

## Normalization of spinal cord displacement during the straight leg raise with resolution of sciatica in patients with lumbar intervertebral disc herniation: a 1.5 year follow-up study

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### INTRODUCTION

Sciatica is described as pain radiating from the buttock down the lower extremity with the vast majority (85%-90%) of cases being caused by lumbar intervertebral disc herniation (LIDH).<sup>1,2</sup> In our previous study we found that in patients with sub-acute single level posterolateral LIDH a significant limitation of neural movement (66.6%) was evident during SLR performed on the symptomatic side.<sup>3</sup> In this study, we followed up on the same patients over 1.5 years to ascertain if changes in cord excursion accompany changes in clinical symptoms.

### METHODS

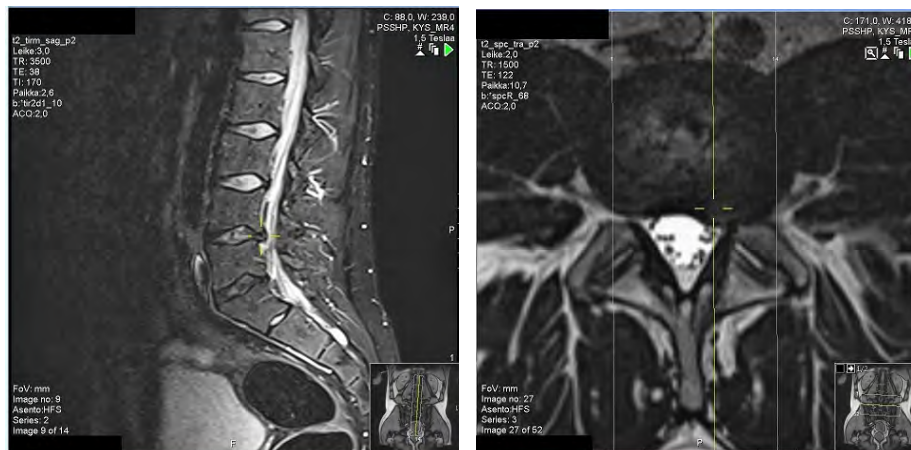
14 patients, who originally had sciatic symptoms due to subacute LIDH, were re-assessed both clinically and radiologically with a 1.5T magnetic resonance (MR) scanner. First a diagnostic MRI was performed to assess the current status of the previously herniated disk. Following this the subjects were scanned using different scanning sequences for planning and measurement purposes. Displacement of the conus medullaris during the unilateral and bilateral SLR was quantified reliably with a randomized procedure and compared between maneuvers. Multivariate regression models and backward variable selection method were employed to identify variables more strongly associated with decrease in low back pain and radicular symptoms.

### RESULTS

Conus medullaris caudal displacement in response to SLRs increased significantly in all the tested subjects. Compared to previously presented baseline values, the data showed an extensive increase in neural sliding of 323.4% (2.52mm,  $p \leq 0.001$ ) with the symptomatic SLR, 37.1% (0.82mm,  $p = 0.0058$ ) with asymptomatic SLR, and 48.2% (1.64mm,  $p \leq 0.001$ ) with the bilateral SLR. The increase in neural sliding correlated significantly with the decrease of, and resolution of, radicular symptoms in the ipsilateral limb (inverse correlation) (Pearson = -0.719,  $p \leq 0.001$ ) as well as with low back pain (Pearson = -0.693,  $p \leq 0.001$ ). Backward variable selection method indicated improvement of neural sliding effects ( $p \leq 0.004$ ) and degrees of hip flexion with symptomatic SLR ( $p = 0.025$ ) as the main variables being associated with improvement of self-reported painful symptoms at follow up for radicular pain. Likewise, reduction of self-reported low back pain symptoms showed to be associated with improvement of neural sliding effects ( $p = 0.006$ ).

### DISCUSSION

In this study we have shown a significant association between the improvement of neural adaptive movement during the SLR and resolution of both radicular and LBP symptoms in patients with posterolateral LIDH during 1.5 years follow-up time. These findings substantiate the SLR test as a useful tool in assessment of neuromechanical impairment in patients with sciatica from the nerve root. To our knowledge, these are the first non-invasive data to objectively support the association between magnitude of neural adaptive movement and clinical symptoms in in-vivo and structurally intact human subjects.



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## Neonatal mouse intervertebral discs restore function following herniation injury

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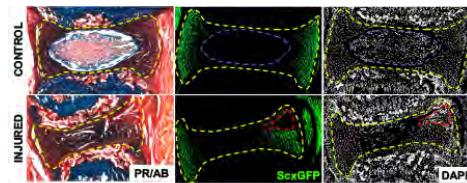
**Introduction:** Endogenous healing of the adult intervertebral disc (IVD) is limited due to its avascular microenvironment [1] as well as its complex biomechanical demands [2]. There are no regenerative strategies available to improve IVD healing and restore its function. One limitation of establishing effective strategies for repair is the paucity of available models for IVD regeneration. Inspired by studies in neonatal tendon [3] showing that neonates regenerate functional neo-tendons after full transection injury, we recently established a model for neonatal mouse IVD injury and demonstrated improved AF healing compared to adults at early stages [4]. The objectives of the current study were to determine the structural and biomechanical properties of neonatal and adult mouse IVDs after long-term healing.

**Methods:** *In vivo* injuries were induced in neonatal (postnatal day 5, n=7) and adult (4-5 month, n=6) caudal IVDs of *ScxGFP* mice with a syringe needle tip of 80% IVD height [4,5]. Picrosirius red/alcian blue (PR/AB) staining was used to determine structural and compositional changes at day 28 and disc height index and axial and torsional mechanical behaviors were assessed at day 56. Statistical analyses were performed using paired Student's t-tests for disc height index and unpaired Student's t-tests for normalized mechanical parameters.

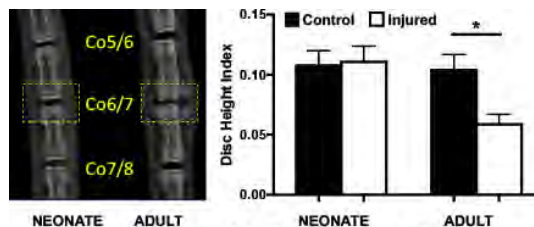
**Results:** AB staining for the proteoglycan-rich nucleus pulposus (NP) at day 28 confirmed sustained loss of NP, indicating successful induction of puncture (Fig.1). For neonates, co-staining with PR revealed a collagenous matrix occupying the repair region within the puncture track, although staining intensity was reduced compared to adjacent AF tissue and organization was not restored (Fig.1). While AF cells adjacent to the injury site retained *ScxGFP* expression at day 28, the presence of non-*ScxGFP* cells in the repair region suggested infiltration of new fibrotic cells (Fig.1). Disc height index of punctured adult IVDs was significantly impaired relative to uninjured internal controls at day 56, and no difference was detected in neonates (Fig.2). Normalized torsional stiffness, torque range, and axial tensile stiffness were lower than control IVDs in adults (62%, p=0.038, 53%, p=0.019, and 48%, p=0.015, respectively), while neonatal values remained normal (Fig.3, axial data not shown).

**Discussion:** The neonatal AF has remarkable capacity to restore biomechanical function following severe injury, highlighting the promise of this model for investigating mechanisms of healing. Understanding improved healing processes will help point towards potential strategies to improve functional healing of adult IVDs following injury. In contrast to our previous studies in transected neonatal tendon, which healed via recruitment and tenogenic differentiation of *ScxGFP* tenocytes [3], our findings suggest that neonatal AF healing is regulated by an undiscovered population of *ScxGFP*-negative cells occupying the repair site. Although tendon and AF share similar embryonic origins and cell markers [6], differences in the local microenvironment, mitotic potential, structure, and loading are likely factors driving distinct biological responses post-injury. Ongoing studies will elucidate the cellular mechanisms underlying neonatal IVD healing, such as the identity of these *ScxGFP*-negative repair cells and their source.

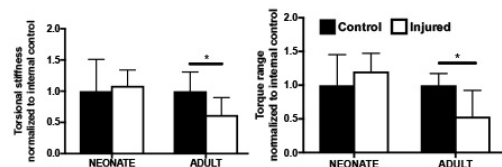
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**Figure 1:** PR/AB and *ScxGFP* post-injury in neonates at d28. PR/AB staining demonstrated the puncture tract was filled with collagenous ECM. *ScxGFP* expression was retained following injury in AF cells adjacent to injury site. A population of non-*ScxGFP* expressing cells was observed in the repair region (red outline). Yellow outline: AF, blue outline: NP, magnification=20X.



**Figure 2:** X-rays of injured (yellow boxes) and adjacent uninjured IVD caudal (Co) levels at d56 in adults and neonates. Disc height index was normal in neonates but impaired in adults (n=5-7, \*p<0.001).



**Figure 3:** Torsional stiffness and torque range were lower in adults but normal in neonates at d56 compared to internal, uninjured controls (n=5-7, \*p<0.05).

- [1] Li+Curr Stem Cell Res Ther, 2015
- [2] Guterl+Eur Cell Mater, 2013
- [3] Howell+Sci Rep, 2017
- [4] Torre+Trans ORS, 2017; Poster#1829
- [5] Martin+J Orthop Res, 2013
- [6] Sugimoto + Development, 2013

## Does inflammatory stimulation and mechanical loading weaken the annulus fibrosus? Preliminary investigations in a bovine AF-organ-culture approach

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**INTRODUCTION** Annulus fibrosus (AF) disruption can lead to prolapse or herniation of intervertebral discs (IVDs)<sup>1</sup>. The trans-lamellar bridging network (TLBN) is a proteoglycan and elastic fiber-rich structure which separates the orthogonal collagen rich lamellae. Additionally, it forms transverse bridges which connect the concentric layers of the AF<sup>2</sup>. Little is known about how mechanobiological factors influence the TLBN and annular wall integrity<sup>2,3,4</sup>. We hypothesize that matrix components of the TLBN are altered by mechanical overloading in the presence of inflammatory factors, thereby contributing to tissue structure weakening. The current study established a bovine AF organ culture model (AF-OC) which allows defined cyclic strains to be applied to the tissue *in vitro*. Additionally, IL-1 $\beta$  media supplementation was used as a concurrent pro-inflammatory stimulus.

**METHODS** Standardized AF rings were cut and punched from bovine caudal discs. After a pre-incubation period of 7 days, AF-organ cultures (AF-OCs) were transferred to a custom-made electro-mechanical device (Fig 1A) and exposed to high physiological cyclic tensile strain (CTS) for 5 days (9% 1Hz, 3 hours/day). A sub-group was cultured in the presence of IL-1 $\beta$  (10ng/ $\mu$ L) to simulate a pro-inflammatory environment. Afterwards AF-OCs were assessed for PGE<sub>2</sub> release (ELISA) and the expression pattern of COX-2, IL-6, and MMP3 in the tissue (Immunohistochemistry). The mechanical strength of TLBN was evaluated using a peel-test. AF segments were dissected into a 'Y' configuration, and a uniaxial material testing machine was used to measure the force required to separate the AF segment along a lamellar boundary<sup>5</sup>. Data were evaluated by descriptive statistics (IHC) or by multiple comparison t-test (PGE<sub>2</sub>).

**RESULTS** The combination of cyclic strain and IL-1 $\beta$  (CTS+IL-1 $\beta$ ) resulted in a significant 25-fold increase in PGE<sub>2</sub> release compared to controls (p = 0,001). In contrast, CTS or IL-1 $\beta$  alone had no effect (Fig 1B). Immunohistochemistry (IHC) analyses showed that the CTS+IL-1 $\beta$  group was associated with a higher percentage area expression of COX-2, IL-6 and MMP3. Additionally, within these samples the TLBN regions were always associated with darker staining of MMP3 and IL-6 compared to adjacent lamellar matrix. Mechanical testing found a decrease in the adhesive strength (N/mm) in the CTS+IL1 $\beta$  group compared to all other groups (Figure 1C).

**DISCUSSION** The adhesion of adjacent AF lamella is an important factor in annular wall integrity. Our unique AF organ-culture and mechanical loading approach enables investigation of the AF and TLBN structure-function relationship. Across all assessments our results show that cyclic strain together with IL-1 $\beta$  had a synergistic effect. These preliminary findings suggest that the combination of cyclic-strain and IL-1 $\beta$  act to increase pro-inflammatory and catabolic molecules within the AF, particularly the TLBN matrix, which consequently leads to a weakening of the tissue structure. This unique AF-OC model will contribute to a better understanding of the pathomechanism of disc herniation. **References:** 1. Adams et al. Spine 2006, 2. Schollum et al. J Anat 2009. 3. Han et al. J Orthop Res 2015, 4. Yu et al, Spine 2015. 5. Gregory et al. 2012. **Acknowledgement:** Supported by the German Spine Foundation.

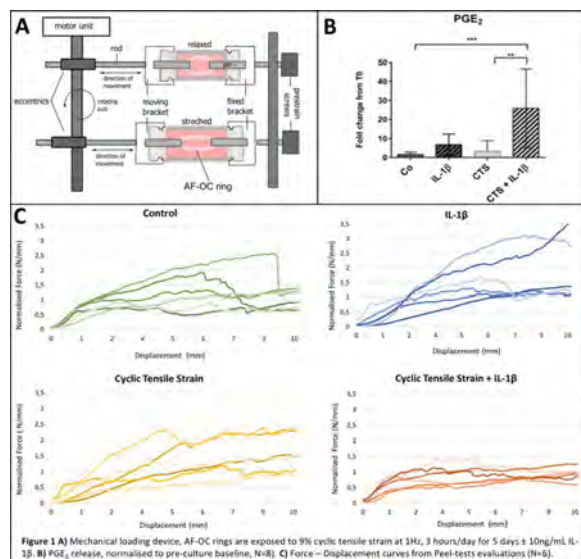


Figure 1 A) Mechanical loading device. AF-OC rings are exposed to 9% cyclic tensile strain at 1Hz, 3 hours/day for 5 days + 10ng/ml IL-1 $\beta$ . B) PGE<sub>2</sub> release, normalised to pre-culture baseline, (N=8). C) Force – Displacement curves from Peel-tests evaluations (N=6).

## Macrophage-derived inflammatory cytokines promote upregulation of pain-related molecules in degenerated human intervertebral discs

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**Introduction:** Intervertebral disc (IVD) pathology is a significant contributor to chronic low back pain. Multiple human and animal studies have suggested that the upregulation of inflammatory cytokines and various growth factors in degenerated or injured IVDs may lead to discogenic low back pain. We previously reported that macrophages in the IVD in injured mice produced inflammatory cytokines, but not growth factors. However, there were some discrepancies between the findings in an experimental IVD injury model and patients with chronic low back pain in the acute and chronic phase. The aim of the current study was to evaluate the regulation of inflammatory cytokines and pain-related molecules by macrophages in human degenerated IVDs.

**Methods:** IVD samples were harvested from 11 patients including 8 with lumbar spinal stenosis and 3 with adult spinal deformity during spinal interbody fusion surgery. All IVD samples showed Pfirrmann Grade 4 or 5 on MRI. Harvested IVD-derived mononuclear cells were obtained and CD14 positive (+) and CD14 negative (-) cells were separated using CD14 antibody and streptavidin-labeled magnetic beads. Inflammatory cytokines including tumor necrosis factor alpha (TNF-alpha), Interleukin 1 beta (IL-1beta), and IL-6, and pain-related molecules including nerve growth factor (NGF) and calcitonin gene-related peptide (CGRP) in the CD14(+) or CD14(-) cells were determined using real-time polymerase chain reaction (RT-PCR). We compared expression levels of each molecular between CD14(+) and CD14(-) cells. To evaluate factors controlling the regulation of pain-related molecules, cultured CD14(-) cells from IVDs were stimulated with TNF-alpha and IL-1beta and the levels of NGF and CGRP were determined using RT-PCR.

**Results:** The levels of TNF-alpha, IL-1 beta, and IL-6 in CD14(+) cells were significantly increased compared with those in CD14(-) cells ( $p < 0.05$ ). However, the levels of NGF and CGRP were not significantly different between CD14(+) and CD14(-) cells ( $p > 0.05$ ). NGF and CGRP levels increased significantly following TNF-alpha and IL-1beta stimulation ( $p < 0.05$ ).

**Discussion:** In the present study, CD14(+) macrophages produced more TNF-alpha, IL-1 beta, and IL-6 compared with CD14(-) cells in human degenerated IVDs. In addition, CD14(+) macrophage-derived inflammatory cytokines including TNF-alpha, IL-1 beta, and IL-6 promote the upregulation of pain-related molecules including NGF and CGRP. We previously reported that macrophage-derived inflammatory cytokines regulate growth factors and pain-related molecules in mice with IVD injury, similar to the findings in the present study. The study findings indicated that macrophage-derived inflammatory cytokines and pain-related molecules were stimulated by macrophage-derived inflammatory cytokines and were associated with the pathomechanism of chronic discogenic low back pain in humans.

## Age-related molecular changes in the intervertebral disc of natural aging rabbits

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**Introduction:** The molecular changes that occur over time in naturally aged discs are not yet well-characterized. The most commonly used models of intervertebral disc (IVD) degeneration involve some type of unnatural injury, which unfortunately cannot provide good insight into the disc degeneration that occurs with natural aging. As such, there is a pressing need to better characterize a naturally occurring disc degeneration animal model. While our group<sup>1</sup> and one other<sup>2</sup> have previously described natural disc degeneration in rabbits related to their age and found interesting differences compared to injury-induced degeneration, these studies have only evaluated animals up to 3 years of age. Here, we present quantitative data from IVDs of naturally aged rabbits up to 9 years old, thereby providing the longest-term assessment to date of the molecular changes that occur naturally in the disc over time with age.

**Methods:** Six-month-old and 3-year-old female New Zealand rabbits were purchased and maintained to age 6 years and 9 years, respectively. To study the effect of aging on the extracellular matrix of discs, 11 total rabbits were used: three 6-month-old, three 3-year-old, three 6-year-old rabbits, and two 9-year old rabbits. From each individual rabbit, the lumbar discs were harvested and pooled to make one sample. Once the discs were homogenized, protein levels were determined by Enzyme Linked Immunosorbent Assay (ELISA) and Western blots. mRNA levels were measured by real-time PCR. The data presented are the mean  $\pm$  S.D. of three independent experiments. A 2-tailed t-test was used to compare between the results of two groups.

**Results:** ELISAs demonstrated that, when compared 6-month-old rabbits discs, the level of aggrecan protein decreased 25% in the 3-year-old rabbits, 65% in the 6-year-old rabbits, and 78% in the 9-year-old rabbits (Fig1). Older discs also expressed significantly lower levels of collagen II protein and higher levels of collagen I protein when compared to younger discs. Real-time PCR demonstrated that the mRNA levels of ADAMTS-4 increased 1.9x in the 3-year-old discs, 3.1x in the 6-year-old discs, and 6.5x in the 9-year-old discs when compared to discs from the 6-month-old rabbits. Similarly, the expression of ADAMTS-5 and MMP3 remarkably increased with aging (Fig2). Western blot & real-time PCR also demonstrated that, when compared to the 6-month-old rabbits, the levels of SOX9 protein decreased over time. Finally, the expression of BMP-2, but not BMP-7, was observed to increase over time when compared to younger discs (Fig3).

**Discussion:** Naturally aged discs in rabbits undergo degeneration at a biochemical level as evidenced by decreased expression of aggrecan, collagen II, and SOX9 over time. Also, increased expression over time of ADAMTS-4, -5, and MMP3 was found. In contrast to what is known to occur in injury-induced degeneration,<sup>3</sup> the expression of BMP-2 increased in aging discs over time, suggesting that lack of BMP-2 is not associated with disc degeneration in natural aging. Such an age-related disc degeneration model may be a more useful tool than an injury-induced model to study the pathogenesis of and test potential therapies for disc degeneration.

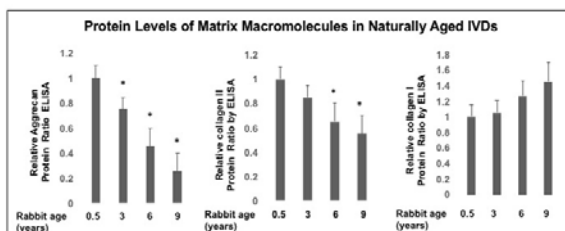


Fig1. Expression of the matrix macromolecules aggrecan, collagen II, and collagen I from the discs from 0.5-year-old, 3-year-old, 6-year-old, and 9-year-old rabbits. Data are normalized with GAPDH and compared to 0.5-year-old rabbits. \* P < 0.01 was considered significant.

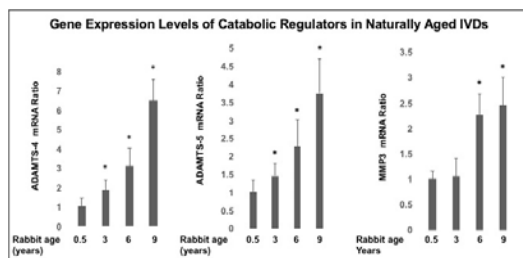
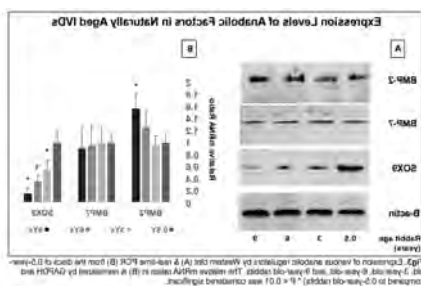


Fig2. Expression of the catabolic regulators ADAMTS-4, ADAMTS-5 and MMP3 from the intervertebral discs of 0.5-year-old, 3-year-old, 6-year-old, and 9-year-old rabbits. Data are normalized with GAPDH and compared to 0.5-year-old rabbits. \* P < 0.01 was considered significant.



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## Wnt5a suppresses inflammation-driven intervertebral disc degeneration via a TNF- $\alpha$ - Wnt5a negative-feedback loop

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**Introduction:** Inflammation has been considered to play a vital role in the pathogenesis of intervertebral disc degeneration (IVDD). Recent studies have shown that Wnt5a may be related to inflammation-related matrix degeneration. However, little is known about the regulatory effects of Wnt5a in IVDD. The aim of this study was to investigate the molecular role of Wnt5a on inflammation-driven IVDD.

**Methods:** The expression of Wnt5a was analyzed in human nucleus pulposus (NP) tissues with immunohistochemical staining. The effects of Wnt5a on matrix production were assessed by RT-qPCR and western blotting. Small interfering RNAs (siRNAs), promoter deletion assay, and promoter binding site mutant were used to reveal the molecular role of Wnt5a in TNF- $\alpha$ -induced matrix metalloproteinase (MMP) expression. The regulatory effects of TNF- $\alpha$  on Wnt5a was investigated with pharmacological inhibitors and siRNA experiment.

**Results:** The expression of Wnt5a was elevated in moderately degenerated human NP tissue with similar expression pattern of TNF- $\alpha$ . In NP cells, Wnt5a significantly increased aggrecan and collagen II expression. Inhibition of JNK or interfering Sox9 gene expression significantly suppressed Wnt5a-induced matrix production. AP-1(JunB) binding sites were located in Sox9 promoter and mutation of these sites sabotaged Wnt5a-induced Sox9 up-regulation and subsequent matrix genes expression. Notably, Wnt5a, which was induced by TNF- $\alpha$ , on the other way round suppressed TNF- $\alpha$ -NF- $\kappa$ B (p65) signaling and subsequent MMPs expression. In vivo studies with MR imaging confirmed the protective role of Wnt5a in IVDD.

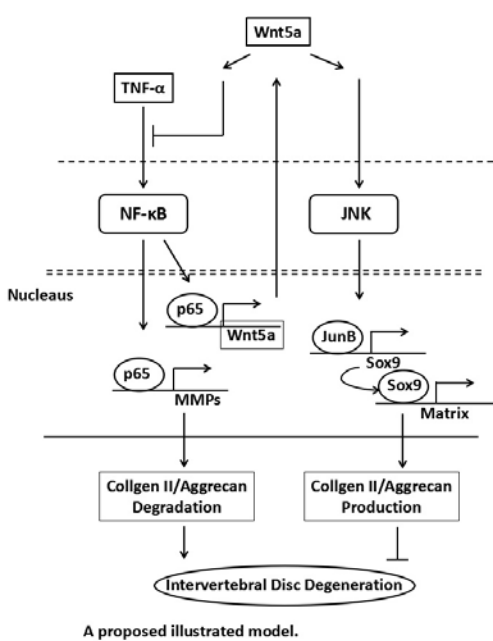
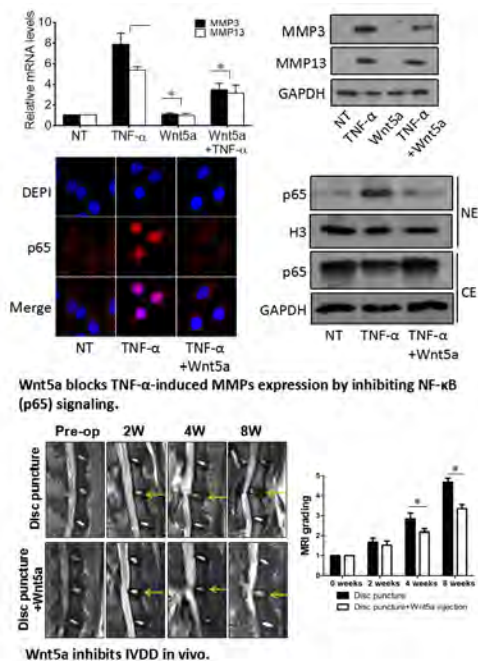
**Discussion:** Wnt5a has been reported to play catabolic roles in matrix homeostasis in skeletomuscular system. However, the current study revealed an anabolic effect of Wnt5a on NP matrix metabolism. The different effect of Wnt5a on matrix homeostasis may be cell-type specific. Besides, the local environment like hypoxic-ischemic setting which NP cells stay in may determine different effects of Wnt5a on matrix metabolism under inflammation. It may to some extent explain the different roles of Wnt5a in matrix maintenance in different systems.

The signaling cascades that are regulated by Wnt5a are so far not well defined. Wnt5a has been shown to induce activation of the MAP kinases JNK, ERK, and p38 in different systems. In this study, we for the first time described a Wnt5a-JNK/AP-1(JunB)-Sox9 signaling cascade in NP cells with no previous report.

The most interesting finding of our study is that TNF- $\alpha$  induces Wnt5a expression in NP cells; on the other way round, Wnt5a antagonized TNF- $\alpha$ -induced MMP-3 and MMP-13 up-regulation in NP cells. These data suggested that Wnt5a regulates TNF- $\alpha$ -induced matrix degradation via a negative-feedback loop in IVDD.

There were several limitations in this study. First, the sample size of human IVD tissues is relatively small due to difficulty to achieve grade I/II discs. Second, results were generated from only normal rat NP cells. Third, the exact receptor and binding partners of Wnt5a is not addressed and further studies will be needed.

In summary, our results indicate that Wnt5a regulates TNF- $\alpha$ -induced matrix reduction and IVDD via a negative-feedback loop mechanism, implying that Wnt5a can be a natural therapeutic agent in the treatment of IVDD.



## Spine-on-a-chip ; Human annulus fibrosus degeneration model for simulating the severity of IVD

Min Ho Hwang, Joo Han Kim, Hong Joo Moon, Hyuk Choi

### Introduction

Degeneration of the intervertebral disc (IVD) is a significant cause of low back pain (LBP) and is a large socio-economic burden. IVD degeneration is also one of the highly prevalent conditions in spinal disease. However, the etiology of IVD degeneration accompanied by LBP is largely unknown and there are no effective fundamental therapies. We hypothesize that this phenomenon is associated with a concentration of pro-inflammatory cytokines which can lead to altered histologic features and cellular phenotypes observed during IVD degeneration. This study investigated the effects of the concentration of pro-inflammatory cytokines and macrophages derived soluble factor on the painful response of human AF cells using a newly developed spine-on-a-chip.

### Methods

Human AF cells were treated with range of concentrations of pro-inflammatory cytokines for a time- (1 ng/mL treatment for 12, 24, 48, and 72 hours) and dose- (1.0, 0.75, 0.5, and 0.25 ng/mL and control for 72 hours) dependent experiment. and macrophage-like THP-1 cell derived soluble factors. We designed an IVD co-culturing microfluidic gradient platform composed of three distinct chambers connected with a micro-patterned gradient channel using standard photolithographic techniques. Fig. 1 depicts a schematic diagram of the newly developed spine-on-a-chip and experimental design. The 1<sup>st</sup> and 2<sup>nd</sup> chambers were directly connected through a micro channel. The 2<sup>nd</sup> and 3<sup>rd</sup> chambers were connected through arrays of thin hydrogel channels for studying the paracrine signalling between 2<sup>nd</sup> and 3<sup>rd</sup> chamber cells without direct contact. Micro patterned gradient channels were connected to the 1<sup>st</sup> chamber for pro-inflammatory gradient stimulation (Fig. 1B, C, and D). The diffusion and gradient profile were simulated by COMSOL Multiphysics computational software. We analysed AF cell kinetics using a live cell imaging system and measured concentrations of matrix metalloproteinase-1 and -3 (MMP-1, MMP-3); interleukin-6, -8, and -1beta (IL-6, IL-8, IL-1 $\beta$ ); and tumour necrosis factor-alpha (TNF- $\alpha$ ) using Enzyme-linked immunosorbent assay (ELISA). we also performed immunofluorescence staining of nuclear factor kappa-light-chain-enhancer of activated B cells (NF- $\kappa$ B) p50 protein and alpha-smooth muscle actin ( $\alpha$ -SMA).

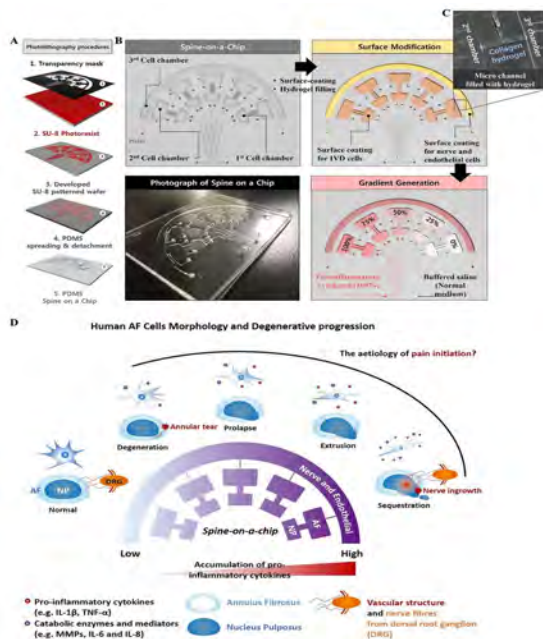
### Results

Our results show increasing the concentration of inflammatory initiator caused modulated expression of pain-related factors, angiogenesis molecules, and catabolic enzymes. Furthermore, accumulated macrophage derived soluble factors resulted in morphological changes in human AF cells, and kinetic alterations such as velocity, dendritic length, cell area and growth rate, similar to that reported within degenerative IVD.

### Conclusions

Our study shows for the first time that the concentration of pro-inflammatory cytokines is strongly linked to the severity of IVD degeneration using molecular and kinetic analysis. In this study, our data also showed that the molecular expression patterns and cellular phenotypic changes were induced by increasing the initiating factors using a newly developed spine-on-a-chip. It will provide fundamental information regarding the pathology of IVD degenerative progression, and inhibition will be a useful therapeutic target for IVD treatment.

Figure 1



## Ingrowth of nerves and blood vessels into degenerated intervertebral discs requires free surfaces

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**INTRODUCTION** The blood and nerve supply of healthy adult intervertebral discs is confined to the peripheral annulus and endplate. In degenerated discs, however, these vessels can grow inwards, possibly as far as the nucleus, and this ingrowth is associated with discogenic pain. Nerve ingrowth may possibly be stimulated by signals from ingrowing blood vessels, but it is not clear if (or how) hollow blood vessels could grow into a pressurised disc. We have shown previously that physical disruption of the disc matrix, which is a defining feature of disc degeneration, creates free proteoglycan-depleted surfaces which appear to be physically and chemically conducive to cell migration and ingrowth. We now hypothesise that ingrowth of blood vessels and nerves into degenerated and herniated discs is largely confined to the vicinity of such free surfaces.

**METHODS** Disc tissue was obtained from 40 patients (aged 37-75 yrs) who were undergoing surgery for disc herniation (n=21), disc degeneration with spondylolisthesis (n=11), or adolescent scoliosis ('non-degenerated' controls) (n=8). Thin (5µm) sections were stained with H&E and toluidine blue for semi-quantitative assessment of blood vessels, fissures, proteoglycan loss and tissue type. From each specimen, 10 thick (30µm) frozen sections were immunostained for CD31 (an endothelial cell marker), PGP 9.5 and Substance P (general and nociceptive nerve markers) and examined by confocal microscopy. Image analysis software was used to calculate the cross-sectional area of each labelled structure, and its distance from the nearest free surface (disc periphery or internal fissure). Results were analysed separately for the three tissue types distinguished by histology: nucleus pulposus, inner annulus fibrosus, and outer annulus fibrosus.

**RESULTS** Nerve terminals in 30µm sections were punctuate and arborizing, and confined to proteoglycan-depleted annulus tissue of herniated or degenerated discs. None were identified within nucleus tissue of any disc. Maximum distance of any blood vessel or nerve from the nearest free surface was 888µm and 247µm, respectively. Blood vessels were greater in number, grew deeper, and occupied a larger area in comparison to nerves. The number and area of labelled blood vessels and nerves increased significantly with grade of disc degeneration. Dense neo-vascularisation and re-innervation were confined to the outer annulus, or to proteoglycan-depleted regions within annulus fissures.

**DISCUSSION** Using multiple thick sections combined with confocal microscopy and fluorescent markers facilitated the detection of filamentous structures within a dense matrix, and showed where they were *not* present. These techniques suggest that blood vessels and nerves occur only in physically-disrupted and proteoglycan-depleted regions in the outer annulus, and adjacent to free surfaces within annulus defects. However, very short nerves growing (vertically) through an endplate into the nucleus may have been missed. Previous reports of nerves in the nucleus may be attributable to such short nerves, or to designating annulus tissue collapsing into the nucleus cavity as 'nucleus'. Also, other nerve markers may be better able (than PGP 9.5 or Substance P) to identify very fine nerve fibres.



## Traceability of mesenchymal stromal cells after transplantation into degenerated discs in patients with low back pain

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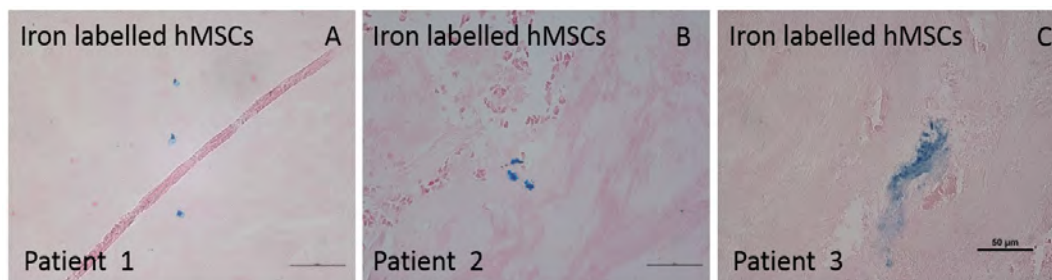
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**Introduction** Low back pain is a major health issue in the western world and one main cause to this condition is believed to be intervertebral disc (IVD) degeneration. Stem cell therapy for degenerated discs using mesenchymal stromal cells (MSCs) has been suggested. The possibility to label MSCs before transplantation has previously been described in animal models. The aim of the present study was to investigate the presence and distribution pattern of autologous MSCs transplanted into degenerated IVDs in patients with chronic low back pain and explanted 6-12 months post transplantation.

**Methods** IVD tissue from 3 patients (41, 45 and 47 years of age, 1 man/2 women) with chronic low back pain participating in a clinical feasibility study on MSC transplantation to degenerative discs were investigated. These three patients decided to undergo surgical fusion surgery 6-12 months post transplantation, including a transforaminal lumbar interbody fusion (TLIF) procedure. Pre-transplantation, the MSCs were prepared from iliac crest bone marrow aspirate, where the MSCs containing fraction were isolated by centrifugation in FICOLL® test tubes and the primary cells cultured to passage 2 in DMEM-LG cell medium. Before transplantation the MSCs were labeled with 1 mg/mL iron sucrose (Venofer®) during 16 h in a cell incubator and thereafter  $1 \times 10^6$  MSCs were transplanted into degenerated IVDs by injection under fluoroscopic guidance. At the time of fusion surgery (6-12 months post transplantation) the IVD tissues were collected. The IVD tissue samples were fixated in 4 % formaldehyde, embedded in paraffin and tissue sections prepared. The IVD samples were stained with Prussian blue staining which visualize iron deposits in cells (blue color) and examined under light microscopy.

**Results** Cells positive for iron deposits were observed in the IVD tissues in all of the three investigated patients. The cells were both observed in clusters and/or as solitary cells displaying an elongated migratory phenotype with visible cellular protrusions. **Figures 1A-1C.**

**Discussion** This is to our knowledge the first study investigating IVD tissue from patients with chronic low back pain where MSCs have been transplanted in an attempt to halt the degeneration and influence the pain. The result demonstrated that MSCs, labelled with iron sucrose, transplanted into degenerated IVDs were detectable 6-12 months after transplantation. The cell morphology (an elongated shape) among the traceable cells further indicated that the transplanted cells has survived and that they were distributed throughout the IVD, either by the injection, but more probable by migration to different parts of the IVD.



**Figure 1.** Images of iron sucrose labeled human MSCs (blue color) detected in transplanted IVDs. Staining: Prussian blue

## Dietary advanced glycation end products cause murine intervertebral disc stiffening

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**INTRODUCTION** Intervertebral disc (IVD) degeneration is a major cause of back pain in obese and diabetic individuals. Modern diets include thermally processed foods that contain high levels of pro-inflammatory advanced glycation end products (AGEs), known contributors to diabetic complications. Crosslinking of AGEs in collagenous tissues has been shown to alter tissue structure<sup>1</sup> and biomechanical properties with increased stiffness and fragility<sup>2</sup>. In diabetic rat IVDs, increased mechanical stiffness was associated with increased AGE accumulation<sup>3</sup>; yet, a mechanistic relationship between AGEs and IVD pathology, independent of hyperglycemia and obesity, has not been demonstrated. This study used a dietary AGE mouse model to assess if chronic AGE ingestion affects IVD structure and mechanics.

**METHODS** All experiments were approved by Mount Sinai IACUC. Twenty female C57BL/6J mice were pair-fed isocaloric diets with either low AGE content (n=10, L-AGE; 7.6 µg/mg AGE), or high AGE content (n=10, H-AGE; 40.9 µg/mg). Mice were euthanized at 6 months; lumbar (L3-5) and caudal (CC4-5) motion-segments and IVDs were harvested for histological, biochemical and biomechanical testing. Caudal motion-segments underwent axial tension-compression and torsional testing. Custom Matlab code was used to calculate stiffness and range of motion. Histological sections of lumbar IVDs were assessed for annulus fibrosus (AF) morphology using polarized light and collagen structure using second-harmonic imaging. Unpaired Student's t-tests determined statistical significance (p<0.05).

**RESULTS** For both groups, body weight and blood glucose levels were normal. AGE content was increased in serum (78%; p=0.03)<sup>4</sup> and IVDs (153% p=0.002) of H-AGE compared to L-AGE mice (**Figure 1a**). Morphologically, detrimental effects of AGE accumulation were demonstrated by second-harmonic (SH) imaging of the AF, which showed less organized collagen structure in H-AGE having lower SH intensity (36% p=0.03) compared to L-AGE mice (**Figure 1g-h**). Polarized light further demonstrated increased birefringence in AF of H-AGE compared to L-AGE mice, suggesting increased AGE accumulation (**Figure 1i-j**). AGE ingestion significantly altered motion segment biomechanical behaviors. H-AGE compared to L-AGE animals had increased compressive stiffness (60%, p=0.007) and decreased axial range of motion (60%, p=0.13). For torsional loading, H-AGE compared to L-AGE animals had increased torsional stiffness (10%, p=0.14) and significantly increased torque range (52%, p=0.04).

**DISCUSSION** This study is among the first to identify a direct link between diet and spinal health, and demonstrated that dietary AGE ingestion increased AGE accumulation in IVDs, resulting in functional biomechanical changes with IVD stiffening in a murine model. The H-AGE diet significantly altered IVD composition and structure, and increased IVD stiffness, independent of other systemic factors such as diabetes or obesity. Assessment of AF structure with SH intensity and polarized-light birefringence suggested increased crosslinking altered collagen fiber structural properties. This is a likely mechanism responsible for the observed biomechanical stiffening, since IVD compressive properties are sensitive to collagen crosslinking<sup>5</sup>. This relationship between diet and IVD health improves understanding of the complexities occurring with IVD aging and degeneration and may help identify novel treatment strategies for low back pain.

**ACKNOWLEDGEMENTS** NIH/NIAMS-R01AR069315

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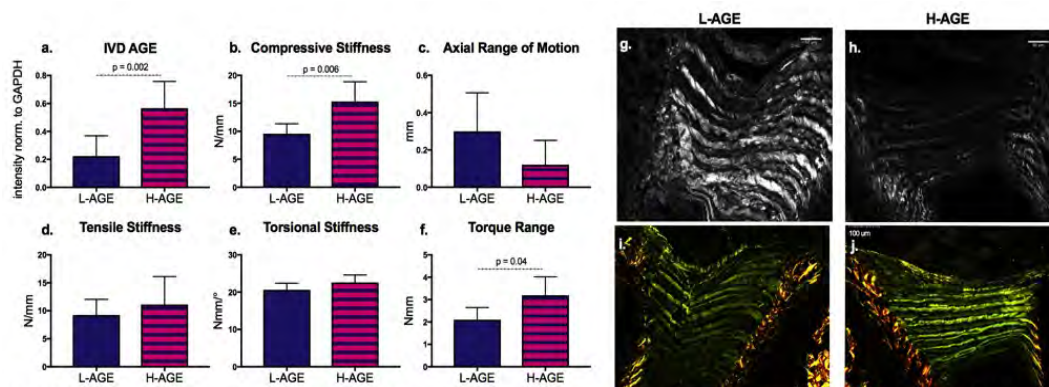


Figure 1 a) Increased AGE protein in H-AGE IVDs. b) Increased compressive stiffness in H-AGE with no differences in c) axial range of motion or d) tensile stiffness after axial tension-compression. No change in e) torsional stiffness with increased f) torque range in H-AGE after torsional testing. n=5-8, data presented as mean ± SD, significant if p<0.05. Representative second harmonic (g-h) and polarized light images (i-j) of L-AGE(left) and H-AGE(right) IVDs.

## Comparison of inflammaging in cervical and lumbar degenerated intervertebral discs: analysis of proinflammatory cytokine and TRP channel expression

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**Introduction:** Disc degeneration (DD) is an age-related process that occurs early in life and is associated with low back pain, with approximately ~80% of the population suffering from it at some point in their lifetime [1]. Certain individuals experience age-related chronic inflammation of the intervertebral disc (IVD), termed "inflammaging", which is characterized by up-regulation of proinflammatory cytokines such as interleukin-6 (IL-6) [2, 3]. Due to their putative role in pain-transduction and inflammation, Transient Receptor Potential (TRP) channels may contribute to DD and discogenic pain and hence be of mechanistic relevance in disc inflammaging [4-7]. The aim of this study was to investigate and compare the occurrence of inflammatory processes in the sites of disc degeneration in the lumbar and cervical spine and to investigate the mechanistic involvement of Transient Receptor Potential Channels TRPC6 and TRPV4.

**Methods:** A total of 51 disc samples were obtained after informed consent from 45 patients (18 men, 27 women, mean age=52) undergoing elective spinal surgery in the cervical (n=24) or lumbar (n=21) region. The procedures were approved by the local ethical committee. Gene expression of inflammatory cytokines and TRP channels was analyzed for differences with regard to spinal level (lumbar vs cervical), pathology (disc herniation (DH) vs DD), Pfirrmann degeneration grade, Modic grade, age, sex, disc region (annulus fibrosus (AF) vs nucleus pulposus (NP)) and surgical extent. For statistical analysis, the Wilcoxon-matched pairs test, Mann-Whitney U test and Spearman correlation were used. All reported tests were two-sided, and p-values < 0.05 were considered as statistically significant.

**Results:** Aside from genes with known implication in DD and DH, four previously unreported genes from the interferon and TRP families (IFNA1, IFNA8, IFNB1, TRPC6) could be detected. A correlation between gene expression and age (IL-15) as well as degeneration grade (IFNA1, IL-6, IL-15, TRPC6), but not Modic grade, was identified. Significant differences were detected between cervical and lumbar discs (IL-15, Figure 1a), NP and AF (IL-6, TNF- $\alpha$ , TRPC6), single-level and multi-level surgery (IL-6, IL-8) as well as DD and DH (IL-8), while sex had no effect. Multiple gene-gene pair correlations, either between different cytokines or importantly also between cytokines and TRP channels (Figure 1b), exist in the disc.

**Discussion:** Our study unveiled a potentially crucial role of Ca<sup>2+</sup> permeable cation channels, specifically of TRPC6, in the disc inflammaging. Furthermore, we confirmed the presence of the pro-inflammatory cytokines IL-1B, TNF- $\alpha$ , IL-6 and IL-8 in degenerative disc disease and highlighted the expression and relevance of cytokines that have previously gained little or no attention in disc research (IFNA1, IFNA8, IFNB1, IL-15). Importantly, we were able to demonstrate that the expression of IL-15, IFNA1, IL-6, IL-8 and TRPC6 was affected by central patient/tissue characteristics, such as the degeneration grade, age, spinal level and/or pathology. These molecules may hence constitute targets to modulate the process of disc degeneration and pain development.

**Acknowledgements:** Financial Support was obtained from the Swiss National Science Foundation (SNF PP00P2\_163678/1) as well as from the Spine Society of Europe (Eurospine 2016\_4).

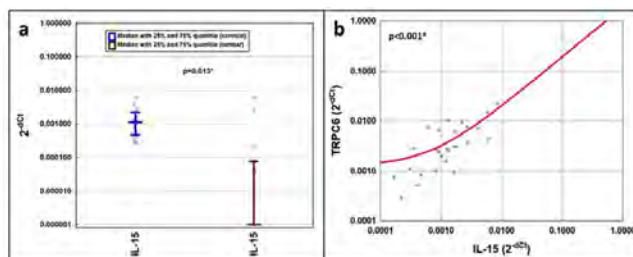


Figure 1. Statistical difference in gene expression of IL-15 between matched cervical (n=14) and lumbar (n=14) samples (a) and statistically significant correlation between the expression of IL-15 and TRPC6 (n=64). Results were calculated as z-score values (relative to GAPDH).

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## Human Wharton's jelly cells activate degenerative nucleus pulposus cells in vitro

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**Introduction:** Degenerative disc disease (DDD) is a main concern of spine surgeons. Stem cell therapy has been developing for many years to treat DDD. In our previous studies, WJCs exhibited potential to differentiate towards nucleus pulposus (NP)-like cells via coculturing with healthy nucleus pulposus cells and ability to revert lumbar disc degeneration in a canine model. However, it is still unclear whether WJCs are capable of elevating the function of resident degenerative nucleus pulposus cells (NPCs) to facilitate the therapy progress. Therefore, this study was aimed to investigate the interplay between human WJCs and degenerative NPCs.

**Methods:** WJCs were isolated from a human umbilical cord and degenerative NPCs were obtained from the nucleus pulposus tissue of degenerate lumbar discs. We simulated implantation of WJCs into intervertebral disc using *in vitro* coculture systems consisted of WJCs and NPCs with or without cell-cell contact. Different cell ratios of WJCs versus NPCs (25%:75%; 50%:50%; 75%:25%) were adopted. After 7 days coculture, relative gene expressions of NP-marker genes (aggrecan, type II collagen, and SOX-9) were investigated.

**Results:** The isolated WJCs positively expressed CD73, CD105, CD90, CD29, CD166 and human leukocyte antigen (HLA)-ABC, but negatively expressed CD34, CD45, and HLA-DR. After coculturing with 3 different WJCs:NPCs ratios for 7 days, the expression of NP-marker genes of both WJCs and dNPCs (aggrecan, type II collagen, and SOX-9) were significantly upgraded in all groups (all P values < 0.05 compared with the control groups). In the cell-cell contact group with WJCs:NPCs at 25%:75%, the gene expression of aggrecan, type II collagen, SOX-9 of WJCs yielded the highest increase by 721-, 1507-, and 1463-folds, respectively (all P < 0.05 compared with the WJCs control). In contrast, as to NPCs in the cell-cell contact group, the highest increase of the expression of aggrecan, type II collagen, SOX-9 for NPCs was achieved by 112-, 84-, 109-folds comparing with the NPCs control (all P < 0.05) when WJCs:NPCs was 75%:25%. Additionally, coculture with cell-cell contact yielded a higher gene expression than coculture without cell-cell contact.

**Discussion:** In this study, we demonstrated the positive effect of WJCs on degenerative NPCs. The data indicated that human WJCs could differentiate towards NP-like cells and restore the biological status of degenerative NPCs in the coculture system. These data might reveal the key early effect of WJCs on the degenerative NPCs, providing the prospective evidence for the further application of WJCs to treat disc degeneration.

## Ex vivo biomechanical evaluation of a combined annulus fibrosus and nucleus pulposus hydrogel repair in a large animal model of severe intervertebral disc herniation injury

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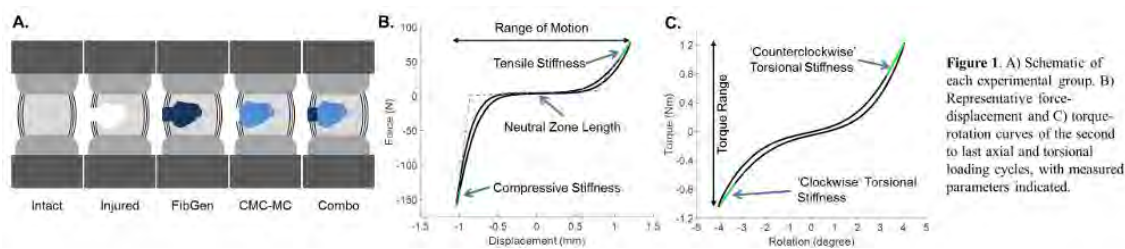
**INTRODUCTION:** Intervertebral disc (IVD) herniation causes pain, and disability when nucleus pulposus (NP) tissue protrudes through annulus fibrosus (AF) defects. Microdiscectomy removes herniated tissue but does not replace lost NP or repair injured AF, which can lead to recurrent pain via altered biomechanics, reherniation, and/or degeneration[1]. We believe effective IVD repair strategies can be applied during discectomy to replace the herniated tissue and recover IVD height loss and biomechanical properties using injectable biomaterials. Carboxymethylcellulose-methylcellulose (CMC-MC) is an injectable hydrogel formulated to match NP mechanical properties[2] and genipin-crosslinked fibrin (FibGen) is an injectable sealant formulated to match AF shear and compressive mechanical properties[3]. We investigated individual and combined use of CMC-MC and FibGen to restore IVD height, axial and torsional biomechanics and prevent herniation, and hypothesized the combined repair will best restore IVD function.

**METHODS:** FibGen and CMC-MC were prepared and injected as described[3,4]. Bovine caudal motion segments (n=8/group) were potted and submerged in PBS overnight at 4°C. Repeated measures biomechanical testing included 0.1MPa preload for 5 minutes then 20 cycles axial tension-compression from 0.25 to -0.50MPa at 0.1Hz and 20 cycles of ±4° torsion at 0.1Hz. Samples recovered overnight, and were tested again after assignment to five experimental groups (Fig. 1), with the injury created via 4mm biopsy punch and removal of 0.18-0.22g of tissue. Samples were lastly subjected to failure testing as described[5]. Compressive stiffness, tensile stiffness, range of motion, neutral zone length, torsional stiffness, and torque range ratios (Fig. 1B,C) to initial intact values were determined. ANOVA with Tukey's post-hoc test compared groups.

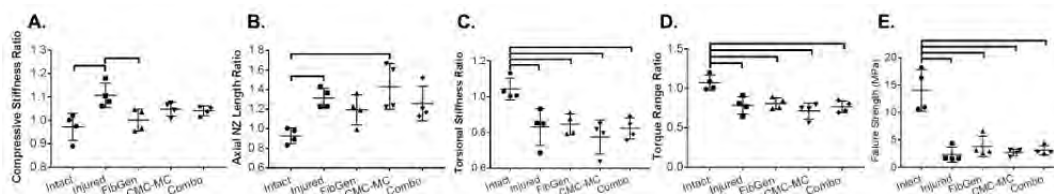
**RESULTS:** Compressive stiffness increased with injury and was restored with FibGen. CMC-MC and Combo repairs were not significantly different from Intact or Injured values indicating partial restoration (Fig. 2A). Axial neutral zone length also increased with injury and was partially restored by FibGen and Combo (Fig. 2B). Axial range of motion (not shown) was significantly increased in Injured, CMC-MC and Combo groups and partially restored for FibGen. Torsional stiffness, torque range and failure strength were significantly decreased for Injured and all repaired groups with no significant differences between Injured and repair groups (Fig. 2C-E).

**DISCUSSION:** We investigated the ability of a combined AF sealant and NP replacement repair strategy to restore IVD biomechanics following a simulated severe herniation and discectomy procedure. FibGen and the combined repair had similar performance restoring compressive stiffness and axial neutral zone length but the combined repair did not display a statistically significant advantage in these parameters over FibGen alone. Furthermore, torsional parameters and failure strength were not restored by any repair, suggesting AF tension was not fully restored and some herniation risk remained. Increased herniation risk for FibGen in this study compared to prior studies may be associated with the more severe injury being evaluated here. Ongoing work will further optimize hydrogel formulations and injection procedures to determine if CMC-MC and FibGen can effectively fill voids, have low herniation risk, and restore biomechanical behaviors following IVD injuries of varying severity.

**ACKNOWLEDGEMENT:** Funded by NIH/NIAMS 2R01AR057397.



**Figure 1.** A) Schematic of each experimental group. B) Representative force-displacement and C) torque-rotation curves of the second to last axial and torsional loading cycles, with measured parameters indicated.



**Figure 2.** A) Compressive stiffness, B) axial neutral zone length, C) torsional stiffness, and D) torque range ratios were calculated by comparing each sample to its own intact value. E) Failure strength showed injured and all repair groups significantly decreased from intact samples. Bar = p<0.05

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- [2] Varma+ ORS 2016
- [3] Likhitpanichkul+ Eur Cells Mater 2014
- [4] Reza+ Acta Biomater, 2010
- [5] Vergroesen+ Spine, 2015

## Regenerative potential of the intervertebral disc by using *the Low Adhesive Scaffold Collagen (LASCOL)*

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**INTRODUCTION:** Spheroid formation has increased attention in the tissue-engineering field, because of its three-dimensional cell-culturing structure capable of mimicking the *in-vivo* environment. We developed the Low Adhesive Scaffold Collagen (LASCOL), which is characterized by a high spheroid-forming ability and low antigenicity. This study was designed to assess the regenerative potential of damaged intervertebral discs by using the LASCOL gel.

### **METHODS:**

*In-vitro* study: Human disc nucleus pulposus (NP) and annulus fibrosus (AF) cells were isolated from 15 patient samples undergoing lumbar surgery (Age, 46.1±24.1 years; male:female = 8:7; Pfirrmann degeneration grade, 2.5±0.6). Cells were cultured on the LASCOL-gel or atelocollagen (AC)-gel plate for 192 hours. (1) Time-lapse microscopic photographing and counting were conducted. (2) Multi-color immunofluorescence for brachyury, Tie2, PAX1, aggrecan, and DAPI was performed.

*In-vivo* study: Sixteen 12-week-old male Sprague-Dawley rats were used. Caudal 8-9, 9-10, and 10-11 disc nucleotomy was conducted through small skin incisions. LASCOL gel, AC gel, and solvents as a control were injected into the disc spaces, respectively. (3) Radiographs were taken at postoperative day 0, 7, 14, 28, and 56. Time-course changes in the disc height index (DHI) were calculated. (4) Mid-sagittal disc sections were stained with H&E or Safranin-O fast green.

Statistical analysis: Multi-way ANOVA with the Tukey-Kramer post-hoc test was used with significance of  $P<0.05$ .

### **RESULTS:**

*In-vitro* study: (1) The number of NP and AF cells increased progressively on the AC-gel plate, but did not increase apparently on the LASCOL-gel plate. However, spheroid formation was observed in both cell types only on the LASCOL gel. Spheroid increased significantly on the LASCOL compared to AC gels. (2) Immunofluorescence showed maintained expressions of brachyury, Tie2, and aggrecan in NP-cell spheroids on the LASCOL gel but to a much lesser extent on the AC gel. In AF cells, PAX1 and aggrecan expressed on both the LASCOL and AC gels. However, more abundant aggrecan expression was found in AF-cell spheroids on the LASCOL gel.

*In-vivo* study: (3) In radiographs, %DHI of the LASCOL-gel group was higher than that of the AC-gel and control groups from postoperative day 7 to 56 with statistical significance compared to the control ( $P<0.01$ ). While a progressive loss of %DHI was observed in the control group, the LASCOL-gel group maintained disc heights throughout (LASCOL, 77.3±11.4%; control, 50.0±14.1% at day 56). (4) Histological H&E staining exhibited that cells existed and migrated into the LASCOL-gels whereas reduced population and no migration of cells were observed in the AC-gels. Cell counting showed significant differences in number between the LASCOL-gel and AC-gel groups ( $P<0.01$ ). Safranin-O staining revealed the presence of proteoglycan-rich matrix in the LASCOL group unlike the control group. Significantly larger Safranin-O-positive area was detected in the LASCOL than AC and control groups ( $P<0.01$ ).

**DISCUSSION:** *In vitro*, the LASCOL gel facilitated the spheroid formation with maintained disc NP-cell and AF-cell phenotype. *In vivo*, LASCOL gel preserved disc heights with cell migration and proteoglycan-rich matrix. The LASCOL itself has the potential to regenerate damaged discs without cell and/or growth factor transplantation, providing advantages in safety aspects.

## Effective disc height restoration following hydrogel injection is dependent on degeneration severity

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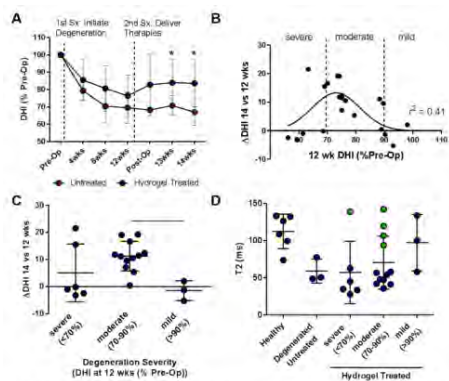
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**Introduction:** Injectable therapeutics, including stem cells, hydrogels, and/or growth factors, hold considerable promise for treating patients with mild to moderate, symptomatic intervertebral disc degeneration.<sup>1,2</sup> We previously described a large animal model of disc degeneration in the goat lumbar spine in which moderate degeneration was achieved 12 weeks following intradiscal injection of 1U chondroitinase ABC (ChABC).<sup>3</sup> Our group has also shown that a triple interpenetrating network hydrogel composed of dextran, chitosan, and teleostean (DCT) mimics nucleus pulposus (NP) mechanics and is an effective carrier for mesenchymal stem cells (MSCs).<sup>4</sup> The purpose of this study was to establish the degree to which the acute efficacy of a combined stem cell and DCT hydrogel injection depends on disc degeneration severity.

**Methods:** Surgery was performed on 6 adult male large-frame goats to induce disc degeneration at four levels of the lumbar spine via intradiscal injection of 1U ChABC.<sup>3</sup> Following progressive degeneration for 12 weeks, a second surgery was performed to deliver therapies. Three groups were randomized to the degenerated lumbar discs: DCT hydrogel alone (n=8), and 3 allogeneic cell types + hydrogel (MSCs (n=6), MSCs preconditioned for 1 week in 2% O<sub>2</sub> (n=4), and NP cells (n=3)). Controls included levels which received no therapy (n=3) and adjacent healthy, non-degenerated levels (n=6). Longitudinal changes in disc height index (DHI) were quantified from lateral *in vivo* radiographs and normalized to pre-operative values. Two weeks following therapy delivery, animals were euthanized and discs assessed via MRI T2 mapping.<sup>3</sup> To investigate the degree to which therapeutic efficacy depended on degeneration severity, results were stratified according to the relative decrease in DHI at 12 weeks vs pre-op. Mild degeneration was defined as ≥90%, moderate as <90% and ≥70%, and severe as ≤70% pre-op DHI after 12 weeks.

**Results:** Two-way ANOVA indicated no significant effect of cell treatment on MRI or DHI outcome measures at this early time point, thus, data were pooled for analysis. Overall, a partial recovery of disc height was achieved following hydrogel delivery to the degenerate disc; DHI was 16.6% higher in hydrogel treated discs than degenerate controls at 14 weeks (Fig. 1A). The improvement in DHI following hydrogel injection at 14 weeks was dependent on the degenerate state of the disc at the time of injection (12 weeks), with the greatest increases in DHI occurring in moderately degenerate discs (Fig. 1B). DHI was unaffected by hydrogel delivery in mildly degenerate discs, where in severely degenerate discs the response was bi-modal (Fig. 1C). The distribution of MRI NP T2 values 2 weeks following therapeutic delivery was also bimodal, with a group of moderately degenerated discs exhibiting increased T2 compared to degenerate controls (green points, Fig. 1D).

**Discussion:** Results from this study suggest that injectable hydrogel therapies for disc degeneration are most effective for restoring disc height in moderately degenerate discs. Treatment was not beneficial for mildly degenerate discs, and the response in severely degenerate discs was variable. Future work will explore the long-term regenerative potential of combined cell and hydrogel therapies in this preclinical model.



**Figure 1.** (A) DHI as a function of time for hydrogel treated discs compared to degenerated controls (\* = p<0.05 compared to 12 weeks). (B-C) Change in DHI from 12 to 14 weeks as a function of 12 week DHI. (D) NP T2 values at 14 weeks for healthy and degenerated controls, compared to T2 values for hydrogel treated discs, as a function of severity of degeneration (12 week DHI). Levels with increased T2 are highlighted in green.

- References: [1] Sakai+2015, [2] Mizuno+2006 [3] Gullbrand+2016 [4] Gullbrand+2017

## Blunting age-associated intervertebral disc degeneration in old mice by exposure to young circulatory factors

**Nam Vo**

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**Introduction:** Aging is the main risk factor for intervertebral disc degeneration (IDD). We have previously demonstrated IDD in the spines of aging mouse models. Recent research reported rejuvenation of multiple old organs in parabiosis experiments in which old mice are surgically paired with young mice to allow sharing of blood circulation. In this study, we performed parabiosis to investigate if exposure to youthful circulatory factors could delay age-related degeneration of the spines in both natural and accelerated aging/progeroid mice.

**Methods:** 4 groups (5 pairs of mice per group) of parabiotic pairs of mice were generated as described: old WT/old WT, young WT/young WT, old WT/young WT, old *Ercc1*<sup>-Δ</sup>/ young WT. The ages of the mice at the time of surgical pairing are 3 months (young WT), 3 months (progeroid *Ercc1*<sup>-Δ</sup>), and 18 months (old WT). Systemic injection of Evans blue dye and fluorescent nano-beads was used to demonstrate development of shared circulation in all pairs after surgery. Mice were surgically paired for 5 weeks and then sacrificed for spine isolation and analyses. Disc proteoglycan (PG) content was assessed by immunofluorescence, safranin-O histological staining, and DMMB colorimetric assay. Disc aggrecan proteolytic fragmentation was measured by Western blot using the anti-G1 antibodies.

**Results:** Compared to the unpaired controls, the accelerated aging *Ercc1*<sup>-Δ</sup> mice heterochronically paired with young WT mice had a significantly improved disc PG content (0.378 vs 0.727,  $p < 0.0023$ ) by DMMB assay, and greater disc aggrecan immunofluorescence. Similarly, when paired with young WT mice, the spines of natural aging WT mice showed significantly reduced protein expression of ADAMTS4 and MMP13, decreased disc aggrecanolytic fragmentation, and increased disc total aggrecan immunofluorescence compared to those isochronically paired with old WT mice.

**Discussion:** Our results show that it is possible to delay IDD in aging mice by shared circulation with young mice. More importantly, our findings are also significant in that they demonstrate that aging of the disc is contributed at least in part by systemic processes and not simply by local changes. The blood-borne systemic factors or cells in young circulation that blunt the aging progression of the intervertebral discs are being investigated.



## **Autologous nucleus pulposus cell-seeded hydrogel implantation to isolated human intervertebral discs promotes tissue repair during physiological culture.**

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### **INTRODUCTION:**

Over the past decade, several high-level *in vitro* and *in vivo* animal studies have paved the way for novel tissue engineering strategies to repair or reverse painful IVD degeneration. However, translation to human IVD repair has not been as rapid. We previously developed a whole disc organ culture system for physiological loading of human IVDs and showed feasibility of monitoring cell injection therapy. Here we use our unique platform for determining NP cell biocompatibility and matrix production within a hydrogel. We also assess tissue repair in intact human IVDs following cell implantation by both a novel T1 $\rho$  MRI sequence and histology following.

### **METHODS:**

Human lumbar IVDs (n=4 donors) were isolated with consent from Organ Donors. NP cells were isolated of the same individual donors (n=4). Cells were tested for viability and matrix production within hydrogels *in vitro* in a custom bioreactors system for 3 weeks, followed biochemical and histological analysis. Discs were scanned in sagittal and axial planes using a custom quadrature volumetric coil in a 7T Bruker Biospec 70/30 and a T1 $\rho$  sequences. Discs were then injected laterally with ~500  $\mu$ L of either HA-pNIPAM hydrogel alone or hydrogel seeded with  $2 \times 10^6$  cells/mL and placed in the bioreactor with intermittent cyclic load of 0.1-0.6 MPa. After 5 weeks of physiological culture, discs underwent follow-up MRI in the same orientation. Paraffin embedded sections were stained with safranin-O and antibodies against collagen types I and II. T1 $\rho$  image quantification was performed using MIPAV software (NIH). Statistical analysis was performed using paired t-tests in Microsoft Excel.

### **RESULTS SECTION:**

Loaded constructs generated more proteoglycan and collagen type II production than the unloaded controls. T1 $\rho$  scans of human lumbar IVDs revealed high quality images of tissue health status which also showed "hot spots" in the NP which we then aimed to treat. After 5 weeks of culture, post-treatment scans revealed increased signal in the treated areas. Image quantification showed significant improvement in T1 $\rho$  values for cell seeded hydrogels. Histological analysis showed positive safranin-O staining and signs of neo-matrix production. Discs injected with cell-seeded gel displayed collagen type II staining surrounding implanted cells.

### **DISCUSSION:**

This study presents an *in vitro* physiological culture tool to assess any number of hydrogel and cell combinations for tissue engineering and drug delivery applications. Specifically, we show feasibility of assessing cell and biological therapy strategies in *ex vivo* isolated human lumbar IVDs under dynamic culture conditions for 5 weeks. This study focused on implantation of autologous NP cells within an injectable thermoresponsive hydrogel, which would theoretically produce disc matrix proteins at a high level. Increased matrix and proteoglycan is detectable within the hydrogels using T1 $\rho$  MRI scanning and histological analysis suggesting enhanced tissue repair over hydrogel alone. Obtained T1 $\rho$  values suggests appropriate quantification of proteoglycan content pre- and post-treatment, which may have clinical significance. Since most current clinical focuses on delivery of mesenchymal stem cells, future studies will assess MSC-NP co-culture using this approach

## Therapeutic effects of cell therapy with neonatal human dermal fibroblasts and rabbit dermal fibroblasts on disc degeneration and inflammation

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### Introduction

Increasing evidence suggests transplanting viable cells into the degenerating intervertebral disc (IVD) may be effective in treating disc degeneration and back pain. Clinical studies utilizing autologous or allogeneic mesenchymal stem cells to treat patients with back pain have reported some encouraging results. Animal studies have shown that cells injected into the disc can survive for months. The objectives of these studies are to determine the impact of donor source on the therapeutic effects of dermal fibroblast treatment on disc degeneration and inflammation. In these studies, we compared transplantation of neonatal human dermal fibroblasts (nHDFs) and rabbit dermal fibroblasts (RDFs) into rabbit degenerated discs on host immune response, disc height and IVD composition.

### Methods

New Zealand white rabbits received an annular puncture using an 18-gauge needle to induced disc degeneration. Four weeks after injury, rabbit IVDs were treated with  $5 \times 10^6$  nHDFs, RDFs or saline. At eight weeks post-treatment (n= 33 per group), animals were sacrificed. X-ray images were obtained. IVDs were isolated for inflammatory and collagen gene expression analysis using real-time PCR and biochemical analysis of proteoglycan contents using dimethylmethylene blue assay.

### Results

Eight weeks after treatment, disc height indexes of discs treated with nHDF increased significantly from 73% to 81% ( $p < 0.01$ ) while those treated with saline or RDF increased by 1 and 2%, respectively. Gene expression analysis showed that discs transplanted with nHDFs and RDFs displayed similar inflammatory responses ( $p = 0.2$  to  $0.8$ ). Expression of both collagen types I and II increased significantly in nHDF-treated discs ( $p < 0.05$ ), trending towards significance in RDF-treated discs, and not significantly in saline treated discs. The ratio of collagen type II/ collagen type I was higher in the IVDs treated with nHDFs (1.26) than those treated with RDFs (0.81) or saline (0.59) and intact discs (1.00). Lastly, proteoglycan contents increased significantly in discs treated with nHDF ( $p < 0.05$ ) and trending towards significance in the RDF-treated discs compared to those treated with saline.

### Discussion

In summary, the results of these studies showed that cell transplantation with nHDF into degenerated IVDs can significantly increase markers of disc regeneration: disc height, collagen type I and II gene expression and proteoglycan contents. Transplantation with RDFs showed similar regenerative trends but these trends were not significant. One difference between these cells other than species origin is the RDFs in this study were from adult rabbit tissue while the HDFs were from neonatal tissue. Adult fibroblasts may need a higher dosage or longer time period to achieve a similar therapeutic response. This study also showed that the human cells transplanted into the rabbit discs did not induce a higher immune response than the rabbit cells. These results support that the intervertebral disc is immune privileged and would tolerate allogeneic or xenogeneic grafts.

### Acknowledgements

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## Lumbar vertebral endplate defects on magnetic resonance images: prevalence, distribution patterns, and associations with back pain in a population-based sample of Chinese

Lunhao Chen, Michele C. Battié, Ge Yang, Ying Yuan, Zhong Chen, Yue Wang

**INTRODUCTION:** While the roles of Modic Changes (MCs) and disc degeneration in back pain remain controversial, clues from cadaveric studies suggest that lumbar vertebral endplate lesions may be important in back pain. Endplate lesions can be detected on magnetic resonance (MR) images as various endplate defects, including focal, corner, and erosive defects. Yet, the clinical significance of such endplate defects remains unknown. Using high-resolution MR and structured questionnaire data, this study investigates the associations between lumbar endplate defects and back pain in a general population sample of Chinese adults.

**METHODS:** Subjects randomly selected from a community register each underwent a structured interview and lumbar MR imaging. Subjects with known history of spinal surgery, tumors, infections, or inflammatory diseases were excluded. Measurements of lifetime exposures of interest, occupational physical demands and back pain history today, over the past 4 weeks, 12 months, and lifetime were acquired. On sagittal MRIs, endplate defects, MCs and disc degeneration were assessed using established protocols. The prevalence and distribution patterns of various endplate defects were characterized. Logistic regressions were used to determine the associations of endplate defects with back pain, adjusting for age, gender, body mass index (BMI), lifetime exposures, occupational physical demands, MCs, and disc degeneration.

**RESULTS:** There were 478 subjects (53.4±14.4 years, range 20-88 years) studied. Among them, 15.5% had back pain today, 7.1% had back pain lasting for ≥1 day over the past 4 weeks, 42.7% had back pain in the past 12 months, and 33.9% recalled having had back pain lasting for ≥1 day during their lifetime. Endplate defects presented in 301 (63.0%) subjects and 842 (16.0%) endplates. Focal defects were the most common (42.0%), followed by erosive (37.3%) and corner defects (20.7%). Endplate defects were more common in the lower lumbar region than in upper, particular for erosive defects. Endplate defects were closely associated with adjacent MCs (OR=6.99, 95% CI=5.55-6.80, P<0.001) and disc degeneration (OR=6.99, 95% CI=2.27-4.31, P<0.001). The presence of endplate defects, but not MCs and disc degeneration, was associated with back pain over the previous year (OR=1.57, 95% CI=1.10-2.46, P=0.047) and lifetime (OR=1.65, 95% CI=1.03-2.65, P=0.039), adjusting for MCs, disc degeneration, age, BMI, and occupational physical demands. Moreover, each type of endplate defect was associated with lifetime back pain history (OR=1.70-2.19, P<0.05 for all), as was a greater number of endplate defects (OR=1.10, P=0.043).

**DISCUSSION:** Lumbar vertebral endplate defects were common MR findings, particularly in the lower lumbar region, and were closely associated with adjacent MCs and disc degeneration. The presence of endplate defects was associated with back pain presence and intensity during the previous year, as well as ever having had memorable back pain lasting more than a day, and these associations remained after adjusting for the effects of MCs, disc degeneration, age, gender, BMI and occupational physical demands. Findings suggested that endplate defects may be an important, previously overlooked confounding factor in studies of other MR findings in back pain.

## MRI reveals significant differences in vertebral and endplate t2-values between low back pain patients and controls

Hanna Hebelka, Helena Brisby, Kerstin M Lagerstrand

### Introduction

Both intervertebral disc (IVD) degeneration and Modic changes (MC) are associated with low back pain (LBP) but their exact relation is not fully elucidated, neither is their relation to compromised endplate (EP) function. To deepen the understanding of the pathophysiology behind these conditions, non-invasive diagnostic tools with ability to detect early biochemical changes in EPs and vertebrae, are desirable. The aim of this study was to investigate if axial loading during MRI (aMRI) affect the EPs and vertebrae, correlate any induced changes with morphological changes (unloaded MRI), with comparison between LBP patients and controls.

### Methods

T2-mapping of L1- S1 was performed on 27 LBP patients (mean age 37 years) and 12 healthy controls (mean age 36 years) during conventional unloaded MRI (uMRI) and subsequent aMRI. Each EP and vertebra was manually segmented with volumetric regions of interest (ROI), covering the entire EP/vertebra except the outermost lateral parts. EP inhomogeneity was termed signal changes (SC) and any Schmorl's nodules or Modic changes (MC) were registered. Each vertebra was subdivided in half to obtain superior respectively inferior vertebral units. A total of 282/119 (patient/control) EPs, and corresponding vertebral units, were evaluated. Median T2-values were compared between uMRI and aMRI, between the groups and the relationship with morphological changes investigated.

### Results

All morphological changes investigated were more common in the patient group (Table 1). With uMRI, the median T2-value differed significantly between the superior and inferior vertebral unit, both within and between the groups (Table 1). Also when adjusting for MC, the T2-values in the vertebral units were higher in the patient group. aMRI did not induce any significant changes in the vertebral T2-value.

In both patients and controls, the median T2-value differed significantly between superior and inferior EPs for uMRI and aMRI. For uMRI, higher T2-values in both EPs were found in the patient group compared with the control group, even when adjusting for MC, SC and Schmorl's nodules. aMRI did not induce any significant EP-changes in the controls. However, in patients aMRI induced increased T2-value in the superior EPs, also when adjusting for MC, SC and Schmorl's nodules.

### Discussion

For the first time, significant differences in vertebral and EP T2-values between LBP patients and controls have been demonstrated. In addition, aMRI induced significant EP-changes in patients but not in controls. Hence, aMRI may reveal functional differences in EPs between patients and controls, but this needs to be confirmed in a larger cohort considering the wide range of induced changes in individual EPs.

Table 1.

		p-value		p-value		p-value
		patients	within group	controls	within group	
uMRI	vertebra superior	100		87		0.01
	vertebra inferior	102		88		0.03
	diff vertebra superior- inferior		<.0001		<.0001	0.9
	EP superior	30		28		0.004
	EP inferior	39		34		0.006
	diff EP superior- inferior		<.0001		<.0001	0.2
aMRI	vertebra superior	99		88		0.02
	vertebra inferior	100		89		0.04
	diff vertebra superior- inferior		0.02		<0.05	0.5
	EP superior	32		29		0.09
	EP inferior	40		37		0.2
	diff EP superior- inferior		<.0001		<.0001	0.5
aMRI-uMRI	vertebra superior	0.5		0.2		0.8
	vertebra inferior	-0.7		-0.7		0.5
	EP superior	2	<0.001	0	0.2	0.9
	EP superior range	(-12 to 33)		(-13 to 67)		
	EP inferior	0	0.95	2	0.1	0.2
	EP inferior range	(-51 to 37)		(-25 to 25)		
Modic changes	39		4			
Schmorl's nodules	23		17			
Signal changes	110		41			

Table displaying median T2-values (ms) in LBP patients and controls with aMRI, uMRI and the differences between the investigations (aMRI-uMRI). Morphological measures (Modic changes, Schmorl's nodules and signal changes) are displayed as number in total (n) within respective cohort, with morphological changes in superior and inferior parts of endplates (EP) respectively vertebrae reported separately. Diff= difference, aMRI= axial loading during MRI, uMRI = unloaded MRI

## Quantitative imaging of bone marrow composition reveals significant alterations in marrow fat content in patients with modic changes

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### INTRODUCTION

The positive association between chronic low back pain (CLBP) and MRI evidence of vertebral endplate bone marrow lesions, often called Modic changes (MC), offers the exciting prospect of diagnosing a “vertebrogenic” phenotype of CLBP. However, there is little quantitative data describing marrow composition inside these endplate lesions, how composition changes during lesion progression, or how it relates to pain severity. Such knowledge may be important for screening patients, developing new treatments, and gauging therapeutic efficacy. Here we measured marrow composition in CLBP patients with and without MC using a novel MRI sequence that quantifies marrow fat content.

### METHODS

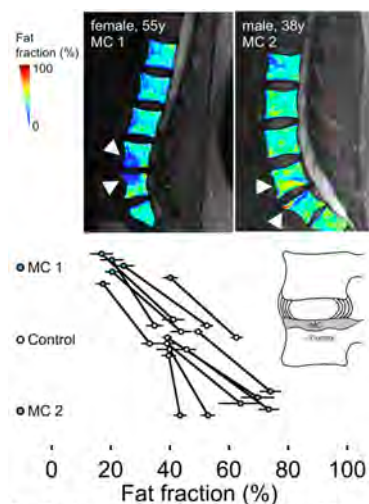
This study was IRB-approved and informed consent was obtained for all subjects. Twenty CLBP patients (VAS  $\geq 4$  or ODI  $\geq 30$ ) without radiculopathy were recruited locally. Subjects were imaged on a 3T GE scanner to evaluate lumbar MC and fat fraction. The MRI protocol consisted of sagittal T1- and fat-saturated T2-weighted fast spin-echo sequences and a 3D SPGR sequence with six echoes and Iterative Decomposition of water and fat with Echo Asymmetry and Least-squares estimation (IDEAL). The IDEAL sequence was validated previously for marrow fat estimation in the presence of trabecular bone. Marrow fat fraction inside MC lesions was averaged for five circular regions of interest (10.08 mm<sup>2</sup> each) and compared to site-matched ROIs placed outside the lesion in the same vertebra. For subjects without MC, fat fraction was averaged in mid-sagittal ROIs placed in the caudal L5 endplates.

### RESULTS

Twelve subjects presented with at least one MC, and MC presence significantly affected marrow fat content (**Figure**). In MC type 1 (MC 1;  $n=6$  subjects), which is known to coincide with fibrovascular replacement of the marrow, mean fat fraction was 47.8% lower than site-matched non-MC regions ( $44.7 \pm 11.2\%$  vs.  $23.3 \pm 8.7\%$ ,  $p < 0.001$ ). By comparison, in MC type 2 (MC 2;  $n=6$  subjects), which coincides with fatty replacement of the marrow, mean fat fraction was 49.2% higher than non-MC regions ( $42.2 \pm 4.4\%$  vs.  $62.9 \pm 12.3\%$ ,  $p = 0.004$ ). A band of hypo-adipose marrow often surrounded the hyper-adipose MC 2 marrow, consistent with conversion from MC 1. As expected, fat fraction in non-MC regions (mean =  $47.7 \pm 12.0\%$ ; range = 27.1-66.9%) was positively associated with age for all subjects ( $p < 0.001$ ; mean age =  $43.7 \pm 11.6$  years; range = 38-66 years), reflecting the physiologic age-related replacement of hematopoietic marrow with fatty marrow.

### DISCUSSION

The magnitude and nature of changes in marrow composition that accompany MC are unclear. *Our data provide the first quantitative evidence that distinct changes in marrow fat fraction coincide with MC.* MC presence/absence is currently inferred from the signal intensity on T1- and T2-weighted images. However, diagnostic sensitivity is highly variable, perhaps reflecting the binary and subjective grading scheme. IDEAL MRI enables quantitative measurements of marrow fat on a continuous scale that may improve sensitivity. Importantly, our data show that IDEAL is sensitive to subtle inter- and intra-lesion differences in marrow composition, which may precede any changes that are discernable with standard structural MRI sequences. Consequently, IDEAL could be especially helpful for sub-classifying patients with MC, monitoring lesion progression, and evaluating treatment efficacy.



Top: Fat fraction maps, acquired at 3T using IDEAL MRI, for CLBP patients presenting with MC 1 and MC 2. Bottom: Fat fraction inside the MC lesions was compared to site-matched regions outside the MC lesions. Horizontal bars show SD for 5 regions/site.

## Upright open MRI for imaging lumbar spinal musculature in varying postures

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### INTRODUCTION

Lumbar spinal musculature is critical for equilibrium, stability, and control of the spine. Recently, the clinical importance of spinal musculature is being emphasized in conditions such as lower back pain, and spinal deformity[1]-[3]. To improve understanding of spinal musculature, models have been developed and refined[4],[5]. Typically however, model validation uses supine magnetic resonance imaging (MRI) which may not be representative of spinal musculature in natural upright weighted postures[5],[6]. This study's objective was to characterize asymptomatic lumbar spinal musculature in varying postures using upright open MRI. Anatomical cross-sectional area (CSA), centroid, radius, and angle of the lumbar muscles (multifidus, erector spinae, psoas major) between L3-S1 were measured. Of interest is how these parameters vary in upright/seated postures compared to supine.

### METHODS

Using an institutionally approved protocol, six healthy volunteers were imaged within the 56cm gap of a 0.5T vertical open MRI (MROpen, Paramed, Genoa, Italy) using a T1-weighted Spin Echo sequence (TR/TE=300/20ms, FOV 20cm, scan matrix 224\*160, slice thickness 7mm with 0.7mm gap, NEX=1, 111s imaging). Each volunteer was scanned in 7 postures: standing, standing holding 8kg, standing bent 45° forward, seated bent 45° forward, seated bent 45° back, seated at 90°, and supine. For each posture, 3 slices were prescribed (parallel to disc) at intervertebral levels-L3/L4, L4/L5, L5/S1.

Image measurements of CSA, centroid, radius, and angle were taken by one rater for the multifidus and erector spinae combined, and psoas major muscles (Figure 1)[7],[8]. Muscle CSA(mm<sup>2</sup>) was determined by manually segmenting the muscle boundary, with its centroid as the geometric center. Angle(°) was relative to the spinous process, and radius(mm) was the distance between the muscle and vertebral body centroids.

The effect of posture on CSA, radius, and angle was evaluated with a repeated measures ANOVA(P<0.05) for each muscle at each level and side(L/R). Posture repeatability was evaluated by comparing CSA in four re-scanned volunteers. Segmentation was repeated for 2/3 of the images for intra-rater repeatability. Both repeatability measures were assessed on CSA by intraclass correlation coefficient (ICC(3,1)).

### RESULTS

Posture affected the right and left psoas major CSA at L3/L4 (one volunteer's images-Figure 2). The largest differences in CSA were; seated bent 45° forward was 51.7% greater than supine (right), and seated at 90° was 60.5% greater than supine (left). Posture also affected the left multifidus/erector spinae angle at L3/L4. The differences in CSA, radius, and angle of all other levels and muscles were not statistically significant. Posture repeatability ICC(3,1) was 0.59-0.92 for the multifidus/erector spinae, and 0.77-0.93 for the psoas major. Intra-rater reliability was 0.96-0.98 for the multifidus/erector spinae, and 0.89-0.93 for the psoas major.

### DISCUSSION

While most effects of posture were not statistically different, there were some interesting differences in the CSA and angle at L3/L4. Intra-rater reliability was excellent despite the MROpen's lower resolution than closed-bore MRI (1.5T-3T). Studies with more volunteers and posture repeatability should be considered before incorporating such results to inform more accurate lumbar spine models.

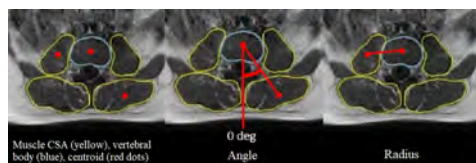


Figure 1: Muscle CSA, Angle, Radius

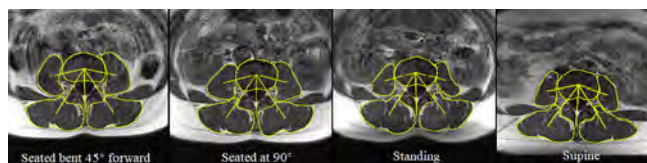


Figure 2: One volunteer's images in different postures at L3/L4

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## Does lumbar disc degeneration predict facet joint changes or vice versa? A 5 year prospective MRI study

Dino Samartzis, Jeffrey Yu, Cora HY Bow, Keith Luk, Jason Cheung

**Introduction:** The facet joints are an integral component of the posterior column of the spine. They provide spinal stability, prevent excessive forward motion and rotation, and accommodate a certain degree of load/stress. The intervertebral discs have been attributed as being the key load-bearing structures of the spinal column. It has been propagated for several decades that disc degeneration (i.e. black disc/disc space narrowing) is the main driver of spine degeneration and, as such, largely precedes facet joint abnormalities or changes. However, such assertions have been based on cross-sectional studies and narrow phenotype assessment. To date, no prospective study has addressed the causal relation of these two spinal regions. Therefore, the following large-scale, prospective study addressed if disc degeneration leads to the development of facet joint changes or vice versa.

**Methods:** A prospective study was performed of 184 non-operative subjects (mean age at baseline: 52 years) who underwent sagittal T2-weighted and axial T1-weighted 3T-MRI of L1-S1 at baseline and were re-imaged at 5 year follow-up. All subjects were part of a population-based cohort of Southern Chinese origin. Disc degeneration was assessed at each lumbar disc level and was graded according to the Schneiderman et al classification scheme, whereby grades 2 and 3 were regarded degenerated (black discs/disc space narrowing). Facet joint changes were assessed of both facets at each level, noting joint space narrowing, irregular and flat shapes, and osteophyte formations. A motion segment with any facet joint expressing changes was noted as a case. All MRI phenotypes were assessed at both baseline and follow-up. Intra- and inter-rater reliability was performed. Subject demographics were also noted.

**Results:** 920 disc levels were assessed. Good to excellent rater reliability was noted. On baseline, 70% of the subjects had disc degeneration in at least one level, whereas on follow-up 92% had degeneration. At baseline and follow-up, facet changes involving at least one level were noted in 98% and 99% of all individuals, respectively. On baseline, disc degeneration (facet joint changes) was noted as follows: L1/L2:9% (41%), L2/L3:11% (50%), L3/4:26% (66%), L4/5:47% (88%), and L5/S1:48% (94%). On follow-up, disc degeneration (facet joint changes) was noted as follows: L1/L2:46% (71%), L2/L3:66% (79%), L3/4:75% (77%), L4/5:84% (86%), and L5/S1:71% (97%). Region-specific lumbar level observations of concomitant disc degeneration and facet joint changes on follow-up were noted.

**Discussion:** Our study is the first large-scale prospective study to assess the natural history of disc degeneration and facet joint changes. Our findings challenge the traditional paradigm of spine degeneration, definitively noting that disc degenerative changes do not always precede facet joint changes. In fact, we noted a substantial number of motion segments that exhibited advance facet joint changes first, followed by degenerative disc changes in time. Our study broadens the understanding of the "drivers" of spine degeneration, and the need to better understand the facet joint phenotype in future research and clinical applications, such as its role in patient selection for novel therapeutics, predictive modeling, adjacent segment degeneration risk profile, preventative spine care and future genetic/omics platforms.

## The effects of compression and traction on lumbar MRI findings in relation to chronic low back pain

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### Introduction

Conventional MRI, a sensitive modality to depict lumbar pathoanatomy, is often clinically inconclusive. This is likely due, in part, to imaging in a relaxed supine position while symptoms are usually worse in sitting or standing. This study aimed to quantify the response of the lumbar spine to compression and traction in participants with and without chronic low back pain (LBP) using MRI to identify promising biomarkers for improving MRI specificity.

### Methods

Fifteen participants with chronic LBP (30.2±10.6 yrs.) were matched for age, weight and gender with 15 healthy volunteers (29.7±10.6 yrs.). All participants rested supine for 20 minutes, followed by 20 minutes with 50% body weight compression, and then 20 minutes traction. MRI scans were obtained during the last 5 minutes of each loading condition. Lumbar discs and nucleus were segmented and the width, mean T<sub>2</sub>, geometric-weighted-centroid (GWC), and T<sub>2</sub>-weighted-centroid (T<sub>2</sub>WC) were calculated using Matlab<sup>®</sup> algorithms developed in house. Disc heights and angles were also measured. A two-way repeated ANOVA with Sidak's post-hoc comparisons was used to compare groups and loading conditions.

### Results

Pain ratings in the unloaded position were 3±2 in LBP and 0±1 in controls. After both compression and traction, pain was 4±2 in LBP and 1±1 in controls. Degeneration grades were similar at all levels between groups.

Four biomarkers presented significant interactions between pain and loading: changes in disc height, the horizontal and vertical coordinates of the disc T<sub>2</sub>WC, and the vertical coordinates of the Nucleus T<sub>2</sub>WC.

**During compression**, the pain group demonstrated an anterior and superior shift of disc T<sub>2</sub>WC, and a superior shift of the nucleus T<sub>2</sub>WC at L5-S1 (Fig.1a), and an inferior shift of the disc T<sub>2</sub>WC at L3-4, relative to the no-pain group (Fig. 1b).

At L1-2, in both groups, disc height increased during compression (Fig.1c).

**During traction**, in the pain group there was a superior shift in the disc T<sub>2</sub>WC at L3-4, and a posterior and inferior shift at L5-S1 (Fig.1d), as well as an inferior shift of the nucleus T<sub>2</sub>WC at L5-S1 (Fig.1e).

Disc height only increased at L1-2 during traction in those with no pain (Fig.1f).

Four biomarkers showed differences between groups by comparing unloaded images. The following were moderately to largely more anterior in the pain group: disc T<sub>2</sub>WC at L3-4 and L4-5; nucleus T<sub>2</sub>WC at L4-5; and nucleus GWC at L3-4, L4-5 and L5-S1. The disc height of the pain group was taller at L3-4 and L4-5.

### Discussion

This study investigated new MRI biomarkers of differences between participants with and without chronic LBP. Comparisons of responses to contrasting loading conditions yielded more differences between pain groups than measurements from unloaded images. The biomarkers reflecting the direction of shifts in fluid distribution within discs and nucleus, as well as disc height, showed promise to improve the specificity of MRI for LBP.

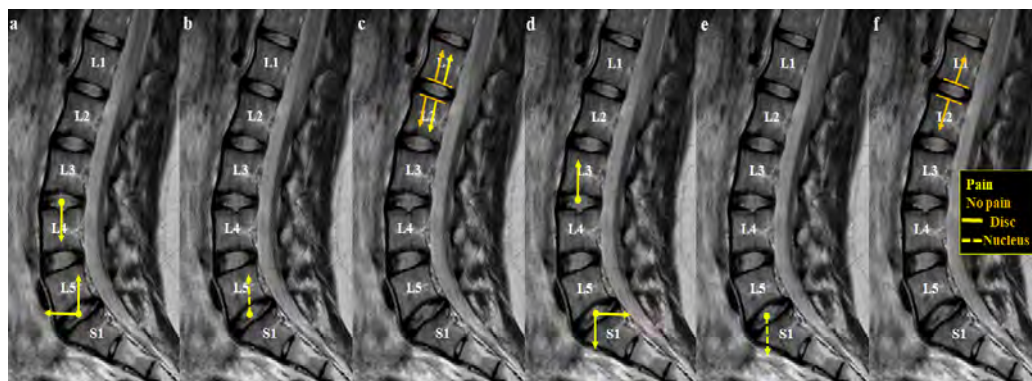


Fig.1 Significant interaction effects between pain and loading. **Compression:** a) disc T<sub>2</sub>WC b) nucleus T<sub>2</sub>WC c) disc height. **Traction:** d) disc T<sub>2</sub>WC e) nucleus T<sub>2</sub>WC and f) disc height



## Serum biomarkers for Modic changes among chronic low back pain patients

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**Introduction:** Lumbar Modic change (MC) can serve as a diagnostic marker, and might also be considered an independent source of chronic low back pain (CLBP). Consequently, establishment of MC-specific serum biomarker profiles could provide an appropriate and cost-efficient method to augment magnetic resonance imaging (MRI) and clinical examination for differential diagnosis and follow-up of patients suffering from CLBP. The aim of this study was to test for the existence of serum biomarkers that are significantly elevated or reduced in CLBP patients with MC.

**Methods:** Study population consisted of patients with CLBP and a confirmed MC on lumbar (L1-S1) MRI (N = 40) and voluntary subjects with no current symptoms in lower back and no MC on MRI (N = 40). Controls were matched for age and gender. The MC were classified into M1 (M1 (100%)), predominating M1 (M1/2 (65:35%)) or predominating M2 (M1/2 (35:65%)), and M2 (M2 (100%)). The first two were considered M1-dominant, and the latter two M2-dominant. Volumes of MC were calculated.

Fasting blood samples were taken for the assessment of inflammatory mediators, signalling molecules, growth factors and markers of bone turnover. Serum concentrations of 41 biomarkers were measured using electro-chemiluminescent based multi-array immunoassays from MesoScale Discovery; a high sensitivity cytokine/chemokine magnetic bead panel premixed 13-plex; a cytokine human magnetic bead panel 30-plex; a commercial Luminex kit, and a Quantikine Elisa kit. Luminex assays were performed using Luminex xMAP Technology. Plasma alkaline phosphatase (AFOS) activity was analysed using an enzymatic method. Serum high-sensitive CRP (hs-CRP) was analysed using nephelometry. Intact PINP (iPINP) and CTX-I analyses were performed using the IDS-iSYS multi-discipline automated system.

Mann-Whitney's U-test was used to compare the differences of biomarker concentrations between the patients and controls, and within patients between M1- and M2-dominant MC. Benjamini-Hochberg procedure was used to correct for multiple comparisons. Spearman's correlation coefficient was used to test for association between MC volume and biomarker concentration.

**Results:** Median concentrations of IL-12/23p40, IL-16, IL-17A, IL-7, IL-6, IL-2R, VEGF, VEGF-A, TNF-beta, IP-10, MCP-4, MDC-1, MIP-1beta, IFN-alpha, bFGF, TARC, IFN-gamma, SAA-1, MIG-1, RANKL, COMP, AFOS, iPINP and hs-CRP did not differ between MC patients and controls, while concentrations of IL-15 (p<0.001), IL-8 (p<0.001), TNF-alpha (p<0.001), Eotaxin-1 (p<0.05), Eotaxin-3 (p<0.001), MCP-1 (p<0.05), MIP-1alpha (p<0.01), Tie-2 (p<0.001), VCAM-1 (p<0.001), RANTES (p<0.001), CTX-1 (p<0.001), VEGF-C (p<0.001), VEGF-D (p<0.05), Flt-1 (p<0.01) and ICAM-1 (p<0.01) were significantly higher among controls. Serum concentrations of IL-1sRII (23.2 vs. 15.5 ng/ml, p<0.001) and hepatocyte growth factor (HGF-1, 169 vs. 105 pg/ml, p<0.01) were significantly higher among patients vs. controls. The type or volume of MC were not associated with serum biomarker concentrations after correction for multiple comparisons.

**Discussion:** Several biomarkers were suppressed while two markers (IL-1sRII and HGF) were elevated among MC patients compared to asymptomatic controls. However, these were not related to MC type or size. Further studies are needed to establish whether these serum biomarkers have diagnostic and prognostic value for CLBP patients.

## Lumbar spine morphometrics predict back pain

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**Introduction.** Since the 1950s, the search for causes of idiopathic back pain has focused mainly on disc degeneration. However, as disc degeneration phenotypes have only been modestly associated with an increased likelihood of back pain, the search has broadened.

**Methods.** In a study of back pain and MRI-based lumbar structural measures, 108 men who initially ranged from 35-63 years of age were followed for 15 years. Custom software was used to measure distances and areas of vertebrae and discs from ROIs on axial and sagittal images, and to calculate the morphometric measurements. The associations of baseline morphometric measurements and changes in measurements from baseline to 15-year follow-up were examined with respect to back pain frequency and disability at follow-up.

**Results.** Individually, baseline measures of disc and vertebra widths and several weight/area ratios were associated with more frequent back pain at 15-year follow-up after adjusting for age, height, weight, and back pain frequency at baseline. Once the most significantly associated predictor, disc volume, entered the multivariable model predicting back pain frequency, no other morphometric factors entered. When both baseline and change morphometric variables were considered, the best multivariable model for back pain frequency at follow-up included lesser change in disc area in the upper lumbar region (OR per 100\*kg/mm<sup>2</sup> 0.72 (95% CI=0.56-0.93) for a 1 point increase on the 7-point scale; p=0.013) and more baseline weight/vertebra area in the lower lumbar region (OR per cm<sup>3</sup> 1.92 (1.06, 3.47); p=0.031). There were no baseline morphometric predictors of disability at 15-year follow-up. When considering change variables, lesser change in upper lumbar axial disc areas was also most strongly related to low back pain disability at follow-up (OR per cm<sup>2</sup> 0.72 (0.58, 0.89) predicting 1 point on the 4-point back pain disability scale; p<0.003), though other measures were nearly as strongly related, including weight/disc area and weight/vertebra area (p=0.008). A change in weight or BMI did not enter into any multivariable model.

**Discussion.** A variety of baseline disc and vertebra morphometric measures are predictive of back pain frequency at long-term follow-up, which may offer clues to conditions contributing to back pain. Within men, the association of greater back pain frequency at follow-up with smaller discs and vertebrae, as well as more weight per disc or vertebra area, may point to a biomechanical risk factor for pain, such as larger forces (e.g. pressure or compression) transmitted through the spinal structures due to size or weight. These findings call for replication and further study.

## Associations of low back pain and long-term sciatica with autonomic nervous system regulation

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**Introduction:** Autonomic nervous system (ANS) contributes substantially to the modulation of pain perception. The measurements of heart rate variability (HRV) and baroreflex sensitivity (BRS) provide noninvasive, yet reliable, methods of assessing ANS activity. Chronic pain conditions such as fibromyalgia are associated with altered ANS responses and, importantly, also altered HRV and BRS. We hypothesize that similar autonomic dysregulation could be detected among subjects with low back pain (LBP) and long-term sciatica when compared to a reference population without pain.

**Methods:** The study sample consisted of the prospective Northern Finland Birth Cohort 1966 (NFBC1966). As part of the 46-year follow-up examination, the participants were invited to 3-minute recordings of electrocardiogram and blood pressure in seated and standing positions, allowing the analysis of heart rate (HR, bpm), vagally mediated HRV (root mean square of the successive differences in R-R intervals, rMSSD, ms), and cross-spectral BRS (ms/mmHg). The frequency (0, 1-7, 8-30, >30 days/yr, or daily; last two were combined for the analyses), intensity (numerical rating scale, NRS, 0-10), and bothersomeness (NRS 0-10) of pains including LBP and long-term (> 3 months) sciatica during the past 12 months were enquired using a questionnaire. The participants' body mass index (BMI) was measured. We also evaluated participants' physical activity (PA), smoking habits, and symptoms of depression and anxiety (the Hopkins Symptoms Checklist-25, HSCL-25). Sex-stratified crude and adjusted (BMI, PA, smoking, HSCL-25) linear regression analyses were conducted to analyze the association of HR, HRV, and BRS with the frequency of LBP and sciatica. HR variables were normally distributed per se, whereas rMSSD and BRS had to be log-transformed in order to meet the normality assumption. We had all necessary data for 4358 individuals (57% women) for the analyses of HR and HRV, and 2025 (54% women) for the analysis of BRS.

**Results:** The intensity and bothersomeness of pain increased in accordance to its frequency (Figures 1-2). After adjustments, the women with the highest frequency of LBP (> 30 days/yr) had higher seated HR, lower seated and standing rMSSD, and lower standing BRS than those without pain. The women in other LBP frequency categories showed similar but more inconsistent trends in ANS response. Among men with LBP, the findings were more inconsistent and attenuated after adjustments (Figure 1). The sciatica patients showed similar associations to those of the LBP patients. After adjustments, the women with the highest frequency of sciatica had higher seated and standing HR, lower seated rMSSD, and lower standing BRS than those without pain. Other frequency categories and male subjects showed inconsistent results (Figure 2). Restricting the sample to those with pain intensity > 4 on NRS did not essentially change the results.

**Discussion:** Our cross-sectional population-based results demonstrate ANS dysregulation especially among middle-aged women with frequent (> 30 days/yr) LBP and sciatica. The findings were more inconsistent among men and those women with less frequent pain. It is interesting to evaluate whether subjects with ANS dysregulation are more prone for work disability and use of health care resources during the follow-up.

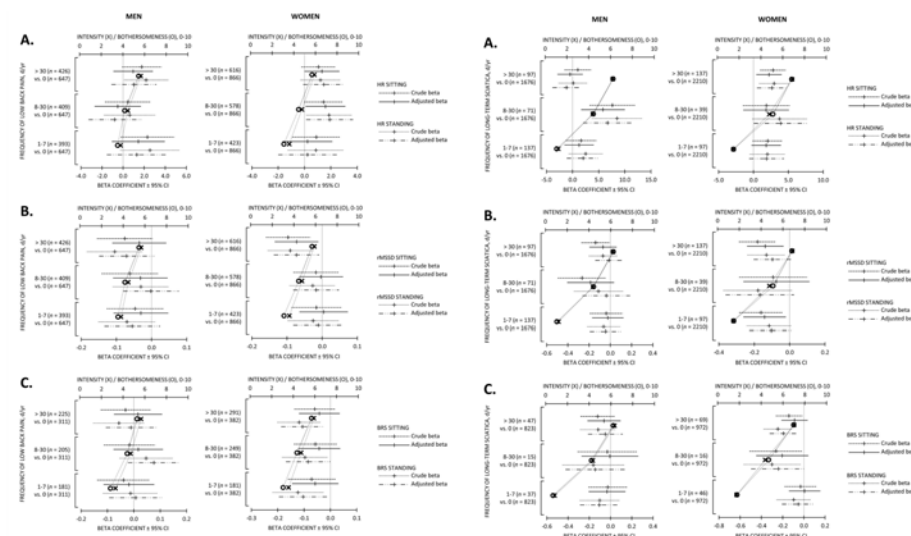


Figure 1. Beta coefficients from linear regression models illustrating the association between autonomic nervous system function (A, heart rate (HR, bpm), B, heart rate variability (rMSSD, ms, log-transformed), C, baroreflex sensitivity (BRS, ms/mmHg, log-transformed)) and the frequency of low back pain among men and women. Additionally, the intensity and bothersomeness of pain are illustrated across the pain frequency categories.

Figure 2. Beta coefficients from linear regression models illustrating the association between autonomic nervous system function (A, heart rate (HR, bpm), B, heart rate variability (rMSSD, ms, log-transformed), C, baroreflex sensitivity (BRS, ms/mmHg, log-transformed)) and the frequency of long-term sciatica among men and women. Additionally, the intensity and bothersomeness of sciatica are illustrated across the pain frequency categories.

## Local associations between intervertebral disc biochemistry, muscle health, physical activity, and clinical disability

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### Introduction

Despite the high prevalence of low back pain (LBP), its etiology and pathogenesis remain unclear. There is a growing need for non-invasive imaging biomarkers which may better differentiate LBP patient subgroups and characterize disease phenotypes in order to effectively target treatments. Intervertebral disc degeneration is associated with LBP. Previous studies have shown MR imaging sequences such as T1 $\rho$ /T2 relaxation are sensitive to the biochemical changes of early stage disc degeneration: proteoglycan loss, dehydration, and disorganization of annular collagen. These studies use region-of-interest (ROI) methods to calculate average relaxation values for the nucleus and annulus. However, it is difficult to accurately and reproducibly separate these regions, especially in patients with severe deformity and degeneration. This work uses voxel-based-relaxometry (VBR) to examine the association between local biochemical composition of the disc, muscle health, and patient reported outcomes (pain, disability, physical activity).

### Methods

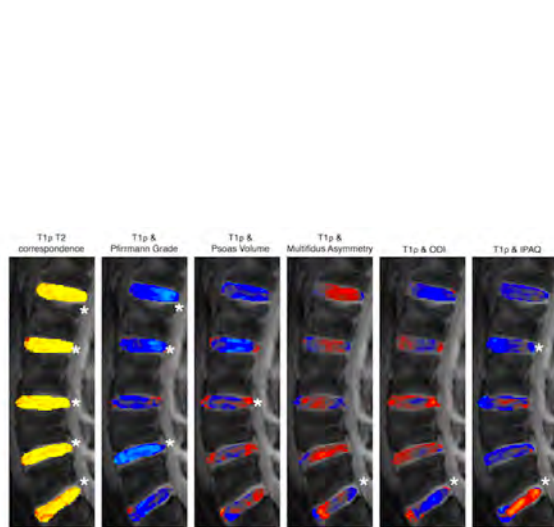
Twelve LBP patients (4 males, 20-67y) were recruited with Committee on Human Research approval. MR images of lumbar spine were acquired on a 3T GE750W scanner. Water, proteoglycan, and collagen content were investigated using a 8min sagittal T1 $\rho$ /T2 (MAPSS) sequence. Modified Pfirmann grading was performed on a 5min sagittal T2W image and a 7min axial IDEAL sequence was acquired for manual segmentation and quantification of spinal muscle volume and fat fraction. Whole lumbar intervertebral discs were segmented semi-automatically using active contours and corrected manually for cases of severe degeneration. Rigid and non-rigid registration was performed, matching each patient image to the atlas lumbar spine. Statistics were computed using Pearson's partial correlations adjusted for age and gender.

### Results

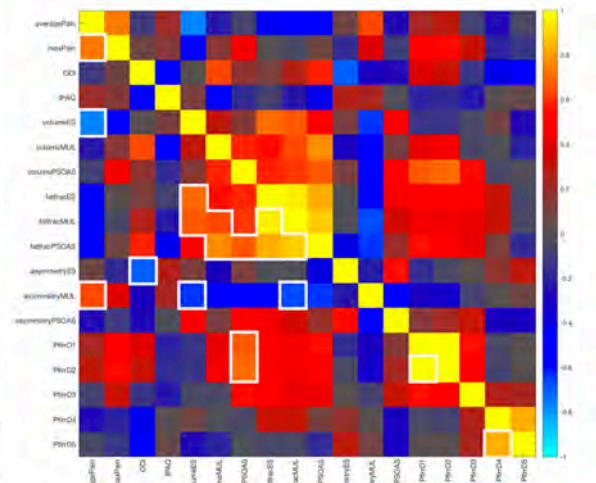
T1 $\rho$  and T2 were significantly correlated throughout the disc, with greatest variations in spatial distribution appearing at the disc periphery **Figure 1**. Modified Pfirmann grade of each disc showed strong negative correlations with T1 $\rho$ . *Psoas*, *erector spinae*, and *multifidus* volume and asymmetry showed disc-level correlations. There was moderate negative association between *psoas* volume and T1 $\rho$  in L1/L2 and L2/L3. *Multifidus* asymmetry was positively correlated with T1 $\rho$  in the disc center at all levels. Greater disability was associated with lower T1 $\rho$  (a more degenerative biochemical state) in L1/L2 and L5/S1. Higher physical activity was associated with higher T1 $\rho$  in L5/S1, with a strong correlation in the nucleus and the posterior annulus. Adjusting for pain, the relationship between IPAQ and T1 $\rho$  remained statistically significant. Between variable relationships visualized in **Figure 2**. Average pain was positively correlated to *multifidus* asymmetry and negatively correlated to *erector spinae* volume. *Psoas* volume showed positive correlations with Pfirmann grade in L1/L2 and L2/L3.

### Discussion

Strong correlations were found between muscle health, physical activity, disability, and T1 $\rho$ /T2. Associations were level-specific, and varied within the disc along the AP direction. A larger patient population with age and gender matched controls would be necessary to confirm the significance of moderate associations. VBR is more reliable and faster than ROI methods to explore differences in local disc biochemistry between LBP patient groups. Future work will attempt to differentiate non-pathological degeneration from pathological degeneration and track responses to treatment within LBP patient subgroups.



**Figure 1** Pearson's partial correlation coefficients for associations between T1 $\rho$  and patient reported outcomes (ODI, IPAQ), Pfirmann grading, and muscle variables, adjusted for age and gender. Similar spatial trends in relaxation times and levels of significance were observed in T2 maps. A white asterisk indicates correlations at this disc level were statistically significant with at least 5% of voxels  $p < 0.05$ .



**Figure 2** Pearson's partial correlation coefficients for associations between patient reported outcomes, Pfirmann grading, and muscle variables, adjusted for age and gender. Pixels outlined in white are statistically significant correlations with  $p < 0.05$ .

MUL, PSOAS, ES = *multifidus*, *psoas*, *erector spinae*

## Genome-wide meta-analysis of 158,000 individuals of European ancestry identifies two loci associated with chronic back pain

Pradeep Suri, Melody Palmer, Yakov Tsepilov, Maxim Freidin, Lennart Karssen, Gail Jarvik, Cindy Boer, Michelle Yau, Traci Bartz, Tuhina Neogi, Caroline Hayward, Blair Smith, Archie Campbell, Liubov Arbееva, Joanne Jordan, Maria Nethander, Magnus Karlsson, Claes Ohlsson, Dan Mellstrom, Dan Evans, Nancy Lane, Carrie Nielson, Eric Orwoll, Lynn Marshall, Marc Hochberg, Rebecca Jackson, Braxton Mitchell, Joyce Van Meurs, Andrea Skelin, Ozren Polasek, Gordan Lauc, Nicholas Smith, Yurii Aulchenko, Frances M Williams

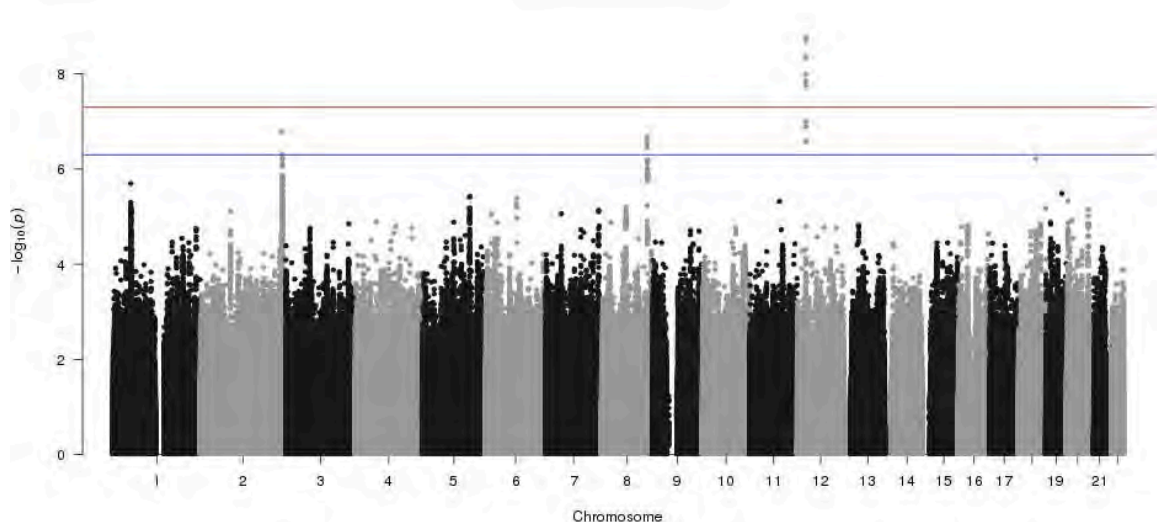
**INTRODUCTION:** Back pain is highly heritable (40%), and results in an associated societal burden driven mainly by those with persistent ('chronic') back pain (CBP). Knowledge regarding specific genetic associations could potentially shed light on biological mechanisms underlying CBP. We conducted the first genome-wide association study (GWAS) meta-analysis of CBP.

**METHODS:** Adults of European ancestry (EA) were included from 16 cohorts: Cardiovascular Health Study, Framingham Heart Study, Generation Scotland, Johnston County Osteoarthritis Project, Osteoporotic Fractures in Men Study (MrOS) Sweden (Gothenburg and Malmo), MrOS US, Osteoarthritis Initiative, Rotterdam Study (RS1, RS2, and RS3), Study of Osteoporotic Fractures, 10,001 Dalmatians (Vis and Korcula), TwinsUK, and UK Biobank. CBP cases were defined by questionnaire as those reporting back pain present for at least 3-6 months. Controls included those with no back pain or back pain of insufficient duration to count as cases. Each cohort conducted genotyping using commercially available arrays followed by imputation using 1000 Genomes or Haplotype Reference Consortium reference panels. GWAS was performed using logistic regression models with additive genetic effects to examine associations between genetic variants and CBP, adjusting for age, sex, study-specific covariates, and population substructure. After quality control, we conducted fixed-effect inverse-variance weighted meta-analysis with genomic control correction. The threshold for genome-wide significance was  $p < 5 \times 10^{-8}$ . Three variants of at least suggestive significance ( $p < 5 \times 10^{-7}$ ) were carried forward for replication (Bonferroni-corrected  $p < 0.017$ ) in a separate GWAS of UK Biobank participants not included in discovery.

**RESULTS:** The discovery sample included 29,531 cases and 128,494 controls (total  $n=158,025$ ). The mean age of participants in all cohorts was 50-76 years. A genome-wide significant association was found for the intronic variant rs12310519 (Figure) on chromosome 12p12 in *SOX5* (OR 1.08,  $p=1.64 \times 10^{-9}$ ), with six other significant variants at this locus. No other loci reached genome-wide significance. Variants of suggestive significance at two other loci were the intronic variant rs1453867 in *DIS3L2* (OR 0.95,  $p=1.63 \times 10^{-7}$ ), and the intergenic variant rs7833174 (OR 1.06,  $p=2.1 \times 10^{-7}$ ), located between *CCDC26* (a long non-coding RNA) and *GSDMC* (gasdermin C). The replication sample included 50,915 cases and 232,837 controls (total  $n=283,752$ ). rs12310519 (*SOX5*:OR 1.06,  $p=5.3 \times 10^{-11}$ ) and rs7833174 (*CCDC26/GSDMC*:OR 1.04,  $p=3.7 \times 10^{-7}$ ) replicated, but rs1453867 (*DIS3L2*:OR 0.98,  $p=0.02$ ) did not.

**DISCUSSION:** This study identified and replicated two novel genetic loci associated with CBP at *SOX5* and *CCDC26/GSDMC*. The *SOX* genes are a family of transcription factors involved in many phases of embryonic development. *SOX5* is necessary for efficient chondrogenesis and vital to normal differentiation of spinal structures. CBP-associated variants in *SOX5* had nominally significant associations ( $p < 5.0 \times 10^{-4}$ ) with height and lumbar spine bone mineral density in prior GWAS. *SOX5* was not associated with related phenotypes such as osteoarthritis or intervertebral disc degeneration in prior GWAS. rs7833174 and other CBP-associated variants in the *CCDC26/GSDMC* locus were associated with sciatica requiring lumbar discectomy and height in prior GWAS. These results require functional follow-up, but suggest possible shared biological pathways among CBP, lumbar disc herniation, height and/or skeletal development.

**Figure.** Manhattan plot



## Honokiol prevents oxidation and inflammation through the activation of TXNIP/NLRP3 inflammasome signaling pathway in intervertebral disc

Zhi-Jun Hu, Pan Tang, Shun-Wu Fan

### INTRODUCTION

Intervertebral disc degeneration (IVDD) is a multifactorial disease and responsible for many spine related disorders. Accumulating evidence indicates that oxidative stress and inflammation play a critical role in the pathogenesis of IVDD. And recent studies revealed that NLRP3 inflammasomes were closely related to the IVDD, that the expression of NLRP3 inflammasomes were evaluated in the degenerative IVDs. Honokiol, a naturally occurring flavonoid derived from the root and bark extract of *Magnolia officinalis*, has been traditionally used in the treatment of various diseases without notable side effects for many years. Further, a recent study demonstrated that honokiol, a low molecular weight natural product, could penetrate into and distribute in IVDs to achieve therapeutic effect in a rat tail model *in vitro* and *in vivo*. The aim of this study was to investigate the effect of honokiol in the progression of IVDD.

### METHODS

The activity of cells, apoptosis, the level of SOD and MDA, inflammatory mediators, extracellular matrix, TXNIP/NLRP3 inflammasome axis, and potential signal pathway were evaluated in nucleus pulposus cells. And the effect of honokiol was checked in a rat IVDD model induced by puncture. The mRNA expression of pro-inflammatory cytokines (iNOS, COX-2 and IL-6), metalloproteinases, aggrecanases, TXNIP, NLRP3 inflammasomes, caspase-1, and IL-1 $\beta$  was determined by real-time polymerase chain reaction (PCR) analysis. The protein expression of the above genes and signal pathways were detected by western blot analysis.

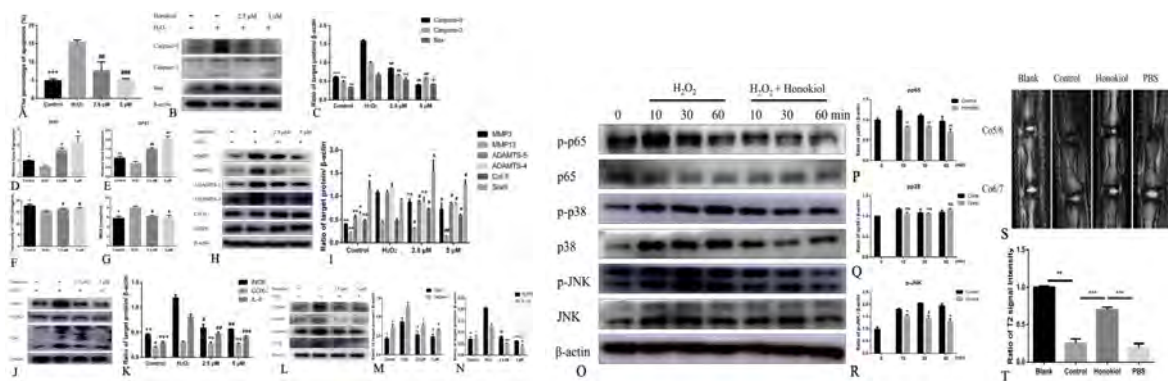
### RESULTS

Our results showed honokiol suppressed the expression of caspase-9, caspase-3 and bax induced by H<sub>2</sub>O<sub>2</sub> in nucleus pulposus cells, and restored the activity of cells. Then, we found that honokiol exhibit potent anti-inflammatory effects through the suppression of inflammatory mediators (IL-6 and iNOS) in nucleus pulposus cells, and restored the balance between the anabolic and catabolic processes by up-regulating Col II and SOX9 and down-regulating MMP-3, MMP-13, ADAMTS-5, and ADAMTS-4. What's more,

H<sub>2</sub>O<sub>2</sub> treatment significantly increased the ROS production in nucleus pulposus cells whereas, pretreatment of cells with honokiol significantly suppressed the H<sub>2</sub>O<sub>2</sub>-induced generation of ROS. Results indicated that the activation of TXNIP/NLRP3 inflammasome and the cleavage of caspase-1 induced by H<sub>2</sub>O<sub>2</sub> can be attenuated by honokiol through inhibition of NF- $\kappa$ B and JNK signaling. In addition, MRI evaluation showed honokiol could not reverse IVDD progression, but it delayed the progression of IVDD *in vivo*.

### DISCUSSION

Honokiol, a small molecular weight natural product, inhibits the H<sub>2</sub>O<sub>2</sub>-induced apoptosis, levels of oxidative stress, expression of inflammatory mediators, major proteases associated with degradation. Honokiol exerted the protective effect may through suppressing the phosphorylation of NF- $\kappa$ B and JNK, and activation of TXNIP/NLRP3 inflammasome in H<sub>2</sub>O<sub>2</sub>-stimulated nucleus pulposus cells, thereby inhibiting the activation of downstream inflammatory mediators such as IL-1 $\beta$ . Thus, our results suggest that honokiol possess nucleus pulposus protective properties and may be of value in suppressing the pathogenesis of IVDD.



## Autophagy plays protective roles against human disc cellular apoptosis, senescence, and extracellular matrix degradation

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**Introduction:** The intervertebral disc is the largest avascular organ. Autophagy is an important cell survival mechanism by self-digestion and recycling damaged components under stress, primarily nutrient deprivation. Thus, resident cells may utilize autophagy to cope with the stressful conditions (low nutrition, pH, and oxygen concentration). However, the extent to which autophagy affects disc cells is unknown. Pharmacological inhibition difficult to provide specific mechanistic explanations of autophagy due to diverse crosstalks in the pathway. Therefore, our objective was to elucidate roles of autophagy in human disc cells using the RNA interference technique.

**Methods:** Human disc cells obtained from lumbar surgery were used. Cells were cultured in DMEM with or without 10% FBS under 2% O<sub>2</sub> for 0–48 hours to assess serum starvation-induced autophagy. Expression of autophagy marker LC3 and substrate p62/SQSTM1 as well as autophagy-related gene 5 (ATG5), essential for autophagy execution, was assessed by WB. Next, we conducted experiments for autophagy induction or inhibition in human disc cells. ATG5 small interfering RNA (siRNA) was transfected to suppress autophagy. Since autophagy is negatively regulated by the mammalian target of rapamycin complex 1 (mTORC1), RAPTOR, a component of mTORC1, was knocked down using siRNA to enhance autophagy. Cells after transfection of each siRNA were cultured in DMEM with or without 10% FBS for 24 hours. Knock-down efficacy were assessed by WB. To assess mTOR signaling affected by RAPTOR siRNA, phosphorylation levels of Akt and p70/S6K were also evaluated by WB. Then, in no serum-containing DMEM with 10 ng/ml interleukin-1 $\beta$  (IL-1 $\beta$ ) to induce inflammation, the incidence of apoptotic and senescent cells was determined by WB for cleaved PARP, cleaved caspase-9 and senescent p16/INK4A. Further, matrix metabolism was evaluated by WB for MMPs and TIMPs in supernatants and real-time RT-PCR for *aggrecan-1* and *collagen type 2- $\alpha$ 1* normalized to *GAPDH*.

**Results:** (1) Time-dependent increases in LC3-II and decreases in p62/SQSTM1 in response to serum starvation, consistent with autophagy induction. (2) ATG5 siRNA decreased LC3-II and increased p62/SQSTM1, showing autophagy inhibition. On the other hand, RAPTOR siRNA increased LC3-II and decreased p62/SQSTM1, showing enhanced autophagy. (3) Pro-inflammatory IL-1 $\beta$  induced apoptotic and senescent stimuli. Cleaved caspase-9 and cleaved PARP increased by ATG5 siRNA, but decreased by RAPTOR siRNA. Senescent p16/INK4A also increased by ATG5 siRNA, but decreased by RAPTOR siRNA. (4) IL-1 $\beta$ -induced MMP-3, -13 releases were unaffected by ATG5 siRNA, but decreased by RAPTOR siRNA. In addition, ATG5 siRNA was less sensitive to *aggrecan-1* and *collagen type 2- $\alpha$ 1* mRNA expression, but RAPTOR siRNA promoted *collagen type 2- $\alpha$ 1* mRNA expression.

**Conclusion:** Knock down of ATG5 led to increased cell death and aging under stressful conditions, indicating the importance of autophagy in maintaining disc cell homeostasis. mTORC1 suppression by RAPTOR siRNA showed protective effects against human disc cellular apoptosis, senescence, and matrix degradation. Suppressed mTORC1 and p70/S6K lose the p70/S6K-mediated negative feedback loop, leading to Akt induction. Activated Akt provides pro-survival and anti-catabolic effects. Autophagy modulation is a potential molecular treatment strategy preventing degenerative disc disease, which depends on induction of Akt as well as autophagy.

## Melatonin antagonizes intervertebral disc degeneration by promoting mitophagy through the NF- $\kappa$ B signaling pathway

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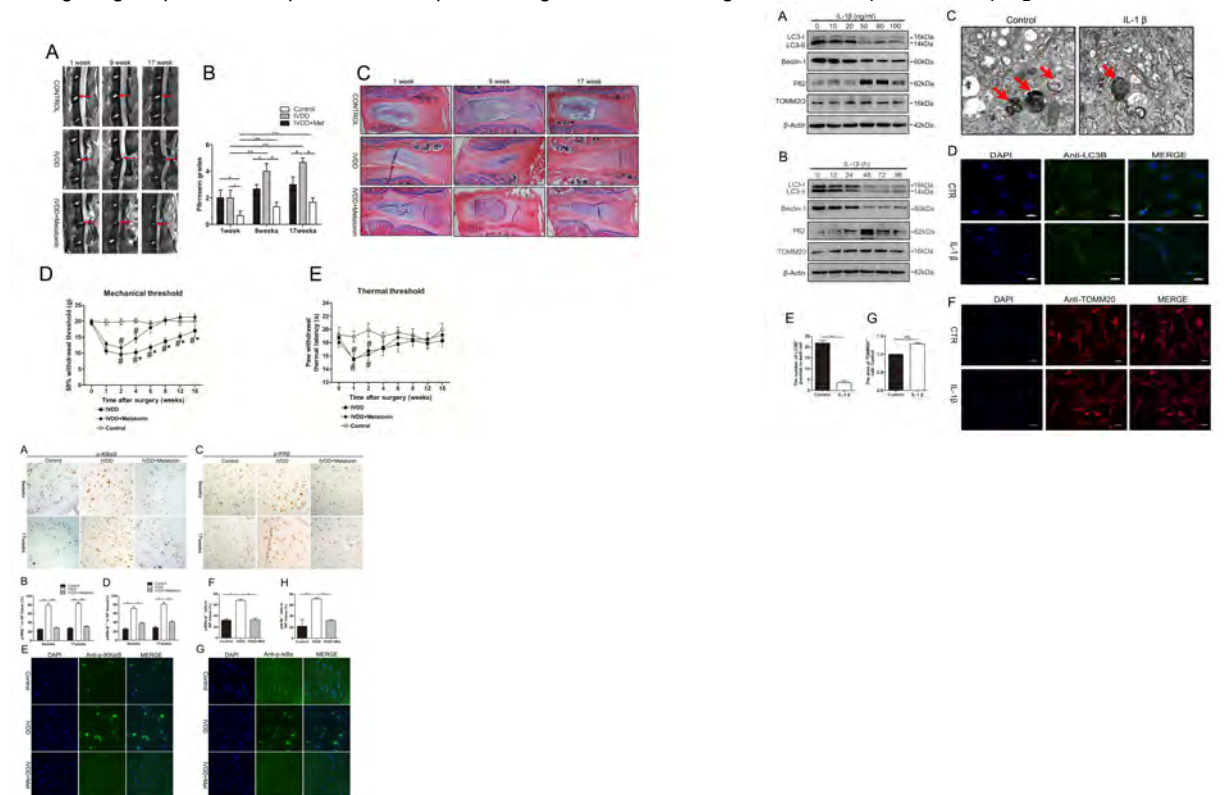
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**Introduction:** Mitophagy is a selective form of macro-autophagy in which the mitochondria are specifically targeted for autophagic degradation. Melatonin has been reported to enhance mitophagy in rats with carbon tetrachloride-induced liver fibrosis and protects against early brain injury after subarachnoid hemorrhage. Intervertebral disc degeneration (IVDD) is a major driving factor of spinal degenerative diseases that lead to disability. These reports make it interesting to study roles of melatonin and mitophagy in IVDD. The objective of this study was to investigate whether exogenous melatonin administration prevents IVDD by promoting mitophagy in cell and animal models.

**Methods:** A rat IVDD model was established to study the role of melatonin on IVDD-related pain behaviors. Immunohistochemical staining, Western blots, RT-qPCR, immunofluorescence staining and transmission electron microscopy were used to analyze the role of melatonin and mitophagy in disc degeneration. Western blots, transmission electron microscopy and immunofluorescence staining were used to study the role of mitophagy in IL-1 $\beta$  induced-IVDD in a cellular model. The role of NF- $\kappa$ B signaling pathway in melatonin-induced mitophagy in intervertebral disc were analyzed by Western blots and immunofluorescence staining and immunohistochemical staining.

**Results:** In a needle puncture-induced rat IVDD model, the application of melatonin prevented IVDD development and improved IVDD-related pain behaviors in vivo. Furthermore, the levels of the specific markers LC3B, Beclin-1, p62 and TOMM20 provide the first demonstration that mitophagy was inhibited in IVDD. Melatonin application attenuated IVDD by promoting mitophagy in vivo. In an IL-1 $\beta$ -induced IVDD cellular model, mitophagy was significantly suppressed in nucleus pulposus (NP) cells, and melatonin antagonized this effect by promoting mitophagy. Following NF- $\kappa$ B siRNA- and Lenti-ShRNA-mediated knockdown, melatonin regulated mitophagy by inhibiting NF- $\kappa$ B signaling pathway.

**Discussion:** This study provides the first demonstration that melatonin prevented IVDD by promoting mitophagy both in vitro and in vivo. A second major observation of our study is that melatonin promoted mitophagy by inhibiting the NF- $\kappa$ B pathway. These findings might provide a possible therapeutic target for controlling the development or progression of IVDD.





## Anti-nerve growth factor therapy attenuates osteoporosis-related cutaneous and deep musculoskeletal pain following ovariectomy in mice

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**INTRODUCTION.** The prevalence of osteoporosis is increasing with the aging global population. In addition to increased risk of fracture, osteoporosis is associated with chronic pain. We previously reported that improvement in bone mineral density is not sufficient to reduce osteoporotic pain in an ovariectomy (OVX)-induced mouse model of osteoporosis, highlighting the need for new treatments. Targeting of Nerve Growth Factor (NGF) with sequestering antibodies is a promising new direction for the treatment of musculoskeletal pain including low back pain and arthritis. Its efficacy is currently unknown for osteoporotic pain. The aim of this study was to examine the efficacy of anti-NGF antibody therapy against behavioural indices of osteoporotic pain and on sensory neuron plasticity in a mouse model of OVX-induced osteoporosis.

**METHODS.** Ovariectomy (OVX, n=20) - and sham-operated (n=10) female C57BL6 mice at 5-7 week of age were assigned to receive either anti-NGF antibody or vehicle (OVX/anti-NGF, OVX/Vehicle, and Sham/Vehicle; n=10 per group) at 8 weeks after surgery. Evaluation of the vertebral and femoral bone mineral density (BMD) were performed prior to the behavioral testing and after anti-NGF treatment. Animals received 2 injections of anti-NGF antibody (Exalpha Biologicals Inc., Shirley, MA, USA, 10mg/kg, i.p) or vehicle (0.01 mL/g, i.p sterile saline), 2 weeks apart. Behaviors were monitored at baseline, and for a maximum of 2 months after the initial treatment. Behavior included measures of cutaneous hindpaw hypersensitivity (von Frey, acetone-evoked behavior, cold plate test and heat test), deep musculoskeletal discomfort (grip test assay) and physical function (rotarod and open-field tests). Sensory nervous system plasticity was evaluated by quantification of the sensory neuropeptide calcitonin gene-related peptide (CGRP)- and neuropeptide-Y-immunoreactivity (-ir) in dorsal root ganglia.

**RESULTS.** There was a significant loss in vertebral and femoral BMD of the OVX mice compared to the sham-operated controls. Anti-NGF treatment had no adverse effect on the vertebral or femoral BMD. Furthermore, anti-NGF treatment attenuated OVX-induced hypersensitivity to mechanical, cold and heat stimuli on the plantar surface of the hindpaw. The OVX-induced impairment in grip force strength, used here as a measure of deep musculoskeletal discomfort, was partially reversed by anti-NGF therapy. No changes were observed in the rotarod or open field tests for overall motor function and activity. Finally, anti-NGF treatment attenuated the increase in CGRP-immunoreactive dorsal root ganglia neurons observed in OVX mice.

**DISCUSSION.** We demonstrated anti-NGF efficacy in the OVX mouse model of osteoporosis-related pain. These data implicate NGF as a driver of long-term osteoporotic pain and suggest that anti-NGF treatment may be a useful therapy for this population.

## The spinal stenosis pedometer and nutrition lifestyle intervention (SSPANLI): results of a randomized trial

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**Introduction:** Owing to mobility limitations, people with lumbar spinal stenosis (LSS) are at risk for diseases of inactivity, including obesity. Body mass index is the strongest predictor of function in LSS, suggesting that weight loss may promote physical activity and provide a unique treatment option for improving function. The goal of this randomized trial was to evaluate an innovative e-health lifestyle intervention aimed at promoting weight loss, increasing physical activity, and quality of life in people with lumbar spinal stenosis who are overweight or obese.

**Methods:** Study Design: Randomized controlled trial. We recruited overweight or obese individuals with LSS confirmed clinically and on imaging. Participants were randomized to either the lifestyle intervention group or control group (usual care). During Week 1, intervention participants received a wearable fitness device (pedometer), a personalized consultation with a Dietitian, and with an Exercise Physiologist. For 12 weeks participants logged on to the e-health website to access personal step goals, nutrition education videos, and a discussion board. Follow-up occurred at Week 13, 6 months and 1 year. Physiologic outcomes included dual energy x-ray absorptiometry (DXA), blood draw, 7-day accelerometry, and Self-Paced Walking Test. Self-report outcome measures included: food record, SF-36, pain scales, Swiss Spinal Stenosis Symptom and Physical Function Scales, Oswestry Disability Index (ODI), Pain Catastrophizing Questionnaire, Tampa Scale for Kinesiophobia, and CES-D Depression Scale. Hypothesis: A 12-week e-health pedometer and nutrition lifestyle intervention will significantly decrease fat mass, increase physical activity (steps/day), and increase health related quality of life in overweight and obese individuals with lumbar spinal stenosis, compared to usual care.

**Results:** Data collection for this trial has just been completed. We had sufficient follow-up data for 44/50 participants. Preliminary analyses of 3-month outcomes demonstrate an average age of  $67 \pm 7$  yrs (60% female), and significant improvements in fat mass (DXA), trunk fat mass, symptom severity (Swiss Symptom Scale), energy intake, steps per day, maximum continuous activity (accelerometry), and quality of life (SF-36) ( $p < 0.05$ ). Qualitative results suggest that participants were supportive of this approach.

**Discussion:** Preliminary analysis suggest that the SSPANLI intervention feasible, attractive to participants, and effective in improving fat mass, physical activity and quality of life. The use of e-health interventions provides an opportunity for patients to take an active role in their own health, making decisions, and managing their condition in co-operation with healthcare providers. E-health interventions that promote permanent behaviour changes will result in healthier patients who are less likely to access health care in the future. Improved overall health will ultimately lead to increased functional autonomy and quality of life. In LSS specifically, weight loss and increased physical activity may delay expensive interventions (e.g. injection and surgery), improve mobility, and reduce the risk of avoidable health deterioration. This study represents the first time electronic media has been used to deliver a lifestyle intervention aimed at managing LSS and risk for diseases of inactivity concurrently.

## **Smoking is associated with increased development of musculoskeletal burden: a longitudinal cohort study from the midlife development in the U.S. (MIDUS) study**

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**Introduction:** Cigarette smoking has been associated with musculoskeletal burden and functional impairment, including decreased bone mineral density, lumbar disk disease, and increased risk of perioperative and healing complications. Prolonged smoking has been associated with lumbar radicular pain and clinically-verified sciatica. However, there is a paucity of literature evaluating the longitudinal association between musculoskeletal pathology and smoking. We sought to further explore the association between the development of smoking and development of musculoskeletal pathology through the MIDUS longitudinal series.

**Methods:** Data was utilized from the MIDUS national study, a longitudinal study assessing health and well-being. MIDUS 1 was conducted in 1995-1996 through random dialing sample of English-speaking, non-institutionalized adults in the U.S. There were 7108 participants who completed the MIDUS 1 survey either by telephone or mail. MIDUS 2 was conducted 9-10 years later, with 4963 participants who were successfully contacted to complete the survey. Three separate outcomes were assessed. Patients were asked to respond to whether they had: 1) experienced or been treated for arthritis, rheumatism, or other bone or joint diseases; 2) experienced or been treated for sciatica, lumbago, or recurrent backache; and 3) in the past 30 days taken prescription medicine for arthritis? Patient who denied musculoskeletal pathology and smoking in the MIDUS 1 survey were included. Evaluating these variables, we conducted two-tailed student's t-tests and chi-square tests to compare demographic data as appropriate and McNemar's tests to assess smoking association with musculoskeletal burden.

**Results:** Of the 4963 participants who completed both MIDUS 1 and MIDUS 2 surveys, there were 1362 participants who did not smoke in the MIDUS 1 survey and had a valid response to the question on smoking in the MIDUS 2 survey. 839 out of 1362 participants answered the question to bone and joint disease; smokers had a higher incidence of bone and joint disease (12 out of 61, 19.7% vs. 147 out of 778, 18.9%,  $p < 0.001$ ). 858 out of 1362 participants answered the question to back pain; smokers had a higher incidence of back pain (12 out of 55, 21.8% vs. 99 out of 803, 12.3%,  $p < .001$ ). 759 out of 1362 participants answered the question to use of prescription arthritis medication; smokers had a lower incidence of use of arthritis medication (7 out of 55, 12.7% vs. 124 out of 704, 17.6%,  $p < .001$ ).

**Discussion:** Our findings suggest a positive association between the development of smoking and the development of musculoskeletal morbidity, including arthritis, rheumatism, lumbago, and sciatica. Our findings also show a negative association between development of smoking and the development of use of arthritis medication. Our findings suggest that prevention and intervention in smoking may have implications on musculoskeletal burden.

## **Type II Diabetes is associated with development of musculoskeletal pathology: a cohort study from the Midlife Development in the U.S. (MIDUS) database.**

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**BACKGROUND:** Both type II diabetes and chronic musculoskeletal pain present substantial burden to the healthcare system. Several studies have reported an association between these two diseases. Metabolic disturbances from diabetes have been linked to microvascular damage and abnormal glycosylation of collagen in connective tissue. However, there is a paucity of literature addressing the longitudinal association between musculoskeletal pathology and type II diabetes. Using the Midlife Development in the U.S. (MIDUS) database, we perform a retrospective cohort analysis on the development of type II diabetes to the development of musculoskeletal pathology.

**METHODS:** The Midlife Development in the U.S. (MIDUS) cohort national survey assessed the health and well-being of non-hospitalized adults in the U.S. The MacArthur Midlife Research Network randomly called 7108 English-speaking Americans between 1995-1996 to complete the MIDUS 1 survey either via telephone call or mailed response. A follow-up survey (MIDUS 2) was completed by 4963 participants, 9-10 years later. Musculoskeletal outcomes were assessed with responses to three questions: whether participants (1) experienced or received treatment for arthritis, rheumatism, or other bone or joint diseases; (2) experienced or received treatment for sciatica, lumbago, or recurring backache; and (3) in the past 30 days, had taken prescription medication for arthritis. Patients without musculoskeletal issues or type II diabetes from the MIDUS 1 survey were included in this study. Data analysis was performed using two-tailed chi-square tests to compare demographic variables and McNemar's tests were used to investigate the association between type II diabetes and musculoskeletal issues.

**RESULTS:** Of the 4963 respondents who completed the MIDUS 1 and MIDUS 2 survey series, there were 3757 who did not have diabetes or high blood sugar in the MIDUS 1 survey and had a valid response in the MIDUS 2 survey. 3021 out of the 3757 participants responded to the question of back pain; a higher incidence of development of back pain was observed in patients that developed type II diabetes (33 out of 196, 16.8% vs. 329 out of 2825, 11.6%). 3035 out of the 3757 participants responded to the question of bone and joint disease; a higher incidence of development of bone and joint disease was observed in patients that developed type II diabetes (42 out of 183, 23.0% vs. 471 out of 2852, 16.5%,  $p < 0.001$ ). 2815 out of 3757 participants responded to the question of arthritis prescription medication usage; a higher incidence of development of use of arthritis prescription use was observed in patients that developed type II diabetes (41 out of 172, 28.9% vs 358 out of 2643, 13.55%,  $p < 0.001$ ).

**DISCUSSION:** Our results indicate a statistically significant relationship between the development of type II diabetes and development of musculoskeletal pain. Patients that developed type II diabetes also had a higher incidence of development of bone and joint disease, back pain and usage of prescription medication for musculoskeletal issues. Our findings highlight the importance of early and accurate diagnosis of comorbid type II diabetes in patients with musculoskeletal pathology with possible implications on overall healthcare economic burden.

## Post-operative single-shot epidural fentanyl and bupivacaine for postoperative analgesia after lumbar decompression: a prospective, double-blind randomized study

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**Introduction:** Despite the success of lumbar decompression in alleviating symptoms of sciatica, radiculopathy, and neurogenic claudication, transient back and buttock pain is still a common complaint in the immediate postoperative period. The purpose of this study was to evaluate the postoperative analgesic effects of a single, postoperatively administered epidural bolus of Fentanyl and Bupivacaine in patients that underwent lumbar decompressive surgery.

**Methods:** We performed a randomized, double-blinded, clinical trial. After approval from the institutional review board and local ethics committee, informed consents were obtained, and 45 patients scheduled for lumbar decompression from December 2015 to August 2017 were randomly assigned to receive a postoperative bolus of 10-mL solution of 25 mcg of Fentanyl, 0.125% Bupivacaine, and 0.9% saline solution via an intraoperatively placed epidural catheter immediately after wound closure, before dressing application. Facial pain scale scores (from 0 to 10) were measured at 3 time points after surgery (fully awake at recovery room, transfer to ward, first postoperative day). Postoperative need for oral analgesics, time to independent ambulation, associated adverse events, and time to hospital discharge were also evaluated.

**Results:** Pain scores were noted to be significantly lower at all time points except upon transfer to recovery room in the epidural group ( $P < 0.05$ ). In turn, they also received less on-demand oral pain medications ( $p = 0.000$ ). The mean time to ambulation was 0.09 days in the epidural group and 0.91 days in the decompression-alone group ( $p = 0.000$ ). Criteria for hospital discharge was usually met on Day 0 in the epidural and Day 1 in the control group ( $p = 0.000$ ). No adverse events or complications related to Fentanyl use were observed.

**Discussion:** This randomized, double blind, prospective study, which included 45 patients, revealed that administration of an immediate postoperative bolus of epidural FB after lumbar decompression can provide effective postoperative analgesia. Better pain control hours after surgery ultimately translated into an earlier time to confidently ambulate independently, a shorter hospital stay and a decreased need for on demand pain medications. The epidural group displayed low and decreasing postoperative pain scores immediately after surgery, upon transfer to ward and on the first postoperative day. Most of these patients were also able to ambulate upon transfer to their ward, as well as meet the criteria for discharge. It was also determined that there was less need for oral medications in the experimental group during their short hospital stay. All of these results were significantly improved compared to the group of patients who underwent decompression without the epidural bolus, except for the pain score upon full consciousness at the recovery room.

## Association of degenerative lumbar scoliosis with the susceptibility genes for adolescent idiopathic scoliosis and disc degeneration

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[Introduction] Degenerative lumbar scoliosis (DLS) is a common spinal deformity that develops and progresses with age. DLS consists of two pathological conditions; degenerative changes superimposed on idiopathic scoliosis, and *de novo* type caused by the intervertebral disc degeneration (IVDD). Although it has been reported that many clinical parameters are different between them, distinguishing the two pathological conditions by clinical and radiographic features is usually difficult. Genome-wide association studies (GWASs) of adolescent idiopathic scoliosis (AIS) have identified four susceptibility genes: *LBX1*, *GPR126*, *BNC2* and *PAX1*. GWASs and several candidate gene approaches also identified IVDD susceptibility genes: *CHST3*, *PARK2*, *CILP*, *GDF5*, *COL11A1*, *THBS2*, *MMP9* and *SKT*. However, a few of them have convincing genetic and functional evidence. We investigated the association of DLS with AIS and IVDD susceptibility genes.□

[Methods] A total of 356 Japanese DLS cases and 3,341 controls were prospectively recruited. In the present study, DLS was defined as Cobb's angle greater than 15 degrees on standing whole spinal anteroposterior radiogram. Furthermore, the patients were diagnosed with DLS between the age of 40 and 75 and not diagnosed with AIS before the age of 20 by the expert spinal surgeons. Single nucleotide polymorphisms (SNPs) associated with AIS (*LBX1*: rs11190870, *GPR126*: rs6570507, *BNC2*: rs10738445, *PAX1*: rs6137473) and with IVDD (*CILP*: rs2073711, *COL11A1*: rs1676486, *CHST3*: rs1245582) were genotyped by the Invader assay. The association between the SNPs and DLS, and Hardy-Weinberg equilibrium of the genotypes were examined by the chi square test for trend. The statistical significance level was set to *P* values less than  $7.0 \times 10^{-3}$  ( $0.05/7$ ) based on the Bonferroni correction.

[Results] Only rs11190870 showed significant association ( $P = 1.14 \times 10^{-3}$ ; OR = 1.27) after correction of multiple testing. rs6137473 showed nominal association ( $P = 1.00 \times 10^{-2}$ ; OR = 1.20). All SNPs associated with IVDD did not show significant association after the correction of multiple testing ( $P < 7.0 \times 10^{-3}$ ). Only rs1676486 showed nominal association ( $P = 1.10 \times 10^{-2}$ ; OR = 1.21).

[Discussion] We found that rs11190870 in *LBX1* had the strong association in DLS. *LBX1* was first identified in AIS GWAS and has the strongest association with the AIS among the genes so far reported. Although we excluded the subjects who were diagnosed with AIS and restricted the age at diagnosis of DLS, the association of *LBX1* was clearly replicated in DLS. Therefore, *LBX1* would be the common susceptibility gene for AIS and DLS. However, all SNPs associated with IVDD were not replicated in DLS. The limitation of the present study was that controls did not have scoliosis and any symptoms, but they were not always diagnosed as whether they have IVDD or not by MRI. It can increase the false negative rate. To increase the sample size and diagnose with IVDD strictly are mandatory to decrease the false negative rate and find the IVDD susceptibility genes associated with DLS.

## A prospective randomized controlled trial of posterolateral lumbar fusion in combination with Platelet-Rich Plasma (PRP)

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### [Introduction]

Platelet-rich plasma (PRP) accelerates bone union in vivo in a rodent model of spinal fusion surgery. However, the advantages of PRP on bone union after spinal surgery remains unclear.

The aim of the present prospective randomized controlled study was to assess the efficacy of PRP when added to autograft bone (local bone) in PLF surgery, and to evaluate the quality of human-derived PRP.

### [Methods]

We randomized sixty-two patients who underwent one- or two-level instrumented PLF for lumbar degenerative spondylosis with instability divided equally into "PRP" and "control" groups. Platelet-rich plasma-treated patients underwent posterolateral fusion with instrumentation using an autograft bone chip (local bone), and PRP was prepared from patient blood samples immediately before surgery and centrifuged to extract platelets. Patients from the control group underwent PLF without PRP treatment. Twenty mL of PRP was obtained, to which thrombin and CaCl<sub>2</sub> were added to form a platelet gel for application to the surgical field. We assessed platelet counts and growth factor concentrations in PRP prepared immediately before surgery. The duration of bone union, the postoperative bone fusion rate, and the area of fusion mass were assessed using plain radiography every 3 months after surgery and by computed tomography at 12 or 24 months. The duration of bone fusion and the clinical scores for low back pain, leg pain, and leg numbness before and 3, 6, 12, and 24 months after surgery were evaluated using VAS.

### [Results]

Data from 50 patients with complete data were included. The bone union rate at the final follow-up was significantly higher in the PRP group (94%) than in the control group (74%) ( $p=.002$ ). The area of fusion mass was significantly higher in the PRP group (572 mm<sup>2</sup>) than in the control group (367 mm<sup>2</sup>) ( $p=.02$ ). The mean period necessary for union was 7.8 months in the PRP group and 9.8 months in the control group ( $p=.013$ ). In the PRP, the platelet count was 7.7 times higher and the growth factor concentrations were 50 times higher than those found in plasma ( $p<.05$ ). There was no significant difference in low back pain, leg pain, and leg numbness in either group at any time evaluated ( $p>.05$ ).

### [Conclusions]

In the present study, patients treated with PRP showed a higher fusion rate, greater fusion mass, and more rapid bone union after spinal fusion surgery than patients not treated with PRP.

## **Sagittal imbalance of the spine-pelvis-lower extremity axis is associated with back-related disability in inhabitant volunteers**

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### **Introduction**

Loss of lumbar lordosis owing to degenerative changes of the lumbar spine results in not only an increase in pelvic tilt (PT) and thoracic kyphosis, but also compensation of the lower extremity axis. The impact of sagittal imbalance on low back pain (LBP) and LBP-related disability in patients has been recently reported. However, there have been no reports regarding the evaluation of the spine-pelvis-lower extremity axis with lateral images of the spine-pelvis axis and the pelvis-lower extremity separately, and the relationships of LBP, LBP-related disability, and knee pain with sagittal alignment of the spine-pelvis-lower extremity axis in inhabitant volunteers. The purposes of this study were to introduce a novel parameter of the spine-pelvis-lower extremity axis using two separate lateral images and to evaluate if this parameter was related to LBP, LBP-related disability, and knee pain.

### **Methods**

This cross-sectional, inhabitant volunteer study included 344 subjects (124 men; mean age, 64.4±7.9 years and 220 women; mean age, 61.6±8.8 years) from Katsuragi town, Japan. The prevalences of LBP and knee pain were examined. LBP-related disability was evaluated using the Oswestry Disability Index (ODI) score. Standing spine-pelvis and standing pelvis-lower extremity radiographs were obtained to assess the sagittal vertical axis (SVA), PT, pelvic incidence, sacral slope, lumbar lordosis (LL), and TK. Additionally, the S1-knee distance (S1-KD), which is the distance from the anterior femoral condyle to the vertical axis at the upper posterior edge of the S1 body, was measured. Furthermore, the SVA/S1-KD ratio was calculated. The volunteers were divided into leg compensated (LC; SVA/S1-KD ratio <0.8) and decompensated (LD; SVA/S1-KD ratio ≥0.8) groups. The SVA was divided into balanced spine (BS; SVA ≤40 mm) and imbalanced spine (IS; SVA >40 mm) groups. All participants were classified into LC+BS, LC+IS, LD+BS, and LD+IS groups. The relationships among the four groups and LBP, ODI, and knee pain were examined.

### **Results**

The prevalences of LBP and knee pain were 31.7% and 24.4% in men, and 34.4% and 20.0% in women, respectively. The ODI score was 10.0±10.4% in men and 9.4±12.2% in women. The SVA, PT, PI, SS, LL, TK, and S1-KD were 1.9±3.4 cm, 23.0±11.1°, 54.5±12.5°, 31.1±8.6°, 35.8±12.9°, 36.6±11.4°, and 4.7±2.8 cm, respectively. There were 228, 29, 29, and 57 individuals in the LC+BS, LC+IS, LD+BS, and LD+IS groups, respectively. There were no significant correlations between groups and radiological parameters in the ANOVA analysis. However, in multinomial logistic analysis, ODI was significantly higher in the LC+IS group than the LD+BS group and the prevalence of knee pain was significantly higher in the LC+IS and LC+BS groups than the LD+IS group.

### **Conclusion**

LBP-related disability was associated with global spinal sagittal imbalance as well as reciprocal change through compensation of the lower extremity. Knee pain was influenced by compensation of the lower extremity, but not spinal sagittal imbalance. Our results suggest global balance is important in the case of LBP, LBP-related disability, or knee pain, and that the SVA/S1-KD ratio is useful for evaluating the spine-pelvis-lower extremity axis and elucidating the possible mechanism of "knee-spine syndrome."



## Variability in self-reported pain score on the same-day in different lumbar degenerative disorders

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### INTRODUCTION:

**Summary of background data.** Visual Analogue Scale or Numeric Rating Scale (NRS) is a common tool to record patient's self-reported pain score. Traditionally, a single NRS score is obtained in each clinic visit. Because pain intensity may vary with activity and rest, one score may not truly represent their pain intensity.

**Objective.** Cluster analysis of various pain patterns, as observed from patients' self-reported pain-score on a 4-item Numeric Rating Scale (NRS) data, and to analyze the relationship between the NRSs spread and different lumbar degenerative disorders.

**Study Design.** A single-center retrospective study on prospectively collected data

**METHODS:** The patients with lumbar disc herniation (DH), degenerative spondylolisthesis (DSP), degenerative scoliosis (DSS) and spinal stenosis (SS) recorded their self-reported HRQOL including NRS of pain prior to surgery, during April 2011 and August 2012. Four separate pain scores (average, at rest, with activity, and pain now) were obtained on NRS, for each clinic visit. The pain patterns were classified according to the variability of pain scores between rest and activity, using k-means cluster analysis.

**RESULTS:** 112 patients (M-53, F-59) were eligible to be enrolled during the study period; 3 cases were excluded for failure to be clustered into any pattern. The remaining 109 cases could be clustered into three distinct patterns. Pattern I (n=37, 33.9%), represented by very high pain score at any time of daily activities. Pattern II (n=42, 38.5%) represented by largest spread in pain scores, between max pain (usually at activity) and minimal pain (usually at rest). Pattern III (n=30, 27.5%) represented by moderate pain score at most of the time. [Multiple Logistics Regression Analysis](#) was used to analyze the relationship between the diagnostic categories and the pain patterns.

DH patients had significant relationship with pattern I (P=0.001); SS patients had strong tendency to show pattern II (P=0.027); DSS had a significant relationship with pattern III (P=0.001). DSP patients had no significant relationship with any pattern, but have more chance (57.1%) to show Pattern II.

**CONCLUSION:** A single NRS pain score may not adequately represent the pain pattern; multiple pain scores may better represent patient's pain perception with activity and rest, and may be helpful in clinical diagnosis.

## Integrating multidisciplinary knowledge of low back pain through collaborative modeling

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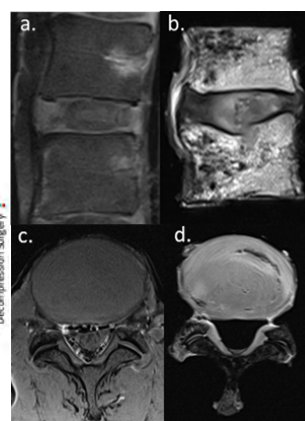
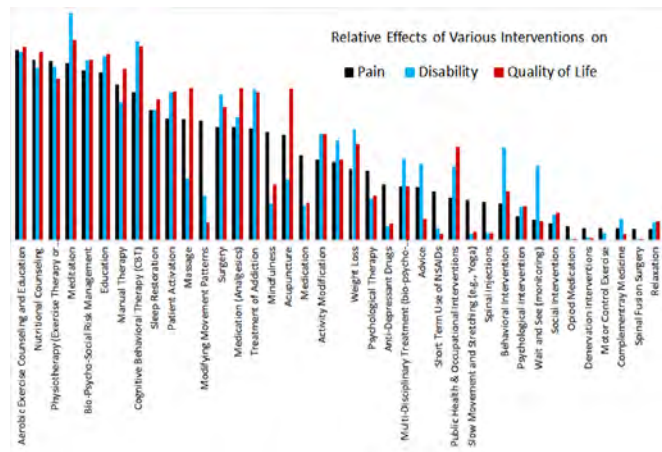
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**Introduction:** Low back pain (LBP) is a very complex problem with numerous bio-psycho-social factors interacting to impact pain, disability, and quality of life. To understand the dynamics of such a complex problem, it needs to be studied in its entirety (systems approach). Although this concept is accepted by the scientific and clinical communities, much research to date is conducted by specialized teams focusing on isolated factors related to LBP. Such a reductionist approach may be useful in some circumstances, but it also creates barriers for integrating knowledge between disciplines and ultimately precludes the understanding of the dynamics of the entire LBP problem. To leverage the knowledge shared among various stakeholders, an innovative process called collaborative modeling was developed within the field of systems science specifically for enhancing the understanding of complex, multi-factorial systems dynamics. This study assessed the feasibility of using this approach for integrating multidisciplinary knowledge of LBP.

**Methods:** Participants (n=29), who have contributed significant knowledge to the area of LBP (e.g., publications, contributions to societies, etc.), were selectively recruited for this study and represented diverse disciplines: Basic Science (n=7), Chiropractic (n=4), Spine Surgery (n=2), Physical Medicine & Rehabilitation (n=2), Physical/Exercise Therapy (n=12), and Psychology (n=2). Each participant underwent a structured one-on-one interview to construct a fuzzy-logic cognitive map (FCM) (Mental Modeler software, [www.mentalmodeler.org](http://www.mentalmodeler.org)) representing his/her understanding of how factors related to LBP interact and affect patient outcomes (pain, disability and quality of life). All individual FCMs were then converted to adjacency matrices and integrated into one meta-model (Gephi software, [www.gephi.org](http://www.gephi.org)). To demonstrate the integrated meta-model's potential, various intervention strategies listed in all FCMs were simulated and their relative effects on pain, disability, and quality of life were investigated.

**Results:** The meta-model, that integrated the understanding of LBP of all participants, consisted of 272 factors and 1429 connections representing interactions among these factors. Simulations of individual treatment interventions predicted that combined aerobic exercise, counseling, and education is likely to be the most effective intervention to reduce pain (Figure 1). Meditation, followed by cognitive behavioral therapy, had the greatest impact on reducing disability and improving quality of life (Figure 1).

**Discussion:** The integration of 29 FCMs, representing diverse participants' views of LBP dynamics, resulted in a model that was extremely complex, but still feasible to produce meaningful interpretations. The simulations provided outcomes that broadly agreed with data in the literature, which suggests that aerobic exercise, counseling, education, meditation, and cognitive behavioral therapy are effective LBP interventions. Although the selection of participants and the relatively small sample size may influence the results, the findings suggest that it is possible to integrate multidisciplinary knowledge of LBP into one meta-model. This approach could provide the framework for a larger, community-wide platform for further development and refinement of this meta-model. Such a meta-model could then be used to simulate other "what if" scenarios, to identify gaps in knowledge, and to inform new essential research directions to ultimately improve patient care and outcomes for LBP.



**Figure 1.** T1 MRI images of FSUs pre- and post-repetitive lifting **a.** Pre-test sagittal. **b.** Post-test sagittal of same FSU. **c.** Pre-test axial. **d.** Post-test axial of same FSU

## In vivo measurement of 3d disc strain and degenerative variation using MRI

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### INTRODUCTION

Disc mechanics are interrelated with disc degeneration and low back pain, which is often triggered by movement. The disc's deformation under load—that is, strain—is a key measure of its function. Measures of in vivo human disc strain are currently limited to local, manual measurements (e.g., height, width), but the disc has heterogeneous properties and pathology. In cadaver discs, we have developed methods to measure 3D strain fields throughout the disc with 3T MRI and no implanted markers [1]. This study's objective was to (a) extend these methods to measure 3D disc strain fields in living humans, (b) verify the results, and (c) test for relationships between in vivo disc strain and degeneration.

### METHODS

Disc strain was measured from 3T MRI of human volunteers' lumbar discs (L1 through S1) in three loading scenarios: morning to evening (AM-PM; n=7), supine to flexed (n=3), and supine to extended (n=4). Age was 23–61 years. Both male & female subjects were included. For AM-PM strain, supine images were acquired at ~ 9 AM (reference) and at ~ 4 PM (deformed). For flexion and extension, images in supine (reference) and flexed/extended postures (deformed; subject propped up on pillows) were obtained in the same session. Images for strain were T1-weighted FLASH (TR = 9.6, TE = 3.65, voxel size = 0.5 mm × 0.5 mm × 3 mm, sagittal slices). Strain for each reference/deformed image pair was calculated using image registration [1]. Axial strain fields were partitioned into anterior, center, posterior, and lateral (left + right) regions to analyze heterogeneity (Fig 1A). Furthermore, disc degeneration in each subject was assessed by both (a) Pfirrmann grade and (b) nucleus pulposus T2 relaxation time (T2; lesser = more degenerate), using standard MRI sequences.

### RESULTS

Axial strain fields from in vivo human MRI were successfully measured in 3D and, using manual measurements, verified (Fig 1B,C). AM-PM compressive strain was relatively homogeneous (Fig 1D,E) and, across all regions, trended to be greater in grade 1 discs (p = 0.07, Fig 1F) and was not significantly related to T2. Both extension and flexion strain significantly varied by region (Fig 1G,H,I,J). Flexion strain in the anterior and center was greater for Pfirrmann grade ≥ 3 (Fig 1K) and, in all regions, was less compressive with lesser T2 (Fig 1L). Extension strain was not significantly related to Pfirrmann grade, but all regions had lesser strain with lesser NP T2 (Fig 1M).

### DISCUSSION

This work is the first successful translation of noninvasive 3D disc strain techniques to in vivo imaging. The results support the hypothesis that degeneration is associated with abnormal disc strain in a region-dependent manner, but further study with more subjects is needed. Although this work focused on axial strain, work is ongoing to expand to other strain components. The ability to measure strain throughout the disc under in vivo loading has great potential to clarify the role of disc mechanics in low back pain and has possible future application as a diagnostic tool.

[1] Yoder+ J Biomech Eng 2014.

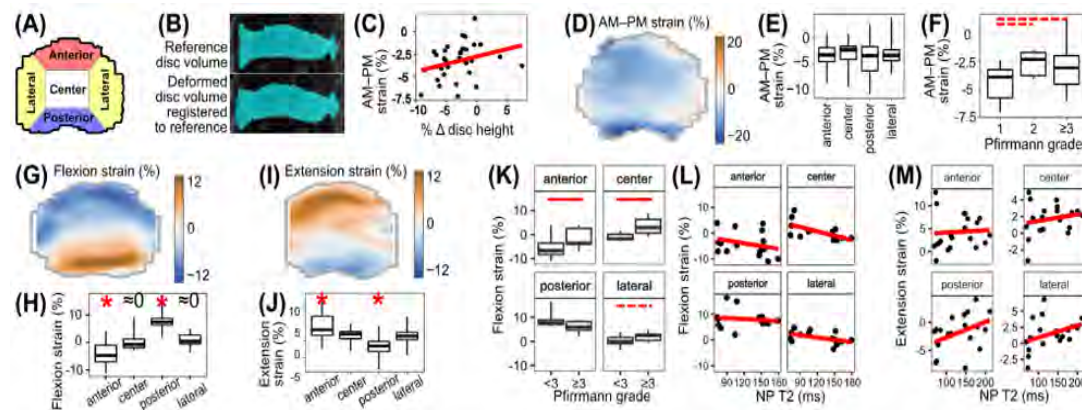


Figure 1: (A) Disc regions. (B) Representative reference and registered disc volumes, in mid-sagittal section, showing good registration accuracy. (C) AM-PM strain was correlated with manually measured change in disc height. (D-E) AM-PM strain regional variation. (F) AM-PM strain degenerative variation. (G-H) Flexion strain regional variation. (I-J) Extension strain regional variation. (K-L) Flexion strain degenerative variation. (M) Extension strain degenerative variation. Stats: — p ≤ 0.05 between indicated groups; - - - p ≤ 0.10 between groups; \* p ≤ 0.05 vs. all groups; ≈ 0 not significantly different from 0. All correlation lines are p ≤ 0.05.

## Evaluation of the effects of loading and disc degeneration on lumbar intervertebral discs and motion segments

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### Introduction

Intervertebral disc degeneration (IDD) is associated with morphological, chemical and metabolic changes. IDD has been implicated in the development of low back pain (LBP). IDD not only affects the magnitude, but also the distribution pattern of fluid within the disc. The effects of the IDD on the disc fluid content and distribution can be best quantified using MR imaging. Loading induces morphologic changes in the lumbar spine, and variations in fluid exchange, which may provide novel biomarkers of degenerative conditions, with possible clinical relevance. The aim of this study was to compare the effects of compression and traction on fluid distribution parameters within lumbar discs in relation to degeneration.

### Methods

Thirty-five volunteers (30±11yrs) with and without chronic LBP rested supine 15 minutes before a 5-minute unloaded T<sub>2</sub>-mapping MRI scan. Participants were then loaded 20 minutes with 50% body weight compression with imaging during the last 5 minutes, and then repeated this process under traction loading. Lumbar discs and the hyperintense area at the center ("nucleus") were segmented semi-automatically and the width, mean T<sub>2</sub>, geometric-weighted centroid, and T<sub>2</sub>-weighted centroid locations were automatically calculated using a custom Matlab program. Disc height and angle were also measured. A repeated measure ANCOVA and Cohen's d compared loading conditions.

### Results

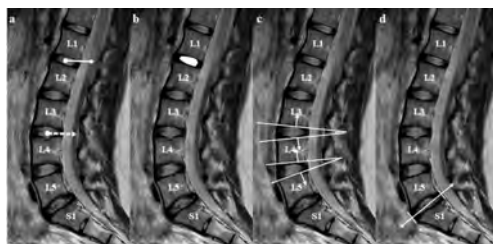
From compression to traction, we observed significant: decrease in L1-2 disc mean T<sub>2</sub> (MT<sub>2</sub>) (ES= -0.35); increase in L3-4 nucleus MT<sub>2</sub> (0.26); inferior and posterior shift in L4-5 (0.4, 0.14) and L5-S1 (0.25, 0.33) disc T<sub>2</sub>-weighted centroid (T<sub>2</sub>-WC); inferior and posterior shift in L5-S1 nucleus T<sub>2</sub>-WC (0.25, 0.31) and geometric-weighted centroid (GWC) (0.22, 0.31), posterior shift in L4-5 nucleus T<sub>2</sub>-WC (0.49) and GWC (0.48) (Figure 1). From unloaded to compression, we observed significant: increase in L5-S1 disc width (ES 0.22); increase in L1-2 nucleus mean T<sub>2</sub> (0.18); anterior shift in L1-2 disc T<sub>2</sub>-WC (0.39); posterior shift in L3-4 nucleus GWC (0.38); and L3-4 (mean 2.1°) and L4-5 (1.8°) motion segment angles (MSA) towards extension (Figure 2).

### Discussion

Examining the response to loading of lumbar discs using MRI helped identify possible biomarkers, which may help define subgroups with different degeneration phenotypes. The location of the disc and nucleus T<sub>2</sub>-WC and GWC, the MSA and disc height were the most promising biomarkers for evaluating the effects of loading. As hypothesised, the pairwise comparisons between compression and traction demonstrated more significant findings than between unloaded and compression, suggesting that this loading contrast may be most effective to detect variations in response to loading. Results also supported our hypothesis that the fluid distribution measurements are more sensitive in capturing the effects of degeneration and loading. The majority of the statistically significant changes and largest effect sizes were observed for T<sub>2</sub> weighted centroid parameters for both the disc and nucleus.



**Figure 1** Significant differences (compression-to-traction) a:) disc T<sub>2</sub>WC b:) nucleus T<sub>2</sub>-WC and GWC and c:) disc height d:) disc and nucleus MT<sub>2</sub>



**Figure 2** Significant differences (unloaded-to-compression) a:) disc T<sub>2</sub>WC and nucleus GWC b:) nucleus MT<sub>2</sub> and c:) MSA d:) disc width

## The biomechanics of the inter-lamellar matrix and the lamella during lumbar disc herniation: which is the weakest link?

Javad Tavakoli, Dhara Amin, Brian J.C. Freeman, John J. Costi

### Introduction:

Microstructural observations have revealed new insights into annulus fibrosus (AF) tissue disruption during herniation [1, 2], as well as the delamination strength of isolated AF samples of the interlamellar matrix (ILM) [3]. While these studies have improved our understanding of where herniation may initiate, the possible pathways of its progression, and ILM delamination strength, no studies have measured the mechanical failure properties of the ILM, nor of the adjacent lamellae during progression to herniation. Therefore, the aim of this study was to develop a new multiscale, biomechanical and microstructural understanding of the effects of progressive herniation on the ILM and lamellae in control, overloaded and herniated discs.

### Methods:

Fourteen ovine spines were dissected into 28 functional spinal units (FSUs) and assigned to three groups: controls (N =14) matched with experimental groups: overload without herniation (N = 7) and load to failure with herniation (N = 7). Experimental groups were subjected to macroscopic compression while held in flexion (13°). Micro-tensile testing of the ILM and the lamella from anterior and posterolateral regions was performed in radial and circumferential directions (224 biomechanical tests) to measure failure stress, modulus, and toughness. Microstructural imaging was performed on adjacent tissue using light microscopy. A univariate ANOVA and unpaired t-tests were conducted for each mechanical and structural parameter.

### Results.

The mean (95% CI) load to failure for herniation and maximum load for overload discs were 10.5(1.5) and 6.4(1.2) kN, respectively. The ILM failure stress was significantly lower for both experimental groups compared to control in each of radial and circumferential loading directions in the posterolateral region ( $p < 0.032$ , Figure 1). Within each experimental group in both loading directions, the ILM failure stress was significantly lower by 36% (overload), and 59% (herniation), compared to the lamella ( $p < 0.029$ ). In overloaded compared to control discs, microstructural imaging revealed significant tissue stretching and change in orientation ( $p < 0.003$ ), resulting in a loss of distinction between respective lamellae and ILM boundaries.

### Discussion.

The ILM failure stress, in both radial and circumferential loading, was significantly reduced in overload and herniation groups, compared to control. However, the ILM failure stress after overloading was not significantly different to after herniation (Figure 1), suggesting that the ILM was susceptible to mechanical damage at loads below those required to create herniation. In contrast, the lamella exhibited no reduction in failure stress between all three groups. In addition, the ILM in the posterolateral region of the disc was significantly weaker than the anterior region, potentially due to a higher number of incomplete lamellae [4]. Our findings provide compelling evidence that the ILM was the weakest link in the outer AF. For the first time, we have demonstrated that the ILM is biomechanically weaker, and provides a pathway of least resistance than the lamella during the process of lumbar disc herniation.

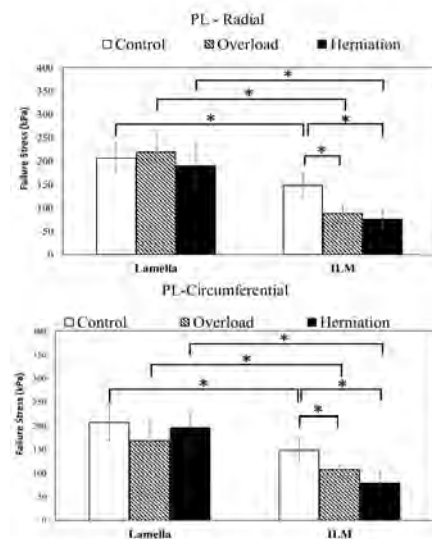


Figure 1. Mean (95% CI) failure stress for the lamella and ILM in the posterolateral (PL) region during loading in the radial and circumferential directions for all groups (control, overload, and herniation). \* denotes significant pairwise differences between and within groups and tissue types (lamella and ILM) ( $p < 0.05$ ).

- [1] Pezowicz CA, Schechtman H, Robertson PA, et al. Mechanisms of Anular Failure Resulting From Excessive Intradiscal Pressure: A Microstructural-Micromechanical Investigation. *Spine* 2006; 31:2891-903. [2] Veres SP, Robertson PA, Broom ND. ISSLS Prize Winner: Microstructure and Mechanical Disruption of the Lumbar Disc Annulus Part II: How the Annulus Fails Under Hydrostatic Pressure. *Spine* 2008; 33:2711-20. [3] Gregory DE, Bae WC, Sah RL, et al. Anular delamination strength of human lumbar intervertebral disc. *Eur Spine J* 2012; 21:1716-23. [4] Marchand F, Ahmed AM. Investigation of the laminate structure of lumbar disc annulus fibrosus. *Spine* 1990; 15:402-10.

## Axial loading during MRI provides new insights into IVD biomechanics in low back pain patients

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### Introduction

To improve the knowledge regarding the relation between intervertebral disc (IVD) degeneration and painful spinal conditions, diagnostic methods with capacity to obtain both detailed IVD matrix composition and functional characteristics are needed. Recently, the combination of T2-mapping and axial loading during MRI (aIMRI) was reported as a promising method to reveal functional IVD characteristics *in vivo* during spinal loading. The aim of the current study was to investigate if low back pain (LBP) patients and controls display differences in functional IVD characteristics by comparing quantitative IVD T2-values before and during spinal loading.

### Methods

120 IVDs in 27 LBP patients (mean age 37 years) were examined with aIMRI (using Dynawell® loading device), but also conventionally, without loading of the spine. For comparison, 60 IVDs in 12 healthy individuals (mean age 36 years) were included. Quantitative T2-value (T2-mapping) of the entire disc was obtained. For each disc, the T2-value, acquired after approximately 20 minutes of loading, was determined in five volumetric regions of interests (ROI); anterior annulus fibrosus (AF) (ROI1), the interface anterior AF- nucleus pulposus (NP) (ROI2), NP (ROI3), the interface NP-posterior AF (ROI4) and the posterior AF (ROI5). The ROIs were equally sized in anterior-posterior direction. T2-values were compared between the unloaded and aIMRI examinations, and between patients and controls. Statistical significance was defined at  $p < 0.05$  and when relevant the analysis were adjusted for Pfirrmann grade.

### Results

In LBP patients, the average T2-value of the entire IVD was 63ms for unloaded MRI and 65ms for aIMRI ( $p=0.03$ ) with corresponding values in controls 70ms and 70ms, respectively ( $p=0.5$ ). Significant load-induced T2- differences (unloaded MRI-aIMRI) were seen in all ROIs in both patients ( $p < 0.001$ - $p < 0.005$ ) and controls ( $p < 0.0001$ - $p < 0.03$ ) (Figure 1). In patients, aIMRI induced higher T2-values in ROI1-3 of 21%, 18% and 5% and lower T2-values in ROI4 (3%) and ROI5 (24%). Significant load-induced T2-difference between groups was detected in ROI4, with a mean decrease of 10% in controls ( $p < 0.001$  respectively  $p=0.03$  when adjusted for Pfirrmann). Significant difference between groups in absolute T2-values at unloaded MRI and aIMRI was detected only at ROI5 and with aIMRI (38ms in patients versus 33ms in controls;  $p < 0.001$ ). Significance remained also with adjustment for Pfirrmann ( $p=0.04$ ).

### Discussion

aIMRI induced large changes in T2-value within all IVD regions, indicating instantaneous IVD matrix reorganization such as redistribution of "water" in the disc. The significant difference between patients and controls in loading behavior regarding the interface NP-posterior AF and posterior AF might indicate structural weakness/biomechanical impairment in these regions. Hence, aIMRI combined with T2-mapping offer a non-invasive, diagnostic tool for biomechanical IVD-characterization that may deepen the knowledge regarding how LBP is related to altered IVD matrix composition.

Figure 1.

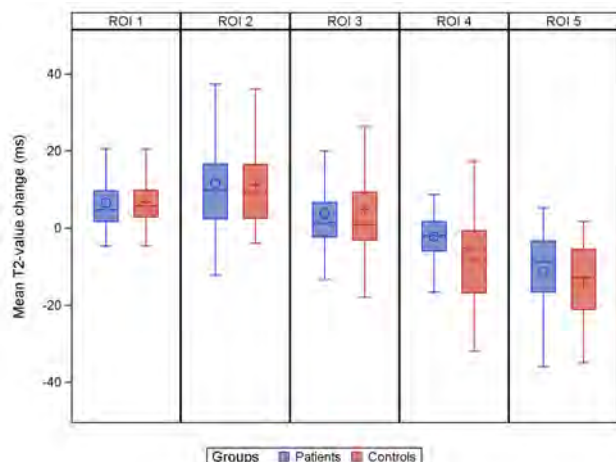


Figure 1. Induced T2-value changes (uMRI-aIMRI) due to re-organization of "water" in the IVD

## Altered multifidus muscle quality following long-duration spaceflight affects lumbar lordosis and compression on the intervertebral disc

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**Introduction:** Prolonged exposure to microgravity increases risk of disc injury and chronic low back pain. Previous work shows that this may be due to *multifidus* atrophy that associates with decreases in both supine lumbar lordosis (i.e., flatter) and lumbar intersegmental range of motion (i.e., stiffer). However, these multifidus findings were based on supine measurements, when the spine is not subject to gravitational loads. This is a significant limitation given that the *multifidus* has an important biomechanical role during upright load bearing, during which it actively stabilizes intersegmental stability and lordotic alignment. The goal of this study was use standing MRI measurements of lumbosacral alignment collected before and after spaceflight to test the hypothesis that longitudinal changes in *multifidus* quality will result in concordant changes in lumbar lordosis (LL) during loaded conditions.

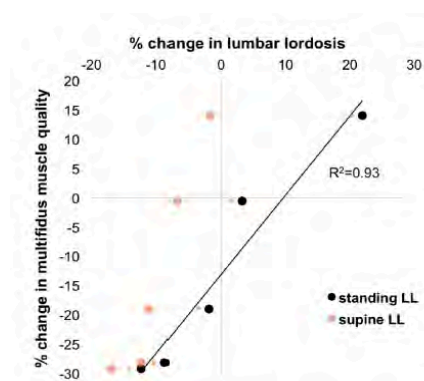
**Methods:** Six NASA astronauts were assessed at two time points: before launch (pre-flight) and one day following six months of weightlessness (post-flight). Standing MRI scans were collected using a Fonar Scanner (0.6T), from which we measured LL and sacral slope (SS) in standing posture. Measures were averaged over four mid-sagittal sections. Previously published data from the same subjects (3T MRI) for multifidus quality (Functional Cross-Sectional Area, FCSA, at L3-L4) and supine LL were also incorporated into our analyses.

**Results:** Following spaceflight, the average standing LL did not significantly change among crew (pre-flight:47.1°± 5.1°; post-flight:47.4°±9.1°; p>0.05). However, on an individual crewmember basis, pre- to post-flight percent change in standing LL correlated strongly with percent change in *multifidus* FCSA ( $R^2=0.93$ , p<0.01; Figure 1). Interestingly, one crew member who actually increased multifidus muscle quality in space also increased their standing LL. These standing data are in striking contrast to previously-reported supine data, where the average supine LL decreased in all crew (pre-flight:37.8°±9.0°; post-flight:34.3°±9.3°; p<0.01). Measures for standing LL and SS correlated among crew before spaceflight ( $R^2=0.89$ , p=0.015), but this correlation was no longer significant following spaceflight ( $R^2=0.60$ ; p>0.05).

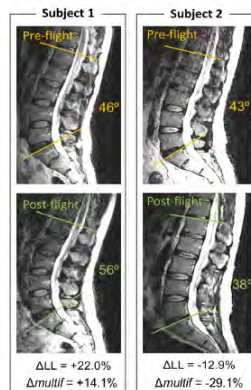
**Discussion:** Our results from longitudinal, standing MRI demonstrate that decreases in *multifidus* muscle quality induced by spaceflight associate with decreases in LL when reintroduced to gravitational load. This finding shows that microgravity disrupts the muscular stability of the lumbar spine, leading to a compensatory flexed posture (flatter LL) when stabilizing the torso under gravitational load. Lumbar spine flexion increases intervertebral disc compression – suggesting a possible mechanism for the reported increases in post-flight disc herniation.

This work underscores the importance of paraspinal muscular health for lumbar spine alignment and stability, as shown by contrasting the multifidus quality/LL relationship when the spine is loaded and unloaded. This conclusion regarding the biomechanical role of the multifidus is reinforced by the fact that two subjects actually maintained or increased *multifidus* muscle quality (likely due to in-flight exercises), with corresponding increases in standing LL (Figure 2).

Our results demonstrate the need for integrating targeted paraspinal muscle exercises as countermeasures to reduce risk of post-spaceflight disc injury. Future crew studies will incorporate additional lumbopelvic alignment measurements to aid our understanding of how microgravity disrupts overall sagittal balance.



**Figure 1:** Scatterplot demonstrating the correlative relationship ( $R^2=0.93$ , p<0.01, Black dots) between percent changes in *multifidus* muscle quality (mm<sup>2</sup> composition of lean tissue within total muscle CSA) and percent change in standing LL following six-months spaceflight. In addition, the correlative relationship between the same *multifidus* muscle quality data and percent change in supine LL (orange dots) is shown for comparison. Supine LL decreased (flattened) for all crew.



**Figure 2:** Mid-sagittal standing MRI images from two crew. Subject 1 demonstrates corresponding increases in LL and multifidus muscle quality following spaceflight. Subject 2 demonstrates corresponding decreases in LL and multifidus muscle quality following spaceflight.

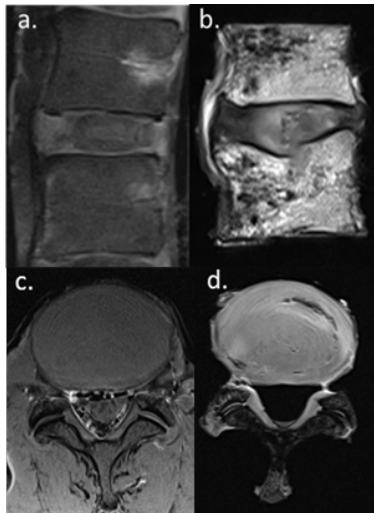
## Analysis of internal disc strains during simulation of repetitive lifting motions

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**Introduction:** Repetitive manual handling was the cause of 31% of all work related musculoskeletal disorders in 2015, with the back being the site of injury 38% of the time [1]. Despite its high resilience, studies have shown that intervertebral discs can be damaged during repetitive loading at physiological motions, causing cumulative damage and disc herniation [2, 3]. To understand the mechanism of disc injury resulting from repetitive loading, it is important to measure disc deformations/strains with MRI imaging to investigate disc damage. Therefore, the aim of this study was to examine associations between the magnitude of 3D internal strains, tissue damage and macroscopic evidence of disc herniation after simulated repetitive lifting on normal human lumbar discs.

**Methods:** Sixteen cadaver lumbar functional spinal units (FSUs) were subjected to pre-test MRI. Eight FSUs (control) underwent 20,000 cycles or until failure (5mm displacement) of loading under compression (1.7 MPa – to simulate lifting a 20 kg weight) + flexion (13°) + right axial rotation (2°) using a novel 6DOF Hexapod Robot [4]. The remaining eight FSUs (experimental) had a grid of tantalum wires inserted, and stereo-radiographs were taken to track internal 3D displacements at increasing cyclic intervals [5]. Maximum shear strains (MSS) were calculated from internal 3D displacements using radio-stereometric analysis. Post-test MRI was conducted to determine the extent of tissue damage and associated with regions of highest internal disc strains. A repeated measures ANOVA was performed on MSS with a within-subjects factor of cycle number and a between subjects-factor of disc region ( $p < 0.05$ ).



**Figure 1.** T1 MRI images of FSUs pre- and post-repetitive lifting **a.** Pre-test sagittal. **b.** Post-test sagittal of same FSU. **c.** Pre-test axial. **d.** Post-test axial of same FSU

**Results:** Pfirrmann grading revealed grades I (N=2), II (N=12), and III (N=2). No significant difference in MSS between control and experimental groups was found for number of cycles to failure ( $p = 0.279$ ). Pre and post-test MRI analysis revealed that all specimens were injured after repetitive lifting: annular protrusion, endplate fracture, posterior nucleus migration, annular fissure, lateral and anterior annular circumferential tears. However, no disc herniation was seen. MSS in all cycles was significantly higher than cycle 1 except for cycles 1000 and 5000 ( $p > 0.055$ ). Significantly higher MSS compared to the nucleus region was found in three regions: left posterolateral (mean (95%CI): 45.9(3.89) % higher than nucleus,  $p < 0.001$ ), anterior (42.5(3.48) %,  $p < 0.001$ ) and posterior (37.4(3.47) %,  $p < 0.001$ ). Macroscopic assessment of the discs revealed circumferential tears in the anterior and left posterolateral regions, corresponding with high shear strains (Figure 1).

**Discussion:** Repetitive flexion + right axial rotation under 1.7 MPa of physiological compression led to largest shear strains in the anterior, posterior and left posterolateral regions that

corresponded to annular tears or annular protrusion. There was no evidence of disc herniation in normal discs, agreeing with current clinical knowledge. In addition, the clinical evidence that discs herniate mostly in the posterolateral region, is consistent with the findings of this study, where annular protrusion was seen in the left posterolateral region. These results may be indi

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3. 3. Adams and Hutton. 1985, Spine.
4. 4. Ding, B, et al. 2014 J. Dyn. Syst-Trans ASME.
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## Can nerves and blood vessels grow through the cartilage endplate in degenerated discs?

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**INTRODUCTION** Discogenic back pain is strongly associated with nerve and blood vessel ingrowth into degenerated discs. However, it is not known if ingrowth occurs primarily through the peripheral annulus fibrosus, or through the vertebral endplates. If ingrowth is possible through the endplates, does it require prior disruption to the dense layer of hyaline cartilage which lies between the bony endplate and the disc? The current study aimed to answer these questions by investigating the location and density of nerves and blood vessels in surgically-removed degenerated human discs.

**Methods** Twenty-five samples of non-herniated lumbar discs (including cartilage endplate) were obtained from 24 individuals, aged 24-71 yrs, undergoing surgery for chronic discogenic back pain. Pfirrmann grade of disc degeneration was assessed pre-operatively from MRI scans. Thin (7µm) tissue sections were stained with H&E in order to identify tissue types. Detailed histological "scores" of degeneration (0-21) were used to grade overall disc degeneration as absent (I), mild (II), moderate (III) or severe (IV). Toluidine blue staining was used to grade glycosaminoglycan (GAG) loss between I (no loss) and IV (severe). Antibodies against CD31 were used to identify blood vessels, and PGP9.5 and substance P were used to identify general and nociceptive nerves, respectively. Blood vessels and nerves were counted in multiple thin sections and their density was determined. Their 3-D location within the disc and cartilage endplate was confirmed in 30µm-thick sections, using immunofluorescence staining with confocal laser scanning microscopy. Data were analysed using one-way ANOVA and Spearman's rank correlation ( $r_s$ ).

**Results** Disc levels ranged from L3-4 to L5-S1, and Pfirrmann grades ranged from III to V. Histology indicated that discs were moderately (12/25) or severely (13/25) degenerated and showed mild (1/25), moderate (11/25) or severe (13/25) GAG loss. Increasing Pfirrmann grade was associated with increased histological degeneration score ( $p < 0.001$ ) and grade ( $r_s = 0.78$ ,  $p < 0.001$ ) and with increased GAG loss ( $r_s = 0.683$ ,  $p < 0.001$ ). GAG loss and histological degeneration were themselves highly correlated ( $r_s = 0.83$ ,  $p < 0.001$ ). Staining for CD31, PGP9.5 and substance P was positive in 76%, 68% and 48% of discs, respectively, and nerves were identified only in discs that were positive for CD31. Density of blood vessels (CD31) and nerves (PGP9.5, substance P) increased significantly with histological and Pfirrmann grades of degeneration ( $p < 0.003$  in all cases) and with GAG loss ( $p < 0.01$ ). Blood vessels and nerves were mostly in outer annulus tissue, usually adjacent to tears and fissures in regions of high GAG loss. None were observed in nucleus pulposus tissue. Only one cartilaginous endplate showed positive staining for PGP9.5 and CD31, and this was associated with a structural defect visible on confocal microscopy.

**Discussion** Results suggest that nerve and blood vessel ingrowth increases with disc degeneration. Their typical location within disrupted and GAG-depleted annulus tissue suggests that this is their normal route into a degenerated disc, and ingrowth may be facilitated locally by low fluid pressure associated with loss of GAG and water. Ingrowth through the hyaline cartilage endplate appears to be rare, and dependent on the presence of a physical defect.

## Characterisation of bone marrow pathologies across the spectrum of modic changes in the human lumbar spine

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3. Calvary Health Care, North Adelaide, South Australia, Australia

### INTRODUCTION

Magnetic resonance imaging (MRI) identified vertebral Modic changes (MC) are associated with intervertebral disc degeneration and low back pain. However, the aetiology and pathobiology of MC in the human lumbar spine remain elusive. Reports on the bone marrow pathology of MC have been limited to MC type 1 and 2, for small sample sizes (n=3 per MC)<sup>1</sup> or bone marrow aspirate analyses<sup>2</sup>. Therefore, the purpose of this study was to perform a comprehensive characterisation of the bone marrow histopathology associated with the spectrum of MC, i.e. MC type 1, 2 and 3.

### METHODS

Forty-one patients (17 women, 24 men; mean age 55±13 years) underwent lumbar spine surgery with pedicle screw instrumentation and showed MC on pre-operative lumbar MRI. Cases were subdivided into MC type 1 (MC1; n=11), MC type 2 (MC2; n=23) and MC type 3 (MC3; n=7). For all patients, a transpedicular vertebral subchondral bone biopsy (10-20mmx3mm) was harvested from the MC region, and then processed for undecalcified histology. Three trained assessors scored the presence and percentage tissue extent of bone marrow pathologies: inflammation (+/- neutrophil aggregates), fibrosis, oedema, and adipocyte necrosis. Inter-observer reproducibility for pathology scoring was high (intraclass correlation coefficient [ICC] 0.82). Bacterial presence/absence was assessed by histological Gram staining. The percentage adiposity of the bone marrow was quantitated by three assessors using Adiposoft-Image J software<sup>3</sup>, with very high inter-observer reproducibility (ICC 0.96).

### RESULTS

Inflammation was present at a moderate extent (20-50%) for all three MC types. MC1 bone marrow was fibrotic (20-50%) compared to MC2 (<5%) and MC3 (<5%), p<0.005. All fibrotic tissue areas were well-vascularised by capillaries. Oedema and adipocyte necrosis were minimal (<5%) for all MC types. There was no difference between MC types for the percentage adiposity of the bone marrow: MC1 29.3% [15.8-40.1%], median [min-max]; MC2 33.3% [16.1-100%]; MC3 36.2% [10.1-73.9%]. There was no evidence of infection present in MC1, MC2, or MC3 bone marrow (no neutrophil aggregates or positive/negative Gram stained bacteria).

### DISCUSSION

This is the first study to characterise bone marrow histopathology across the Modic spectrum. The predominant bone marrow pathology common to MC1, MC2, and MC3 is inflammation. Adipocyte necrosis and oedema are minimal for all MC types, with no evidence of bone marrow infection for any MC type. Increased bone marrow fibrosis in MC1 distinguishes this MC type from MC2 and MC3. These observations are consistent with MC1 representing a bone marrow healing response to disc/endplate injury, whereas MC2 and MC3 are consistent with the persistence of an inflammatory stimulus as a disease model<sup>4</sup>.

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2. Dudli et al. Eur Spine J (2017), 26:1362-1373
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## Cartilage endplate damage strongly associates with chronic low back pain, independent of modic changes

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### INTRODUCTION

A key obstacle in the management of chronic low back pain (CLBP) is identifying which tissues and levels to treat. One potential source of pain is structural damage to the cartilage endplate (CEP), since CEP damage is heavily innervated. Moreover, CEP damage often co-localizes with bone marrow lesions, which appear as Modic changes (MC) on MRI. While MC associate with CLBP, histologic studies indicate that MC assessment may miss the majority of bone marrow lesions, and thus, absence of MC is not very good for ruling out bone marrow lesions and pain. Here we evaluated the relationship between CEP damage and CLBP, and we determined whether CEP damage associates with CLBP after accounting for MC.

### METHODS

This study was IRB-approved and informed consent was obtained for all subjects. Twenty-eight CLBP patients (VAS  $\geq 4$  or ODI  $\geq 30$ ) without radiculopathy and fourteen asymptomatic controls were recruited locally. Subjects were imaged on a 3T GE scanner to evaluate lumbar MC and CEP damage. The MRI protocol consisted of sagittal T1- and fat-saturated T2-weighted fast spin-echo sequences and a high-resolution 3D ultrashort echo time (UTE) sequence. The UTE sequence included TE=0.075 ms, TR=10 ms, voxel size of 0.22x0.22x0.80 mm<sup>3</sup>, and fat suppression. CEP damage was defined as a discontinuity in the bright UTE signal of the CEP.

### RESULTS

Average age was similar for the patients (46.2 $\pm$ 11.2 years; 13 female/15 male) and controls (44.3 $\pm$ 11.5 years; 6 female/8 male). CEP damage strongly associated with CLBP (OR=10.8, CI=2.4-49.5,  $p=0.002$ ), more so than any MC (OR=8.0, CI=1.5-42.7,  $p=0.01$ ) or MC type 1 (OR=2.8, CI=0.5-15.5,  $p=0.23$ ). There was a significant dose response, as the odds of having CLBP increased by a factor of 1.8 (CI=1.2-2.9) for each additional CEP with damage. Overall, CEP damage (101/420 levels) and MC (40/420 levels) predominated at the lower lumbar levels (L4-S1), and CEP damage co-localized to MC in 63% of cases (**Figure**). Importantly, CEP damage remained significantly associated with CLBP (OR=9.1, CI=1.8-46.6,  $p=0.008$ ) after adjusting for MC.

### DISCUSSION

Conventional MRI is unable to show the CEP, and consequently, the clinical significance of CEP damage is unclear. In this case-control study, we used a novel UTE sequence to assess CEP damage. *Our data indicate that CEP damage strongly associates with pain, even after accounting for MC.* MC were also associated with pain, but the association was weaker than for CEP damage. MC assessment misses many bone marrow lesions, perhaps owing to poor image contrast or limited spatial resolution. Our high-resolution UTE sequence provides enhanced contrast for delineating the CEP (including any damage) from the subchondral bone. Taken together, these new data suggest that assessing CEP damage using UTE MRI may improve identification of symptomatic endplate-related pathologies compared to conventional assessments of MC alone.



3T MR images acquired using conventional T1- and fat-saturated T2-weighted sequences and a 3D ultrashort echo time (UTE) sequence. **Top:** CLBP patient with CEP damage and MC type I at L5/S1. **Bottom:** CLBP patient presenting with CEP damage but no clear evidence of MC.

## Impacts of vertebra and endplate fractures on the adjacent disc and vertebral trabeculae: a retrospective MR follow-up study

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**Introduction** Cadaveric studies highlighted that endplate lesions were important pathologies for studying disc degeneration and back pain. Endplate fractures are one type of endplate lesions which occur in vertebral fractures. To date, impacts of endplate fractures on the adjacent disc and trabeculae remain controversial. Using magnetic resonance (MR) imaging, this study investigated the role of endplate fractures in adjacent disc degeneration, progression of segmental kyphosis, and occurrence of Modic changes (MCs) and high-intensity zone (HIZ).

**Methods** In a defined period, patients with AO classification type A fresh vertebral fractures at T11 to L5 and had follow-up MR images were recruited at a territory hospital. On baseline spine images, endplate fractures were evaluated as present or absent. Using image program *Mimics*, disc degeneration measurements, including disc height, disc bulging and cerebrospinal fluid adjusted disc signal intensity, were quantitatively acquired on the mid-sagittal T2 weighted MR images, for the disc immediately adjacent to the fractured vertebra and a proximal control disc. In addition, the area of endplate deformity and kyphosis of the fractured spinal segment were measured on baseline and follow-up MR images. Using t-tests, changes of disc, vertebra, and spinal segment in follow-up were compared between the adjacent and neighbor discs, and between vertebral fractures with endplate fractures and those without. New occurrence of MCs and HIZ were evaluated in the fractured spinal segment.

**Results** Seventy-one subjects (mean age 52 years, range 22 to 65 years) met inclusion criteria and were studied. In total, there were 94 fresh vertebral fractures, with 72 endplate fractures and the other 28 without endplate fractures. The mean follow-up time was 17.6 months. Both the adjacent and proximal discs decreased in height ( $-0.79 \pm 1.08$  and  $-0.48 \pm 0.93$  mm,  $P < 0.01$  for both) and signal intensity ( $-12.22 \pm 14.57 \times 10^{-2}$  and  $-5.49 \pm 8.89 \times 10^{-2}$ ,  $P < 0.01$  for both) in follow-up, and the adjacent disc had greater decrease in height and signal than the proximal disc ( $P < 0.01$ ). Moreover, discs adjacent to endplate fractures had greater decrease of signal intensity than those adjacent to vertebral fractures without endplate fractures ( $-15.18 \pm 15.42 \times 10^{-2}$  vs.  $-4.63 \pm 8.35 \times 10^{-2}$ ,  $P < 0.01$ ). While segmental Cobb angle increased in vertebral fractures with endplate fractures ( $1.80 \pm 4.84$  degrees,  $P < 0.05$ ), that in vertebral fractures without endplate fractures remained unchanged. Endplate fractures were not associated with occurrence of MCs and HIZ.

**Discussion** Endplate fractures can lead to adjacent disc degeneration and progression of segmental kyphosis. Endplate fractures were not associated with occurrence of MCs and HIZ.

## New evidence for structural integration across the cartilage-vertebral endplate junction

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### Introduction

A recent biomechanical study of the interface strength at the endplates of human thoracic spines showed a greater incidence of failure at the cement line, the junction between the cartilaginous endplate (CEP) and vertebral endplate (VEP) [1]. It has been suggested that this junction has poor structural (collagenous) connectivity leading to an increased vulnerability to avulsion of the CEP from the VEP [1]. However, in herniated material, both cartilaginous and osseous material from the endplate are often present suggesting that failure within at the endplate can involve both the CEP and VEP [2]. The mechanical significance of the organic and mineral phases in the endplate thus requires further exploration, especially concerning how these influence endplate strength and its modes of failure.

### Aims

Employing decalcification in combination with a novel partial rupture technique, this study investigated how integration is achieved across the cement line of mature ovine lumbar discs at the micro and ultrastructural levels.

### Methods

Forty-nine vertebra-annulus-vertebra samples, approximately 5mm x 6mm in cross-section, were prepared from the anterior and posterior regions of 25 mature ovine lumbar motion segments such that the lamellar fibres in one of the oblique fibre directions extended from vertebra to vertebra. The samples were then subjected to site-specific decalcification confined to the region of the endplate and then stretched axially to an extent sufficient to achieve partial rupture of the endplate region. The failure regions were analysed using both differential interference contrast microscopy and scanning electron microscopy (SEM).

### Results

In 19 of the 49 samples tested failure occurred within the vertebra proper, distant from the endplate. These were therefore excluded for the analysis. In the remaining 30 samples, macroscopic inspection indicated that partial tearing had occurred at the cement line. However, microstructural analysis revealed that these tears were not necessarily confined to the cement line. Instead, some tears also continued into the underlying vertebral endplate with bone osteon material still attached to the annular bundles. Ultrastructural (SEM) analysis of the ruptured regions of the cement line revealed clear evidence of blending/interweaving between the fibrils of the annular bundles, the calcified cartilage and the bone with no one pattern of association appearing dominant.

### Discussion

This study demonstrates a close association of annular, CEP and VEP fibrils in a highly variable pattern of interweaving *combined* with clear evidence that the cement line is not a preferred plane of weakness, even following decalcification. The data suggest that fibril-based structural cohesion exists across the cement line with stiffening via a mechanism analogous to how the strength in a steel-reinforced concrete structure is achieved. In such a system the various elements comprising the steelwork are brought into a close intermingling association. The concrete matrix then provides that all-important integrating medium and thus parallels that of endplate junction mineralisation. The clinical observation of osseous material extruded with herniated tissue is consistent with this new study showing that there is structural connectivity across the cement line, thus accounting for this osseous material's attachment to the soft tissue extrusion.

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## Spinopelvic alignment and the development of vertebral endplate abnormalities: the "missing link"

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**Introduction:** Vertebral endplates are considered critical for maintenance of intervertebral disc function. The appearance of defects or abnormalities in its structure and adjacent bone marrow changes are highly associated with the pathogenesis of disc degeneration and low back pain. However, factors determining these particular phenotypes are still not clearly understood. Besides age and weight related factors, mechanics may play key role in the development of these phenotypes. Spinopelvic alignment can be one of the elements influencing stress/load distribution as well as kinematics of the spine leading to the production of endplate defects. However, it remains unknown whether spinopelvic parameters are related to endplate abnormalities. As such, the following study assessed the association of spinopelvic parameters with vertebral endplate defects.

**Methods:** 90 Southern Chinese subjects from the Hong Kong Neck/Low Back Pain Cohort were recruited (64.4% females; mean age: 54 years) in this study. Only those subjects with complete clinical profile, no history of trauma and visible structural spine deformity such as scoliosis, spondylolisthesis were included in the study. Standing lateral full-length radiographs and T2W 3T MRI of the lumbar spine were obtained for all subject. C7-S1 sagittal vertical axis (SVA), global tilt angle (GTA), T1pelvic angle (T1PA), T1 sagittal tilt (T1ST), lumbar lordosis (LL), pelvic incidence (PI), sacral slope (SS), and pelvic tilt (PT) were assessed on plain radiographs. Lumbar lordosis index (LLI=LL/PI) was also obtained. Disc degeneration was assessed by the Pfirrmann method and summated. Structural endplate defects were noted on T2W MRI. Subjects were further divided into 4 groups: no endplate defects, only cranial, only caudal or involvement of both endplates. Morphological defect "type" was noted: no defects, only typical, only atypical and both types of endplate defects. Subject demographics were obtained. Data was analysed used one-way ANOVA.

**Results:** Intra-rator reliability for all measurements were excellent. There were 53% subjects with no endplate defects, 14.5% each with cranial and caudal endplates defects while 17% had both endplates involved. There were 17% with typical defects, 24.5% with atypical and 5.5 % having both typical and atypical defects. Age was significantly higher in individuals with both endplates defects ( $p<0.01$ ) and with atypical defects ( $p=0.02$ ). Degeneration scores were higher in individuals having both endplates with defects ( $p=0.001$ ), atypical defects ( $p=0.01$ ) and in subjects having both types of endplate defects ( $p=0.002$ ). LL ( $p<0.001$ ), LLI ( $p=0.02$ ) and SS ( $p=0.001$ ) were significantly lower in subjects with only caudal endplate defects and subjects with both endplates defects. While LL and SS was seen to be significantly lower in individuals having both types of defects ( $p=0.01$  &  $p=0.006$ , respectively).

**Discussion:** This is the first study to note that spinopelvic alignment, specifically decreased LL, LLI, and SS, can alter the spine's stress/load distribution and kinematics, resulting in increased load bearing to the endplates, specifically leading to the development of endplate variants. The endplates, considered as "weak link" of the motion segment, are more vulnerable to be damaged in response to an altered spinal alignment. Future alignment profiling is needed in the context of clinically relevant spinal phenotypes.

ISSLS PRIZE WINNING PAPER

**Growth differentiation factor-6 attenuated pro-inflammatory molecular changes in the rabbit annular-puncture model and degenerated disc-induced pain generation in the rat xenograft radiculopathy model**

**Shingo Miyazaki<sup>1,2</sup>, Ashish D Diwan<sup>2</sup>, Kenji Kato<sup>1</sup>, Kevin Cheng<sup>1</sup>, Won C Bae<sup>3</sup>, Yang Sun<sup>4,5</sup>, Juinchi Yamada<sup>1,5</sup>, Carol Muehleman<sup>6</sup>, Mary E Lenz<sup>1</sup>, Nozomu Inoue<sup>7</sup>, Robert L Sah<sup>1,4</sup>, Mamoru Kawakami<sup>8</sup>, Koichi Masuda<sup>1</sup>**

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**INTRODUCTION:** The intradiscal administration of growth differentiation factor 6 (GDF6) in an *in vivo* sheep model had positive effects on preserving intervertebral disc (IVD) structures by increasing collagen and proteoglycan accumulation. It is unknown if GDF6 affects pain generation in degenerative discs. In this study, we hypothesized that structural and biological modifications of IVDs by GDF6 injection will be associated with relief from pain induced by degenerated IVDs. First, discs after GDF6 injection in the rabbit annular-puncture model were characterized. The recovered nucleus pulposus (NP) tissues were transplanted on nude rat dorsal root ganglion (DRG) as a xenograft transplant to assess potency for pain generation; the status of pain markers in DRGs was then assessed.

**METHODS:**

**Rabbit annular-puncture disc degeneration model and injection of GDF6:** Adolescent female rabbits (n=14) received annular-puncture in two non-consecutive lumbar IVDs (L2/3 and L4/5). Four weeks later, phosphate-buffered saline (PBS) or GDF6 (100 µg) was injected into the NP of punctured discs.

**Gene expression analysis:** Gene expressions of aggrecan (ACAN), collagen-II (Col-II), Interleukin-1β (IL-1β), IL-6, tumor necrosis factor α (TNF-α), vascular endothelial growth factor (VEGF), prostaglandin-endoperoxide synthase 2 (PTGS2), nerve growth factor (NGF) and GAPDH were analyzed using quantitative real-time polymerase chain reaction with standards.

**Nude rat disc xenograft radiculopathy model:** To assess pain induction, female nude rats (n=16) were used for this study. Degenerated NPs from punctured/injected IVDs (L2/3 or L4/5) of annular-punctured rabbits were placed on L5 right DRGs as xenografts.

**Mechanical allodynia:** Mechanical allodynia was evaluated in nude rats using the 50% paw withdrawal threshold response to mechanical stimulation by Von Frey hair filaments.

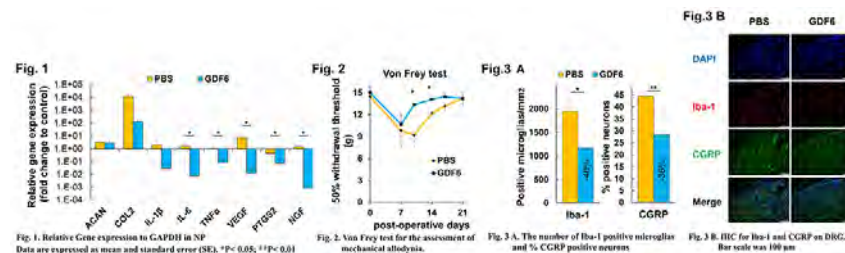
**Immunohistochemistry of DRGs:** The numbers of calcium binding adaptor molecule-1 (Iba-1) positive cells were quantified and expressed as cells/mm<sup>2</sup>. The number of calcitonin gene-related peptide (CGRP)-positive and -negative neurons in DRGs was counted and expressed as percentage of CGRP-positive neurons.

**RESULTS:** Gene expressions (*Fig. 1*): In the NP, genes expressions of inflammatory cytokines (IL-6, TNF-α) and pain-related molecules (VEGF, PTGS2, NGF) in the GDF6 group were significantly lower than those in the PBS group (P<0.05)

**Mechanical allodynia (*Fig. 2*):** Rats transplanted with GDF6-treated rabbit degenerated NPs exhibited reduced mechanical allodynia compared to rats transplanted with PBS-treated rabbit degenerated NPs. on both days 10 and 14 (P<0.05).

**Expression of Iba-1 and CGRP in DRGs (*Fig. 3A, B*):** The expressions of Iba-1 and CGRP in rat DRGs in the GDF6 group of xenograft experiments were significantly lower than those in the PBS group (P<0.05).

**DISCUSSION:** Our two-step disc xenograft model revealed that degenerated rabbit NP tissues, with excessive expression of pro-inflammatory cytokines and pain-related molecules, can induce significant mechanical allodynia in the nude rat radiculopathy model. Importantly, the intradiscal injection of GDF6 into these rabbit IVDs attenuated degenerated NP-induced pain. The decreased inflammatory condition, supported by gene expression analyses, corresponded with less pain generation. The results suggest that pain generation induced by molecules released by degenerated discs may be ameliorated by treatment with GDF6 through the inhibition of inflammatory/pain-related molecules.



**ISSLS PRIZE WINNING PAPER**

**Dynamic imaging of degenerative spondylolisthesis reveals mid-range dynamic lumbar instability not evident on static clinical radiographs**

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**Introduction:** The efficacy of fusion for patients with degenerative lumbar spinal stenosis with concomitant spondylolisthesis remains a contentious topic among spine surgeons<sup>1,2</sup>. Evidence suggests better outcomes with fusion<sup>3</sup> although there are certain patients that can achieve adequate clinical outcome after decompression alone<sup>4,5</sup>. The challenge lies in prospectively identifying which patients will respond favorably to decompression alone and which patients will become unstable and ultimately require fusion. Dynamic instability is currently diagnosed clinically by measurements obtained from static flexion/extension radiographs, which has the potential to miss important mid-range kinematics. The goal of this study was to determine if static clinical radiographs adequately characterize dynamic instability in patients with lumbar degenerative spondylolisthesis (DS) and to compare rotational and translational kinematics in-vivo during continuous dynamic flexion activity in patients with degenerative spondylolisthesis (DS) versus asymptomatic age-matched controls.

**Methods:** Seven patients with symptomatic single level lumbar DS (6 M, 1 F; 66 ± 5.0 years) and seven age-matched asymptomatic controls (5 M, 2 F age 63.9 ± 6.4 years) underwent dynamic biplane radiographic imaging during continuous torso flexion. A volumetric model-based tracking system was used to track each vertebra in the radiographic images using subject-specific 3D bone models generated from high resolution computed tomography (CT) (Figure 1). In-vivo continuous dynamic sagittal rotation (flexion/extension) and AP translation (slip) were calculated and compared to clinical measures of intervertebral flexion/extension and AP translation obtained from standard lateral flexion/extension radiographs.

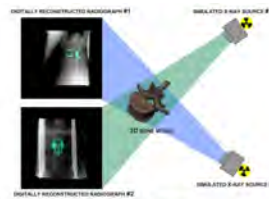
**Results:** Static clinical radiographs underestimated the degree of AP translation seen on dynamic in-vivo imaging (1.0 mm vs 3.1 mm; p=0.03) (Table 1). There were no significant differences identified in intervertebral flexion ROM when comparing static and dynamic measurements (3.3° vs 4.9°, p=0.12). There was no difference in initial AP slip in the neutral position on static versus dynamic measurements (6.8 mm vs 6.9 mm, p=0.75). DS patients demonstrated three primary motion patterns compared to a single kinematic pattern in asymptomatic controls (Figure 2 and Figure 3, respectively). 3/7 (42%) of patients with DS demonstrated aberrant mid-range motion (Figure 2).

**Discussion:** The results indicate that static clinical radiographs underestimate dynamic slip occurring during flexion in DS patients. 42% (3/7) of patients with DS showed maximal change in AP translation during the mid-range, not the end range of motion. Interestingly, four of the seven patients with DS had an increase in slip of more than 1.5 mm on in-vivo dynamic imaging, while the other three had a difference of .3 mm when comparing static clinical to dynamic imaging. Motion greater than 1.25 mm has been shown to be a predictor of delayed instability following decompression without fusion for spondylolisthesis<sup>6</sup>. These results suggest that there may be a sub-group of patients, who have dynamic instability, which is missed when relying on static clinical imaging. While indications for decompression and fusion for lumbar spondylolisthesis remain controversial, this study offers a starting point for identifying patients with occult dynamic instability that may require fusion in addition to decompression surgery. Further studies with larger populations are necessary to further explore this phenomenon.

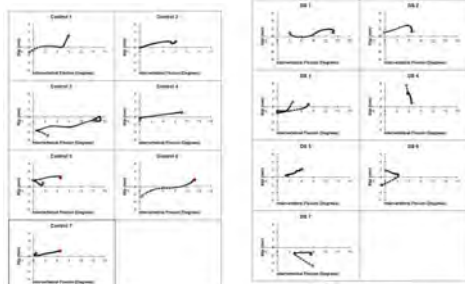
**Table 1:** Static clinical radiographic measurements compared to in-vivo dynamic measurements of intervertebral flexion, maximum slip, and upright neutral initial slip in patients with DS.

Subject	Flexion ROM (°)		Maximum Slip (mm)		Initial Slip (mm)	
	Clinical	In-vivo	Clinical	In-vivo	Clinical	In-vivo
1	8.0	11.0	1.8	2.1	5.6	3.7
2	7.0	6.9	2.0	2.0	5.6	4.7
3	1.0	7.7	0.2	3.0	6.0	6.1
4	2.0	1.3	0.4	4.6	2.1	3.5
5	2.0	4.2	1.9	1.6	9.4	10.0
6	3.0	4.2	1.3	3.7	9.2	7.2
7	5.0	4.9	0.4	3.4	8.7	10.0
<b>Average</b>	<b>3.3</b>	<b>4.9</b>	<b>1.0</b>	<b>3.1</b>	<b>6.8</b>	<b>6.9</b>
<b>P-Value</b>	<b>0.12</b>		<b>0.03</b>		<b>0.75</b>	

Flexion ROM refers to the change in intervertebral flexion seen on clinical flexion-extension radiographs and from in-vivo neutral position to full-flexion. Maximum Slip refers to the maximum AP translation seen on clinical flexion-extension radiographs and in-vivo neutral position to full-flexion. Initial Slip refers to the initial amount of anterolisthesis seen on neutral clinical radiographs and in-vivo upright neutral position imaging.



**Figure 1:** Volumetric model-based tracking technique. Each subject-specific 3D bone model created from CT is placed in a computer-generated reproduction of the spine system (model). Simulated X-rays are passed through the 3D bone model to generate digitally reconstructed radiographs (DRRs). Bone position and orientation are determined by an optimization process that matches the DRRs to the edge-enhanced radiographs. This process is completed for each vertebra.



**Figure 2:** Dynamic in-vivo observation during torso flexion in DS patients. All observed degrees of freedom are shown in the sagittal plane. The graphs show the change in sagittal rotation and AP translation during continuous dynamic flexion activity. The graphs show the change in sagittal rotation and AP translation during continuous dynamic flexion activity. The graphs show the change in sagittal rotation and AP translation during continuous dynamic flexion activity.

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## ISSLS PRIZE WINNING PAPER

### Longitudinal analysis of inflammatory, psychological and sleep-related factors following an acute low back pain episode: the good, the bad and the ugly

David Klyne, Mary Barbe, Wolbert Van den Hoorn, Paul W Hodges

#### INTRODUCTION

Systemic inflammation is observed in chronic LBP and may contribute to the transition from acute to persistent LBP. Longitudinal studies are required to determine whether changes present early or develop over time. Psychological and/or sleep-related factors may be related. **This study aimed** to determine whether systemic cytokines and C-reactive protein (CRP) during an acute episode of low back pain (LBP) differ between individuals who did and did not recover by six months and to identify subgroups based on patterns of inflammatory, psychological and sleep features associated with recovery/non-recovery.

#### METHODS

Individuals within two weeks of onset of acute LBP (N=109) and pain-free controls (N=55) provided blood for assessment of CRP, tumor necrosis factor (TNF), interleukin-6 (IL-6) and interleukin-1 $\beta$  and completed questionnaires related to pain, disability, sleep and psychological status. LBP participants repeated measurements at six-months. Biomarkers were compared between LBP and control participants at baseline, and in longitudinal (baseline/six-months) analysis, between unrecovered ( $\geq$ pain and disability), partially recovered (reduced pain and/or disability) and recovered (no pain and disability) participants at six-months. We assessed baseline patterns of inflammatory, psychological, sleep and pain data using hierarchical clustering and related the clusters to recovery (%pain change) at six-months.

#### RESULTS

CRP was higher in acute LBP than controls at baseline. In LBP, baseline CRP was higher in the recovered than non-recovered groups. Conversely, TNF was higher at both time-points in the non-recovered than recovered groups. Two subgroups were identified that associated with more ("inflammatory/poor sleep") or less ("high TNF/depression") recovery.

#### DISCUSSION

This is the first evidence of a relationship between an "acute-phase" systemic inflammatory response and recovery at six-months. High inflammation (CRP/IL-6) was associated with good recovery, but specific elevation of TNF, along with depressive symptoms, was associated with bad recovery. Depression and TNF may have a two-way relationship.

## Opioids delay healing of spinal fusion: a rabbit posterolateral lumbar fusion model

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### INTRODUCTION

Opioid use is prevalent for management of pre- and post-operative pain in patients undergoing spinal fusion.<sup>1-3</sup> In-vitro and pre-clinical studies suggest a negative effect of opioids on bone healing and turnover.<sup>4-6</sup> However, the effect of opioids on healing of spinal fusion has not been investigated before. Failure of fusion healing remains a concern after spinal fusion as it can result in poor clinical outcome, need for revision surgery, and additional healthcare costs. The objective of our study was to study the effect of systemic opioids on the healing of spinal fusion using a rabbit posterolateral spinal fusion model.

### METHODS

24 adult, New Zealand white rabbits were studied in two groups. The opioid group (n=12) received four-weeks pre-operative and six-weeks post-operative transdermal fentanyl. The control group (n=12) received only peri-operative pain control as necessary. All animals received a bilateral L5-L6 posterolateral spinal fusion using iliac crest autograft. Animals were euthanized at the six-week post-operative time point, and assessment of fusion was done by manual palpation, plain radiographs, micro-computed tomography (microCT) using previously reported scoring systems<sup>7,8</sup>, and histological analysis.

### RESULTS

12 animals in control group and 11 animals in the opioid group were available for analysis at the end of six weeks. The mean serum fentanyl level in the opioid group at pre-operative assessment was 2.73± 0.24 ng/ml, and 1.58± 0.71 ng/ml four-weeks post-operatively. The fusion scores on manual palpation, radiographs, and microCT were not statistically different (Fig 1). Three-dimensional microCT morphometry found that the fusion mass in the opioid group had a lower bone volume (p=0.09), lower trabecular number (p=0.02) and higher trabecular separation (p=0.02) as compared to control (Fig 2). On histological analysis, most of the sections showed 75-100% of the fusion mass composed of new bone, and some sections showed up to 20% of cartilage and fibrous tissue (Fig 3). In the control group, there was remodeling of woven bone to lamellar organization with incorporation of osteocytes, and formation of mature marrow (Fig 4). In the opioid group, there were no sections showing lamellar organization and development of mature marrow elements (Fig 5). Less dense trabeculae on microCT correlated with histological findings of relatively immature fusion mass in the opioid group.

### DISCUSSION

Optimization of modifiable patient factors before spinal fusion represents a cost-effective way to improve chance of fusion success. A biologically plausible and modifiable exposure that has not been studied in spinal fusion is opioid use. Our study using a rabbit posterolateral spinal fusion model is the first to investigate the effect of opioids on the healing of spinal fusion. We found that presence of systemic opioids in the pre- and post-operative period negatively affects the process of spinal fusion healing. Fusion mass in animals with opioid exposure had fewer, and widely spaced trabeculae on microCT analysis. Additionally, there was a delay in the maturation of woven bone on histological analysis in the opioid group. These findings indicate a less mature and inferior quality fusion mass because of opioids, and lay foundation for further research.

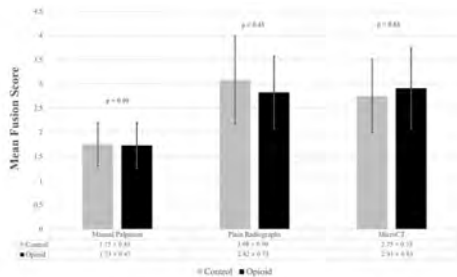


Fig 1 Mean fusion score on manual palpation, plain radiographs, and microCT analysis between control (n=12) and opioid (n=11) rabbit groups

Fig 2 Results from three-dimensional morphometric analysis of intertransverse fusion mass by microCT

	Control group (N=24*)	Opioid group (N=22*)	P value
Bone Volume (mm <sup>3</sup> )	742 ±125	679 ±122	0.09
Trabecular Thickness (mm)	0.73 ±0.11	0.74 ±0.11	0.76
Trabecular Number (mm <sup>-1</sup> )	0.103 ±0.016	0.092 ±0.014	0.02*
Trabecular Separation (mm)	5.14 ±0.60	5.6 ±0.76	0.02*
Bone Mineral Density (mg/cc)	0.783 ±0.024	0.771 ±0.041	0.22

\*Bilateral measurement of intertransverse fusion mass in each animal  
\*Statistically significant

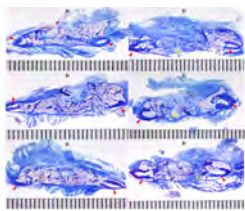


Fig 3 Micrograph of sagittal intertransverse fusion sections. Left - 100% bridging bone between adjacent transverse processes (red arrow). Right - Incomplete bridging of bone with intervening cartilage (yellow arrow) between adjacent transverse processes (red arrow). (Mallory aniline blue connective tissue stain, 10x scale in the field, D: Dorsal)

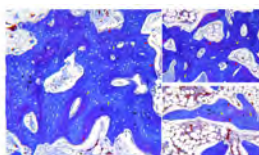


Fig 4 Representative micrograph of fusion in control group undergoing remodeling and maturation of intramembranous woven bone. All images - Lamellar (L) organization of matrix (yellow arrow) with incorporated osteocytes (OC). Small and fine bone trabeculae with bridging new bone (red arrow). Developing mature marrow elements (M). Left - Area of woven bone with haphazard arrangement of incorporated osteoblasts (OB) and unorganized matrix can be seen. Compare to similar and organized osteocytes (OC) in organized lamellar (L) matrix. (Mallory aniline blue connective tissue stain, 75x magnification)

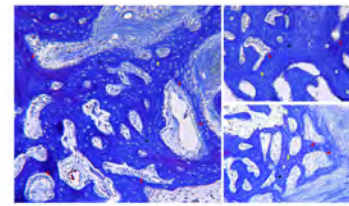


Fig 5 Representative micrograph of fusion in opioid group showing intramembranous woven bone. All images - Woven (W) bone (yellow arrow) with haphazard arrangement of incorporated osteoblasts (OB) and unorganized matrix can be seen. Hypertrophied and dense osteoblasts seen lining new bone (red arrow). (Mallory aniline blue connective tissue stain, 75x magnification)

## **Pre-operative chronic opioid therapy: a risk factor for complications, readmission, continued opioid use and increased costs after one and two level posterior lumbar fusion**

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2. *Orthopaedics, Rush University Medical Center, Chicago, Illinois, United State of America*

### **INTRODUCTION**

Chronic opioid use is associated with poor clinical outcomes and dependence after spine surgery.<sup>1-4</sup> Risk factors, complications, readmissions, adverse events, and costs associated with COT in patients undergoing lumbar fusion are not entirely known. As providers look to reduce healthcare costs and improve outcomes, identification of modifiable risk factors will be important. Our objective was to study patient profile associated with pre-operative chronic opioid therapy (COT), and study COT as a risk factor for 90-day complications, emergency department (ED) visits, and readmission after primary 1-2 level posterior lumbar fusion (PLF) for degenerative disease of the spine. We also evaluated associated costs as well as risk factors and adverse events related to long term post-operative opioid use.

### **METHODS**

Commercial insurance data from 2007 to Q3-2015 was used to study pre-operative opioid use in patients undergoing primary 1-2 level PLF. 90-day complications, ED visits, readmissions, one-year adverse events, and associated costs have been described. Multiple-variable regression analyses were done to study pre-operative COT patient profile, and study opioid use as a risk factor for complications and adverse events.

### **RESULTS**

24,610 patients with a mean age of 65.6±11.5 years were included. 5,500 (22.3%) patients had documented opioid use for >6 months before surgery. On multiple-variable logistic regression analysis, patients who had pre-operative COT were more likely to be associated with diagnosis of anxiety (OR 1.29, 95% CI:1.19-1.40), depression (OR 1.15, 95% CI:1.06-1.25), inflammatory arthritis (OR 1.14, 95% CI:1.06-1.23), tobacco use disorder (OR 1.50, 95% CI:1.37-1.64), and drug abuse/dependence (OR 1.43, 95% CI:1.23-1.67). After adjusting for various demographic and clinical covariates, pre-operative COT was found to be a risk factor for 90-day wound complications (OR 1.19, 95% CI:1.05-1.35), pain diagnoses (OR 1.10, 95% CI:1.02-1.19), ED visits (OR 1.31, 95% CI:1.15-1.49), readmission (OR 1.80, 95% CI:1.24-2.57), and continued use post-operatively (OR 8.08, 95% CI:7.40-8.80). Post spinal fusion long-term opioid users had an increased utilization of lumbo-sacral epidural and facet joint injections (OR 2.24, 95% CI:2.04-2.46), higher risk for revision fusion (OR 1.33, 95% CI:1.14-1.55), and increased incidence of new onset constipation (OR 1.15, 95% CI:1.05-1.25) within one-year after surgery. The cost associated with increase resource use in these patients have been reported.

### **CONCLUSION**

Pre-operative COT is a modifiable risk factor for complications, readmission, adverse events, and increased costs after 1-2 level PLF. The increased risk of complications, readmission, and adverse events with resultant higher resource use in chronic opioid users results in additional healthcare costs, and will have financial implications for all providers in a bundled payment model. With increasing emphasis on cost containment and quality improvement, our findings are intended to caution providers about COT as a risk factor for adverse outcomes and increased costs after lumbar fusion.

## Predicting likelihood of surgery prior to first visit in patients with back and lower extremity symptoms: a simple mathematical model based on over 8000 patients

**Lauren M Boden, Stephanie A Boden, Ajay Premkumar, Michael B Gottschalk, Scott D Boden**

**Introduction:** Low back pain (LBP) and radicular lower extremity (LE) symptoms are common musculoskeletal problems. There is currently no standard data-derived patient triage process based on information that can be obtained prior to the initial physician-patient encounter to more efficiently direct patients to the optimal physician type (spine surgeon versus non-surgeon). This study was designed to identify patient-reported information that can be obtained before a physician office visit associated with an increased likelihood of undergoing surgery in patients with LE radicular symptoms with or without LBP. We hypothesized that a triage scoring system derived from a mathematical model could be created to stratify patients into low, moderate, and high likelihood for undergoing surgery within one year of presentation, and that this data-driven model would more effectively identify patients likely to undergo surgery than the existing triage system at our institution.

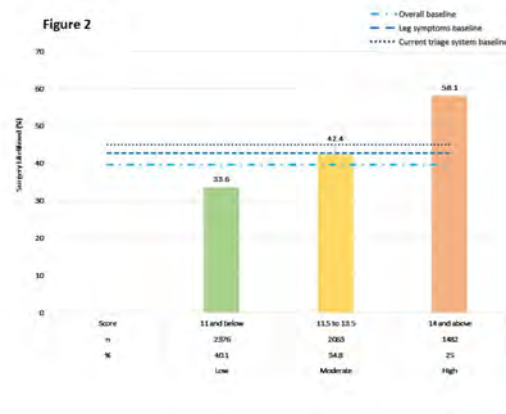
**Methods:** We analyzed patient-reported data from 8006 patients with a chief complaint of LBP and/or LE radicular symptoms who presented to surgeons at a large multidisciplinary spine center between September 1, 2005 and June 30, 2016. Univariate and multivariate analysis identified independent risk factors for undergoing spinal surgery within one year of initial visit. A model incorporating these risk factors was created using a random sample of 80% of the total patients in our cohort, and validated on the remaining 20%. A model using fewer risk factors but still with strong correlation was then validated to better serve as a more practical phone or web-based triage tool.

**Results:** The baseline one-year surgery rate within our cohort was 39% for all patients and 42% for patients with LE symptoms. Those identified as high likelihood by the center's existing triage process had a surgery rate of 45%. Multiple logistic regression analysis indicated that eleven variables were independent predictors of undergoing surgery within one year of presentation (Figure 1). The Hosmer-Lemeshow statistic was not significant, ( $\chi^2 = 5.68, p = 0.68$ ), indicating that the model's overall fit was good. The new triage scoring system proposed in this study was able to identify a high likelihood group in which 58% underwent surgery, which is a 46% higher surgery rate than in non-triaged patients and a 29% improvement from our institution's existing triage system (Figure 2). A shorter model based on the top five variables was able to triage patients in a similar manner.

**Discussion:** To our knowledge, this is the first study to identify patient-reported factors obtained solely before the initial patient encounter that are predictive of ultimately undergoing spinal surgery. Several studies have attempted to predict failure of conservative treatment using elements of patient history, physical exam, and radiographic findings with no clear results. The data-driven triage model and scoring systems derived and validated in this study significantly improved existing triage processes in predicting the likelihood of undergoing spinal surgery within one year of initial presentation. This triage system will allow centers to more selectively screen for surgical candidates and more effectively direct patients to surgeons or non-operative spine specialists.

Figure 1. Triage model for the classification of patient likelihood of undergoing surgery within one year

Triage Question	Univariate OR (95% CI)	p	Multivariate OR (95% CI)	p	Score
Does your pain or problem involve your lower extremity?	44.5 (22.08 – 89.64)	<0.0001	-	-	-
1. Do you have lower extremity pain?	4.14 (3.40 – 5.00)	<0.0001	1.82 (1.10 – 2.99)	0.019	1
2. Is your leg pain worse than your back pain?	1.99 (1.80 – 2.20)	<0.0001	1.68 (1.48 – 1.91)	<0.0001	2.5
3. Do you avoid tobacco and nicotine products, including cigarettes?	1.42 (1.22 – 1.66)	<0.0001	1.56 (1.30 – 1.86)	<0.0001	2
4. Is your lower extremity pain steadily worsening?	2.09 (1.88 – 2.31)	<0.0001	1.51 (1.28 – 1.73)	<0.0001	2
5. Are you over 65 years old?	1.22 (1.09 – 1.36)	0.0004	1.41 (1.22 – 1.63)	<0.0001	1.5
6. Were you employed before your current problem started?	1.14 (1.03 – 1.26)	0.013	1.39 (1.22 – 1.59)	<0.0001	1.5
7. Do you experience pain in over 50% of your waking hours?	1.58 (1.31 – 1.90)	<0.0001	1.37 (1.07 – 1.75)	0.014	1.5
8. Are you male?	1.19 (1.07 – 1.31)	0.0011	1.36 (1.20 – 1.54)	<0.0001	1.5
9. Is your BMI less than 30?	1.17 (1.05 – 1.30)	0.0037	1.33 (1.17 – 1.51)	<0.0001	1.5
10. Is your low back pain steadily worsening?	1.48 (1.32 – 1.67)	<0.0001	1.23 (1.04 – 1.45)	0.017	1
11. Have your parents or siblings had any back or spine problems?	1.17 (1.04 – 1.31)	0.0066	1.15 (1.01 – 1.32)	0.036	0.5



## Outcome after degenerative spine surgery - Do we need longer follow-up than 1 year?

**Catharina Parai<sup>1,2</sup>, Olle Hägg<sup>2</sup>, Bengt Lind<sup>1,2</sup>, Helena Brisby<sup>1,3</sup>**

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### Introduction

In order to evaluate the outcome of degenerative spine surgery in a credible way, variables such as pain, physical function and quality of life should be assessed for an adequate follow-up period. Most authors/journals consider a follow-up period of less than two years to be too short to draw any firm conclusions about the outcome after degenerative spine surgical procedures. The purpose of this study was to explore possible clinically important differences in outcome at 1, 2 and 5 years post surgery for these patients based on the Patient-Reported Outcome (PRO) measures Global Assessment (GA<sub>BACK/LEG</sub>), Visual Analogue Scale for pain (VAS<sub>BACK/LEG</sub>), Oswestry Disability Index (ODI), the quality-of-life measure EQ-5D<sub>INDEX</sub> and Satisfaction of outcome using the Swespine registry.

### Methods

Adult patients with degenerative lumbar spine conditions operated between 1998 and 2016 were retrieved from the "Swedish spine registry" (Swespine) (n=98,732). The mean follow-up rates at 1, 2 and 5 years were 73%, 58% and 32%. The patients were divided into the diagnosis groups Lumbar Disc Herniation (LDH, n=31,314), Lumbar Spinal Stenosis (LSS, n=53,043) and Degenerative Disc Disease (DDD, n=14,375). The values of the PRO measures at the three follow-ups were assessed by the two one-sided test (TOST) procedure. The acceptance criterions were based on Minimal Important Change (MIC) values.

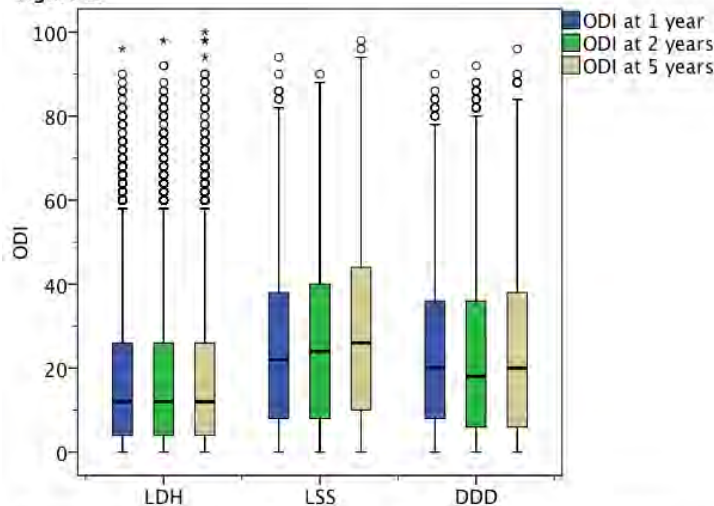
### Results

In the three diagnosis groups, the differences at 1, 2 and 5 years were found to be within the equivalence margins. In the LDH group the mean differences between the first and second follow-up for VAS<sub>BACK/LEG</sub> was 1.40 (SD 22.2) and 1.70 (SD 25.3), for ODI 0.15 (SD 10.5) and for EQ-5D 0.004 (SD 0.23). There were no median differences for GA<sub>BACK/LEG</sub> or Satisfaction. The results were similar for the outcome at 5 years as well as for the other diagnosis groups.

### Discussion

No clinically important changes in PRO measures appear between 1, 2 and 5 years after surgery for degenerative lumbar spine conditions, suggesting that a follow-up period of 1 year is sufficient. Statistically significant differences are to be expected when the sample size is as large as in the present study. However, these differences lack clinical relevance.

Figure 1.



Results at 1, 2 and 5 years of follow-up after surgery for Lumbar Disc Herniation (n at 1 year=17,311; n at 2 years=14,257; n at 5 years=9,647), Lumbar Spinal Stenosis (n at 1 year=33,622; n at 2 years=26,799; n at 5 years=14,485) and Degenerative Disc Disease (n at 1 year=8,914; n at 2 years=7,374; n at 5 years=5,144) with Oswestry Disability Index as outcome variable.

## The influence of preoperative opioid use on hospital length of stay and patient reported outcomes following elective spine surgery.

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**Objectives:** Pre-operative opioid use in spine surgery is very common. Limited studies have demonstrated an association of preoperative opioid use with negative surgical outcomes. Our primary objectives were to assess the influence of preoperative opioid use on 1) hospital length of stay (LOS), and 2) patient-reported pain and disability one year after elective spine surgery.

**Methods:** Retrospective review of Canadian Spine Outcomes and Research Network (CSORN) Registry data across eight provinces. Patients (n=1931) with a primary degenerative diagnosis, hospital LOS, and baseline and 1-year post-surgical patient reported outcomes were included. For objective 2, we examined postoperative patient reported pain from a visual analog scale (0: no pain-10: unbearable pain) and neck or back disability scores for patients with cervical and thoracolumbar diagnoses, respectively. The main covariate of interest was preoperative opioid use (daily, intermittent and no use). Other covariates included socio-demographic (e.g. age, sex, education, work status), lifestyle (e.g. smoking, BMI), and clinical variables (e.g. depressive mood, surgery type) as well as baseline pain and disability scores. Multiple linear regression models were used to examine the associations between preoperative opioid use and LOS as well as 1-year post-surgical pain and disability.

**Results:** Daily, intermittent and no preoperative opioid use was reported by 18.3%, 32.4% and 50.7% of patients respectively. Independent factors significantly associated with preoperative daily opioid use were thoracolumbar diagnosis (Odds Ratio (OR):2.73), depressed mood (OR:2.22), 3+ comorbidities (OR:1.93), disc herniation diagnosis (vs. stenosis) (OR:1.79), positive legal claim (OR:1.56), in labor force but not working (OR:1.54), anxious mood (OR:1.48), degenerative disc disease (OR:1.41), and being a current smoker (OR:1.37). Older patients, those exercising regularly, and those currently working were significantly less likely to report daily opioid use. Mean LOS was 4.4, 5.1 and 5.2 days (p=0.19) for no, intermittent and daily pre-operative opioid use. In multivariable linear regression models, preoperative daily opioid use was independently associated with increased LOS ( $\beta=1.40$ ;  $p<0.0001$ ), whereas intermittent use was not ( $\beta=1.16$ ;  $p<0.072$ ). Daily opioid use was independently associated with worse self-reported pain ( $\beta=0.48$ ;  $p=0.003$ ) and disability ( $\beta=4.83$ ;  $p<0.0001$ ) at 1-year post-surgery as compared to patients not using opioids. Intermittent use was associated with worse disability ( $\beta=2.44$ ;  $p<0.042$ ) but not pain. Legal claims ( $\beta=0.55$ ;  $p=0.001$ ), smoking ( $\beta=0.47$ ;  $p=0.007$ ), anxiety ( $\beta=0.85$ ;  $p=0.004$ ) and higher baseline pain ( $\beta=0.24$ ;  $p<0.0001$ ) were associated with worse pain scores at 1 year. Worse disability scores were associated with older age ( $\beta=0.90$ ;  $p=0.029$ ), legal claims ( $\beta=5.93$ ;  $p<0.0001$ ), smoking ( $\beta=2.83$ ;  $p=0.013$ ), 3+ comorbidities ( $\beta=4.85$ ;  $p=0.003$ ), anxiety ( $\beta=2.28$ ;  $p<0.026$ ) and higher baseline ODI/NDI ( $\beta=0.44$ ;  $p<0.0001$ ).

**Conclusions:** Preoperative opioid use is highly prevalent in patients undergoing elective spine surgery across Canada, with 50% reporting intermittent or daily use. Preoperative use of opioids in this setting is independently associated with greater pain and disability at one year post-surgery, with daily user having a greater negative impact on outcome. Furthermore, daily preoperative use is also associated with increased hospital LOS. Future work will focus on examining efficacy of opioids and predictors of changes in opioid use post-surgery and its associated impact on outcomes.

## Lumbar surgery within two weeks of epidural steroid injection is associated with increased 90-day complications

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### Introduction

The use of lumbosacral epidural steroid injections (ESIs) for lower back conditions has increased dramatically with improved understanding of their efficacy and proper indications for use. ESIs may modulate the immune system and could potentially increase the risk for infection with subsequent spine surgery. While several studies show no association between lumbar ESI and postoperative infection, others suggest a possible increase in risk if ESIs are given within 30-90 days prior to surgery. The goals of the current study were to use nationally-representative claims data to gain more insight into the relationship between lumbar ESI and postoperative complications and better understand the influence of the timing of ESI prior to surgery.

### Methods

A national cohort of primary lumbar spine surgery patients was derived from the Marketscan<sup>®</sup> databases (2007-2014) using well-validated coding algorithms. Inclusion criteria were primary lumbar spine surgery for stenosis and/or disc herniation, age  $\geq 18$  years, health plan enrollment  $\geq 1$  year preoperatively to identify ESIs and screen exclusions, and enrollment  $\geq 90$  days postoperatively to track complications. Patients with lumbar ESI in the year prior to surgery were matched on a one-to-one basis with those who did not have ESI using a propensity score matching algorithm incorporating all available demographics, comorbidities, and surgical details to minimize confounding. Differences in 90-day complication rates were assessed with chi-squared tests. The relationship between the timing of the ESI prior to surgery and complications was assessed via binary logistic regression with receiver operating characteristic (ROC) curves (SAS 9.4,  $\alpha=0.05$ ).

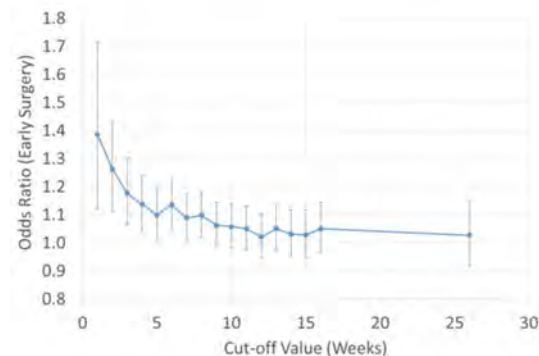
### Results

Of patients having primary lumbar spine surgery for stenosis and/or herniation, 59.0% had lumbar ESI within the prior year. 29,478 patients with ESI were matched successfully to those without ESI (age  $50.2 \pm 14$  years, 41% female). The groups were balanced with respect to all demographics, comorbidities, and surgical details after matching. No difference was observed in the overall rate of complications (ESI=14.0%, no ESI=14.2%  $p=0.530$ ) or inpatient readmissions (ESI=2.7%, no ESI=2.6%,  $p=0.444$ ). Additionally, infection rates did not differ between groups (ESI=2.0%, no ESI=1.9%,  $p=0.475$ ).

Despite no difference overall, 90-day complication rates increased as the time between ESI and surgery decreased (Figure). In ROC-curve analyses, the optimal cut point was identified at 2 weeks preoperatively. Patients having ESI within 2 weeks preoperatively had a 26% increase in the odds for complications (Odds Ratio=1.26, 95% CI=1.11-1.42,  $p<0.001$ ) relative to those with more time between ESI and surgery. To identify the drivers of this increase, a sub-analysis was performed comparing patients with "early surgery" following ESI ( $n=3,082$ ) and their matched pairs. Patients having ESI within 2 weeks prior to surgery had increased rates of infection (ESI=2.5%, no ESI=1.5%,  $p<0.006$ ), DVT (ESI=1.8%, no ESI=1%,  $p=0.017$ ), and inpatient readmissions (ESI=3.3%, no ESI=2.3%,  $p=0.017$ ) within 90 days relative to those not having ESI prior to surgery.

### Conclusion

Lumbar ESI within 2 weeks prior to lumbar surgery for spinal stenosis or disc herniation is associated with a 66% increased risk for infection, an 80% increased risk for DVT, and a 43% increased risk for readmission within 90 days.



**Figure 1.** The odds for 90-day complications versus the cut-off defining "early surgery" after lumbar ESI, demonstrating that the odds for complications increase with decreasing time between ESI and surgery. ROC analysis identified the optimal cut-off as 2 weeks prior to surgery.

## Effect of HbA1c and Perioperative Blood Glucose Control on the Occurrence of Postoperative Infection in Lumbar Instrumentation Surgery

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### Introduction

Diabetes mellitus (DM) is a potential risk for surgical site infection (SSI) in spine surgery, which increases the rate two or threefold. However, it remains unclear how the pre- and perioperative blood glucose control influences the occurrence of SSI. The purpose of this study is to investigate the effect of preoperative HbA1c and perioperative blood glucose control on SSI rate after posterior lumbar instrumentation surgery in DM patients.

### Methods

A total of 807 patients who had undergone a posterior lumbar instrumentation surgery from 2010 to 2016 were reviewed at a minimum of one-year follow-up. They were 339 males and 468 females with a mean age of 70 years. SSI was defined as deep wound infection which required surgical intervention. HbA1c was measured at preoperative general health checkup. Preoperative blood glucose level was monitored by 7-point glycemic profiles immediately before surgery. Relationships among preoperative HbA1c, perioperative blood glucose control and SSI rate were investigated. Patients were divided into three groups: non-DM group, low HbA1c group (HbA1c < 7.0 in DM group), high HbA1c group (HbA1c ≥ 7.0 in DM group). As well, based on the status of blood glucose control, patients were also divided into two groups: good control group (postprandial blood glucose < 200 mg/dl), and poor control group (≥ 200 mg/dl). The rate of SSI was compared among these groups.

### Results

Proportion of DM patients was 24.4% (197 of 807 patients). SSI occurred in 2.1% in non-DM group (13 of 610 patients), 3.0% in low HbA1c group (4 of 132 patients), and 9.2% in high HbA1c group (6 of 65 patients); the rate was significantly higher in high HbA1c group ( $p < 0.001$ ). Regarding perioperative blood glucose control, SSI occurred in 2.0% in good control group (2 of 100 patients), and 13.8% in poor control group (8 of 66 patients); the rate was significantly lower in good control group ( $p = 0.007$ ).

### Discussion

The CDC guideline recommended that blood glucose level should be kept less than 200mg/dl perioperatively to prevent SSI. The current study showed that SSI rate after posterior lumbar instrumentation surgery significantly increased in high HbA1c DM patients. However, the rate could be reduced to the same level as that of the non-DM group, by lowering postprandial blood glucose to less than 200 mg/dl immediately before surgery.



## **A multicenter prospective investigation of thoracolumbar/lumbar perioperative complications in patients aged 80 years or older**

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### **【Introduction】**

To perceive complications of spine surgeries in elderly patients, we have done multicenter prospective survey of perioperative complications of thoracolumbar/lumbar surgeries in patients aged 80 years or older.

### **【Methods】**

Eight spine centers, which board-certified spine surgeons belong to, participated in this prospective survey. A total of 110 consecutive patients (40 males and 70 females) aged 80 years or older underwent thoracolumbar/lumbar surgeries between January and June 2017. Trauma, infection, and tumor cases were excluded. Surgical procedures were posterior decompression in 40, instrumentation surgery in 50, and balloon kyphoplasty (BKP) in 20 patients. Perioperative complications were defined as adverse events which occurred intraoperatively and within 30 days after surgery. Preoperative comorbidity, activity, and nutrition were assessed using (1)Charlson Comorbidity Index (CCI), (2)ASA physical status classification (ASA), (3)ECOG Performance Status (PS), (4)presence of sarcopenia, and (5)Geriatric Nutritional Risk Index (GNRI). Relationship between preoperative health status and systemic perioperative complications were also analyzed.

### **【Results】**

Surgical site complications occurred in 9 patients (8.2%): 2 of 40 in decompression and 7 of 50 in instrumentation surgery. There were 3 dural tears (2.7%), 2 superficial infections (1.8%), and hematoma/fracture of lower instrumented vertebra/pedicle screw back-out after surgery/surgical wound disruption in one each (0.9%). Reoperations were required in 6 patients (5.5%). Seventeen patients (15.5%) developed systemic complications (2 of 40 decompressions, 13 of 50 instrumentation surgeries, and 2 of 20 BKPs). They were deliriums in ten (9.1%), anemia with transfusions in five (4.5%), urinary tract infections and asymptomatic DVTs in two each (1.8%). No patient developed myocardial infarction, cardiac failure, cerebrovascular disease, pneumonia, pulmonary embolism, renal failure requiring dialysis, and digestive complications. As well, there were no perioperative deaths in this series.

Assesment of preoperative general health showed that a majority of patients were in good status (CCI was less than 5 in 101 cases; ASA was 2 in 103 cases; PS was less than 3 in 71 cases). Prevalence of sarcopenia was 22.8%. GNRI in 81 patients was more than 98, which means no nutrition-related risk of morbidity and mortality in the hospitalized elderly. Multivariate analysis showed that preoperative health status was not related to the occurrence of systemic complications.

### **【Discussion】**

To our knowledge, there have been no multicenter prospective studies regarding perioperative complications related to thoracolumbar/lumbar surgeries in consecutive elderly patients. In addition, relationship between systemic complications and preoperative general health status remains unclear. The current study showed that systemic complications occurred in 15.5%, whereas there were no fatal complications. As well, reoperation rate was low as 5.5%. No preoperative general health status was recognized as a risk factor of perioperative systemic complications. The current results suggested that thoracolumbar/lumbar surgeries could be safely performed even in patients over 80 years.

## Retrospective multicenter study of perioperative complications in 1,015 patients who underwent oblique lateral interbody fusion surgery

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**Introduction:** Lateral lumbar interbody fusion (LLIF) has been widely performed and is attracting attention. LLIF is divided into two major techniques according to the approach: oblique lateral interbody fusion (OLIF) and transpsoas LLIF (direct/extreme LIF: D/XLIF).

Perioperative complications associated with D/XLIF have been previously reported, such as transient thigh pain and muscle weakness resulting from the transpsoas approach. On the other hand, OLIF has been reported to have less perioperative complications owing to its mini-open and non-psoas splitting retroperitoneal approach (Abe K, Orita S, et al, Spine 2017; Fujibayashi S, et al. Spine 2017). However, there were issues in these reports such as combined incidence with XLIF or a smaller amount of subjects. We aimed to investigate and report the perioperative complications limited to OLIF surgery by performing a retrospective multicenter survey.

**Methods:** The present study was a retrospective review of operative data collected from 14 orthopaedic institutions all over Japan under the approval of each institutions ethics committee. Each institution included more than 100 OLIF cases at the time of the survey. These study subjects were patients with low back pain (LBP) who underwent surgery under the diagnosis of degenerative lumbar disease such as spondylolisthesis and degenerative lumbar kyphoscoliosis from April 2012 to March 2017. In addition to the basic data such as diagnosis, age, gender, surgical method, intraoperative blood loss, and operative time, the perioperative complication-related collected data was analyzed and arranged according to the following major categories: intraoperative and early-stage postoperative ( $\leq 1$  month) complications. The intraoperative complications were then subcategorized into organ damage (neural, vertebral, vascular, and others) and other complications, mainly related to the instrumentation failure.

**Results:** In total, 1,015 OLIF patients were evaluated (mean 66.7 yo, range 14–87 years). The most frequent diagnosis was spondylolisthesis (68.2%) followed by kyphoscoliosis (22.1%). Overall, 269 complications were reported (incidence rate, 26.5%). The most frequent complication was transient psoas weakness and thigh numbness (8.67%), followed by segmental artery injury (0.49%), dural injury (0.20%), vertebral fracture including endplate injury and cage subsidence (8.37%), ALL injury (2.76%), retroperitoneal hemorrhage (0.59%), wrong level (0.30%), peritoneal injury (0.39%), ureteral injury (0.10%), and intraoperative implant breakage (1.08%). Severe and permanent damage included only the ureteral injury. There was a significant increased complication occurrence with increasing number of levels included in the fusion. (mean 1.89 levels vs. 1.58,  $p = 0.04$ ). Increasing Intraoperative blood loss and operative time during the anterior OLIF approach was associated with higher complication cases.

**Discussion:** The overall incidence of perioperative complications of OLIF surgery amounted to 26.5%, of which only 0.10% resulted in permanent damage in a ureteral. The overall incidence was lower compared with the previous reports of transmuscular LLIF, most of which are transient such as thigh numbness. Increased number of fusion levels was associated with increased Intraoperative blood loss and increased operative time. Considering the low incidence of complications compared with other approaches including posterior interbody fusion, the present study suggests that OLIF may be one if not the most MIS and safe spinal fusion options.

1. Abe K, Orita S, et al. Perioperative Complications in 155 Patients Who Underwent Oblique Lateral Interbody Fusion Surgery: Perspectives and Indications From a Retrospective, Multicenter Survey. Spine (Phila Pa 1976). 42(1):55-62, 2017. 2. Fujibayashi S, Kawakami N, et al. Complications Associated With Lateral Interbody Fusion: Nationwide Survey of 2998 Cases During the First 2 Years of Its Use in Japan. Spine (Phila Pa 1976). 42(19):1478-1484, 2017

## Lumbar epidural steroid injections for herniation and stenosis: incidence and risk factors of subsequent surgery

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### Introduction

The use of lumbosacral epidural steroid injections (ESIs) for lower back conditions has increased dramatically. Aside from pain reduction, one indication for ESIs is the ability to avoid or delay surgery. Surgery rates after ESI have been examined in several randomized trials; however, these are frequently underpowered or hindered by other methodological limitations and often rates in clinical practice do not match those observed in the controlled setting of a randomized trial. Therefore, the goal of this study is to use a large, nationally-representative claims database to determine the proportion of patients who progress to surgery after lumbar ESI. Furthermore, we seek to better understand the typical timing of this progression and to examine factors associated with surgery.

### Methods

Survival analyses were performed using the MarketScan® databases (2007-2014), a large, national administrative claims data resource. Inclusion criteria were ESI for stenosis and/or herniation, age  $\geq 18$  years, and health plan enrollment for 1 year prior to ESI to screen for exclusions. Patients were followed longitudinally until they progressed to surgery or had a lapse in enrollment, at which time they were censored. Rates of surgery were assessed with the Kaplan-Meier survival curves and 99% confidence intervals (99% CI). Demographic and treatment factors associated with surgery were subsequently assessed with multivariable Cox proportional hazard models (SAS 9.4, two-sided  $\alpha=0.001$ ).

### Results

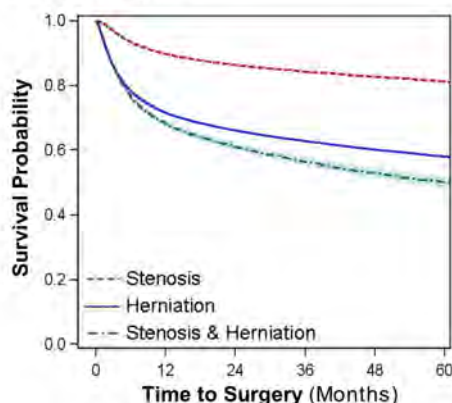
A total of 203,001 patients having lumbar ESI for stenosis and/or herniation were identified (age  $53 \pm 15$  years, 48% female). Within 6 months, 17.6% (99% CI: 17.3%, 17.9%) of patients underwent lumbar surgery. By 1 and 5 years, this reached 23.7% (99% CI: 23.3%, 24.0%) and 36.2% (99% CI: 35.7%, 36.7%), respectively. Additionally, 45.8% (99% CI: 45.2%, 46.3%) of patients had a second epidural, with most occurring in the first 3 months.

In multivariable models, rates of surgery were 2 to 9 times higher for patients with herniation relative to those with stenosis ( $p < 0.001$  for all), with the greatest differences occurring in the younger age groups. Concomitant spine diagnoses (neuritis/radiculitis/radiculopathy, myelopathy, spondylosis, instability, spondylolisthesis, lumbago, and sciatica), male sex, younger age for herniation patients, residence in the Northeastern or rural U.S., and previous treatment for tobacco use were also associated with increased surgery rates after ESI ( $p < 0.001$  for each). Conversely, fluoroscopic guidance was associated with a 12 percent decrease in surgery rates ( $p < 0.001$ ). Younger age for stenosis patients and a number of medical comorbidities (CHF, previous treatment for drug use, chronic pain, obesity, anxiety, hypercholesterolemia, and COPD) were associated with lower rates of surgery ( $p < 0.001$  for each).

### Discussion

In the long-term, more than 1 out of every 3 patients undergoing ESI for lumbar herniation and/or stenosis progressed to surgery, and nearly 1 of 5 did so within the first 6 months. After adjusting for other demographics and comorbidities, patients with herniation were more likely have surgery than those with stenosis. The improved understanding of the progression from lumbar ESI to surgery will help to better inform discussions regarding the value of ESI and aid in the shared decision making process.

**Figure 1.** Univariate Kaplan-Meier survival curves and 99% confidence intervals for the time from ESI to surgery stratified by diagnosis.



## Supervised physical therapy versus unsupervised exercise for patients with lumbar spinal stenosis: a randomized controlled trial

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**INTRODUCTION:** Exercise for patients with lumbar spinal stenosis (LSS) has been reported to lead to better short-term outcomes in terms of disability and back and leg pain than no exercise. However, no reports have compared supervised exercise with unsupervised exercise or quantified physical activity using a pedometer to confirm compliance with the home exercise program. The purpose of this study was to compare the effectiveness of supervised physical therapy with unsupervised exercise for patients with LSS.

**METHODS:** Patients presenting with symptoms of neurogenic claudication caused by LSS, which was confirmed by magnetic resonance imaging (MRI), were enrolled from September 2014 to August 2017. Patients were randomized to a physical therapy group (PT group), which performed supervised physical therapy twice a week for 6 weeks or a home exercise group (control group) using covariate adaptive randomization and online statistical computing web programming. Physical therapy sessions included manual therapy, stretching and strengthening exercises, cycling, and body weight-supported treadmill walking. All patients were asked to undertake a home exercise program. Patients in the control group visited a physical therapist to confirm whether they performed home exercise once a week for 6 weeks. The primary outcome was the difference in improvement in symptom severity scores on the Zurich Claudication Questionnaire (ZCQ) at 6 weeks. Secondary outcomes included: physical function and satisfaction on the ZCQ; self-paced walking test (SPWT) performance; pain indicated using a numerical rating scale; and scores on the SF-36, Hospital Anxiety and Depression Scale, Pain Catastrophizing Scale, and the Tampa Scale for Kinesiophobia. Compliance with the home exercise program was measured using a pedometer and self-report questionnaire. Scores and mean changes after 6 weeks were compared between the groups.

**RESULTS:** Thirty-six patients (16 men and 20 women, average age 72.1 years) were allocated to the PT group and 36 patients (16 men and 20 women, average age 73.1 years) to the control group. At baseline, there were no significant differences in age, gender, body mass index, MRI findings and the outcome measures between groups ( $P>0.05$ ). At 6 weeks, compared with the control group, the PT group showed significant improvements in ZCQ symptom severity (mean difference  $-0.4$ ; 95% confidence interval [CI]:  $-0.7$  to  $-0.1$ ,  $P=0.003$ ), ZCQ physical function (mean difference  $-0.4$ ; 95% CI:  $-0.7$  to  $-0.2$ ,  $P=0.001$ ), walking distance on the SPWT (mean difference 475 m; 95% CI: 305 to 646,  $P<0.001$ ), physical functioning (mean difference 9.0; 95% CI: 0.8 to 17.2,  $P=0.031$ ) and bodily pain (mean difference 10.0; 95% CI: 0.9 to 18.0,  $P=0.016$ ) on the SF-36, and number of daily steps (mean difference 793 steps/day; 95% CI: 208 to 1378,  $P=0.009$ ).

**DISCUSSION:** Supervised physical therapy for patients with LSS produced significant short-term improvements in pain, walking distance, disability, and physical activity compared with unsupervised exercise. The mean difference between groups in improved symptom severity scores on the ZCQ exceeded a minimal clinically important difference of 0.36. Future studies should focus on long-term outcomes and surgery rates after exercise programs.

## **Associations among natural history, conservative treatment and health-related quality of life among patients with symptomatic lumbar spinal stenosis: Locomotive Syndrome and Health Outcomes in Aizu Cohort Study (LOHAS)**

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### **Introduction:**

Few longitudinal studies have examined the natural history of patients with untreated symptomatic, degenerative lumbar spinal stenosis (LSS). The present study compares the health-related quality of life (HR-QOL) between untreated and treated patients with symptomatic LSS.

### **Materials and Methods:**

This retrospective study analyzed data that were prospectively collected from 2134 community-dwelling individuals (male, 795, female, 1,339; age range, 39 – 95 years) for the Locomotive Syndrome and Health Outcomes in Aizu Cohort Study (LOHAS, 2008-9). Symptomatic LSS was assessed using a validated LSS diagnostic support tool (Konno et al. 2007). Exclusion criteria comprised a history of spinal surgery. We evaluated HR-QOL using the Medical Outcomes Study 12-Item Short Form Health Survey (SF-12) and compared changes in SF-12 Physical Function (PF) scores over a one-year follow-up period between patients with untreated and treated symptomatic lumbar spinal stenosis. None of the patients received public health intervention such as secondary health examinations throughout the observational period. Medical care that the patients received was recorded for one year.

### **Results:**

The baseline prevalence of symptomatic LSS was 205 (9.6%) of 2134 participants. Within the year of follow-up, six and 73 patients were treated by lumbar spinal surgery and conservatively, respectively (treated group) whereas 126 patients were not treated (untreated group.). The PF score was significantly lower for the treated, than the untreated group at baseline ( $56.2 \pm 31.9$  vs.  $69.2 \pm 31.0$ ,  $p = 0.0045$ ) and at one year of follow-up ( $54.9 \pm 30.8$  vs.  $73.4 \pm 27.8$ ,  $p < 0.0001$ ), whereas overall one-year scores did not significantly differ between them ( $1.14 \pm 37.1$  vs.  $-3.75 \pm 31.2$ ,  $p = 0.297$ ).

### **Discussion:**

The degree of LSS might be more severe among conservatively treated, than untreated patients because their HR-QOL scores were lower than those of untreated patients at all observational periods. However, scores at baseline and at one-year follow-up did not significantly differ between treated and untreated patients. The natural history of about half of the patients with untreated LSS for one year might favourably affect their HR-QOL.

## **A study on the difference of bone union between unilateral and bilateral lumbar spondylolysis in adolescent patients**

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**INTRODUCTION:** Last year, we reported that bilateral lumbar spondylolysis had lower rate and longer period for bone union compared to unilateral lumbar spondylolysis. However we were not able to compare these two types at the same stages. In this study we added more patients for further analysis.

**METHODS:** From April 2012 to December 2016, 255 adolescent patients (209 men and 46 women, mean age; 14.8 years, range 11 to 18) who came to our hospital and was diagnosed lumbar spondylolysis with both CT and MRI, were included. We retrospectively reviewed both CT and MRI in order to determine their spondylolysis stages: 1) very-early, 2) early, 3) progressive and 4) terminal stage. And we classified patients into three groups; unilateral spondylolysis group (U-group), bilateral spondylolysis with same stage at both sides (B-group) and bilateral spondylolysis with different stages (BU-group). BU group patients had an affected side with preceding opposite side spondylolysis. The decision of bone union was made with CT. We compared the rates and the period of bone union between these three groups. The stages and bone union of BU group was decided as to affected side.

**RESULTS:** The number of patients who selected conservative treatment with lumbosacral corset was 180 (151 men and 29 women) and mean follow-up periods was 8.5 months. U-group consisted of 90, B-group 48 and BU-group 42. Their stages were: U-group; 1) n=24, 2) n=54, 3) n=12, 4) n=0, B-group; n=3, 29, 16, 0, BU-group (affected side); n=4, 30, 8, 0 respectively. Bone union was obtained 84 of 90 patients (93.3%) in U-group, 30 of 48 patients (62.7%) in B-group and 23 of 42 patients (52.3%) in BU-group. There was a significant difference between U-group and B, BU-group. ( $P < 0.01$ ). The periods for bone union was 3.1 months, 4.8 months and 5.1 months respectively. There was also a significant difference between U-group and B, BU-group. ( $P < 0.01$ ).

**CONCLUSION:** In this study, we showed that as to bone union, bilateral lumbar spondylolysis had lower rate and needed longer period than unilateral spondylolysis. Especially in BU-group, concerned side was difficult to cure. We thought we must diagnose and treat unilateral spondylolysis as soon as possible in order not to proceed to bilateral spondylolysis.

## **Risk factors and score for recollapse of the augmented vertebrae after percutaneous vertebroplasty in osteoporotic vertebral compression fractures**

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### **Introduction**

Osteoporotic vertebral compression fractures (OVCFs) are very common in the elderly worldwide. Percutaneous vertebroplasty (PVP) has been traditionally adopted and proved a minimally invasive technique for treating painful OVCFs, which could rapidly relieve the pain, restore vertebral height partially, and provide biomechanical stability. However, recollapse of the augmented vertebrae with significant vertebral height loss and aggravation of kyphotic deformity after surgery, which usually requires further treatment. Recollapse of the vertebral body may be related to previous intravertebral cleft (IVC) and cement distribution pattern, but the significant relationship is not clear. The purpose of the study was to identify risk factors and further develop a risk score for recollapse of the augmented vertebrae after PVP treatment for OVCFs.

**Methods:** Patients treated with PVP for single OVCFs and met this study's inclusion criteria were retrospectively reviewed. The follow-up period was at least 2 years. Associations of recollapse with co-variables (age, gender, bone mass density (BMD) with a T-score, fracture level, IVC, fracture type, cement volume, total cement leakage, intradiscal leakage, cement distribution pattern, Non-PMMA-endplate-contact (NPEC), preoperative fracture severity, reduction rate (RR), reduction angle (RA)) were analyzed and a risk score for recollapse was further developed to predict recollapse.

**Results:** A total of 152 patients were included. Recollapse group was found in 42 (27.6%) patients. Preoperative IVC, solid lump cement distribution pattern, more RR (a cutoff value of 7%) and larger RA (a cutoff value of 3°) was significantly associated with increased risk for recollapse of the augmented vertebrae. A risk score was developed based on the number of risk factors present in each patient. Patients with a score of 4 had an approximately 9-fold increased risk of developing recollapse over patients with a score of 0. The receiver-operating-characteristic curve of the risk score generated an area under the curve of 0.899 (95% CI 0.642–0.836, P=0.000).

**Discussion:** A risk score based on preoperative IVC, cement distribution pattern, reduction rate and reduction angle predicts the rate of recollapse. Additional studies should aim to validate this score and inspect the clinical benefits of recollapse prevention in patients at high risk.

## **Is it feasible to manage osteoporotic vertebral fracture with pharmacologic therapy?: a comparative study with subcutaneously injected weekly teriparatide, daily teriparatide and denosumab**

**Masumi Iwabuchi, Jun Komatsu, Hironari Fukuda, Keigo Kusano, Osamu Shirado**

**INTRODUCTION:** The real efficacy of pharmacological therapy for osteoporotic vertebral fracture (OVF) has not been fully clarified.

**METHODS:** A retrospective cohort study. From April 1, 2012 through October 31, 2016, 41 patients with thoracic and/or lumbar OVF were treated with one of the 3 drugs; weekly teriparatide (TW), daily teriparatide (TD) or denosumab (DM). They were investigated with a minimum follow-up of 1 year. All patients were women with a mean age of 78 years. The patients with severe liver or kidney dysfunction were excluded. On the first diagnosis of the fresh fracture, the patients chose either TW or TD after having the drug information to treat the OVF as well as osteoporosis. DM became to be chosen as another option since June 11, 2013 when it came to market. All patients wore flexible lumbar corset. The following measurements were performed; bone union rate(%), the period for bone union(months), the amount of increase of the local kyphotic angle(degrees) and the incidence of delayed paralysis due to retropulsed bony fragments into the spinal canal(%). The results were compared among 3 groups; TW in 13 patients, TD in 12, and DM in 16. Anterior height of the indexed vertebral body in lateral X-P on sitting and supine position was measured. Fresh fracture was diagnosed if the difference of the height between two positions was observed. Plain X-P were taken by the same way every 3 months after the first diagnosis. Bone union was confirmed when the difference of the anterior height could not be observed. Kruskal-Wallis test was used for statistical analysis, performed with SPSS for the Windows Version 17.0. Significance was defined as a *p*-value of less than 0.05.

**RESULTS:** There was no statistically significant difference among 3 groups in all measurements. The bone union rate was 100%(13/13) in TW group, 75%(9/12) in TD, and 87.5%(14/16) in DM (*P*=0.169). The mean period for bone union was 7 months in TW group, 8.8 in TD, and 6.4 in DM (*P*=0.264). The mean amount of increase of the local kyphotic angle was 3.5 degrees in TW group, -0.2 in TD, 2.5 in DM (*P*=0.183). There was no patient resulted in delayed paralysis in all 3 groups.

**DISCUSSION:** The current study demonstrated that it was feasible to successfully treat the patients with OVF by the subcutaneously injected drugs; TW, TD and DM. The efficacy of 3 drugs was equivalent in terms of the bone union rate, the period for bone union, the amount of increase in local kyphotic angle, and the incidence of delayed paralysis. Three drugs are equally recommended to manage OVF, though future study might be needed to clarify the difference from another perspective, for instance, medico-economical issue.



## Prognostic factors and survival after surgical resection of spinal metastases from renal cell carcinomas with a minimum 3-year follow-up

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**Introduction:** The bone is a common metastatic site in metastatic renal cell carcinoma (RCC), second only to the lung. Spinal metastases from RCC are difficult to manage, because they tend to be large, highly destructive, and more resistant to systemic therapy than other metastases, causing intractable pain and paralysis. The role of surgical resection of metastases from renal cell carcinoma (RCC) is widely accepted. Previous studies reported that complete resection of metastases from RCC was associated with long-term survival. Current Urological Association guidelines recommend complete surgical resection of metastases if achievable. However, spinal metastases from RCC are reported as a poor prognostic factor owing to the difficulty of surgical resection. Previous studies reported that the 5-year survival rate for patients with metastatic RCC was between 10 and 20 %. Our study aimed to examine the survival of patients who underwent complete resection of spinal metastases from RCC and analyze prognostic factors.

**Methods:** We collected data on 50 patients with spinal metastases from RCC, who underwent complete resection at our institution between 1995 and 2014. We retrospectively examined cancer-specific survival (CSS) from the surgery to death or last follow-up, and analyzed a total of 20 potential factors associated with survival such as age, gender, performance status, presence of lung, liver, lymph node, or nonspinal bone metastases, interval between the diagnosis of kidney cancer, tumor size of spinal lesion, history of systemic therapy, Motzer classification grade, and abnormal levels in serum c-reactive protein, corrected calcium, or albumin. The log-rank test and the Cox proportional hazard model were used for univariate and multivariate analyses to identify risk factors for survival, respectively.

**Results:** To achieve complete oncological resection, spondylectomy was performed in 48 patients and partial spondylectomy in 2 patients. Thirty-six patients received a single vertebral resection, 14 patients received two or three consecutive vertebral resections. Twelve patients died less than 3 years after surgery, whereas the other 38 patients survived 3 years or more after surgery. For all patients, the estimated median CSS time was 90 months. The 5 and 10-year CSS rate were 58% and 43%, respectively, for all patients, and 50% and 31%, respectively, for patients with coexistence of lung metastases at the time of surgery. The presence of multiple lesions in the spine and the poor risk group in the Motzer criteria were significantly associated with short-term survival in the multivariate analysis.

**Conclusion:** Our results indicate that patients with multiple spinal metastases or the poor risk in the criteria for patients with metastatic RCC at the time of spine surgery had short-term survival. However, for the selected patients, complete surgical resection of spinal metastases can have the potential to prolong the survival.

## Spinopelvic alignment predicts disc stiffness, herniation, and Modic changes: evidence of an evolutionary etiology for clinically-relevant spinal phenotypes

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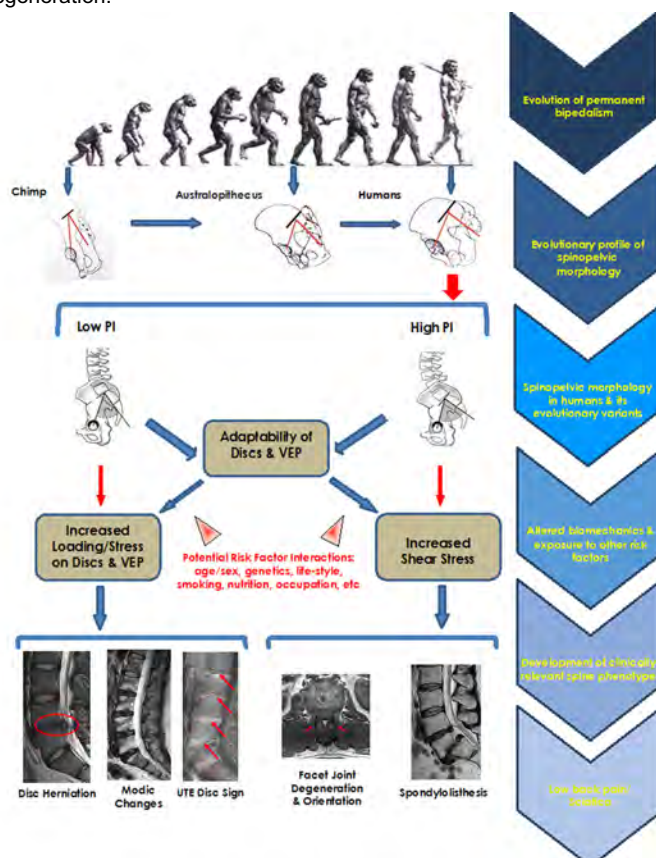
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**Introduction:** Lumbar disc degeneration (i.e. grey/black disc) on T2-weighted (T2W) MRI has not been consistently correlated with pain profiles. Lumbar disc herniation (LDH), Modic changes (MCs) and UTE Disc Sign (UDS, i.e. calcification/stiffness) on MRI are robust spinal phenotypes that can lead to sciatica/low back pain. Not all degenerated discs result in LDH, MCs and UDS, suggesting varied etiologies. Although several etiological factors (e.g. genetics, lifestyle) may exist for the aforementioned spinal phenotypes, variations exist and replication has been unsatisfactory. Spinopelvic parameters have been implicated in various spinal disorders. In particular, pelvic incidence (PI) is a “fixed parameter” since skeletal maturity. Currently, no study has addressed LDH, MCs and UDS in the context of spinopelvic parameters. Therefore, the following study aimed to determine if spinopelvic parameters are associated and predict clinically-relevant MRI phenotypes of LDH, MCs and UDS.

**Methods:** A cross-sectional study was conducted. 108 population-based subjects (mean age: 52.3 years), irrespective of pain, were recruited. Presence of spondylolisthesis, scoliosis, and other co-morbidities were excluded. Lumbar lordosis (LL), PI, sacral slope (SS), and pelvic tilt (PT) were assessed on lateral plain standing radiographs. Disc degeneration was assessed and summated, and the presence or not of LDH and MCs were noted on T2W MRI. UDS was detected on UTE. UDS was mapped to the location of MCs and LDH.

**Results:** Following exclusion criteria, 95 subjects were assessed. LDH (82.1%), MCs (52.6%) and UDS (37.9%) were all associated with lower PIs, SS, LL and LL/PI index. Based on multivariate analyses, a lower PI was significantly related to the development of these MRI phenotypes (adjusted OR range:0.95-0.92;  $p < 0.05$ ), with a cut-off PI value of 42 degrees or lower exhibiting a 4-fold increase risk of these combined phenotypes ( $p = 0.020$ ). Of UDS discs, 39.3% had adjacent MCs and 83.6% had LDH. 87.5% of MC had corresponding UDS directly adjacent to the lesions.

**Discussion:** This is the first study to note that PI may “predict” the development of lumbar LDH, MCs and UDS, suggesting potential sub-variants and a mechanistic susceptibility that may be grounded in spinopelvic evolution. An “evolutionary etiological pathway” (Figure 1) of spinal phenotype development is proposed. An individuals’ spinopelvic morphological profile should be accounted in personalized spine care approaches. PI is a central focus for future “omics” studies to explore pathways of spine degeneration.



## Dynamic sagittal balance associates with patient-reported disability in adult spinal deformity population

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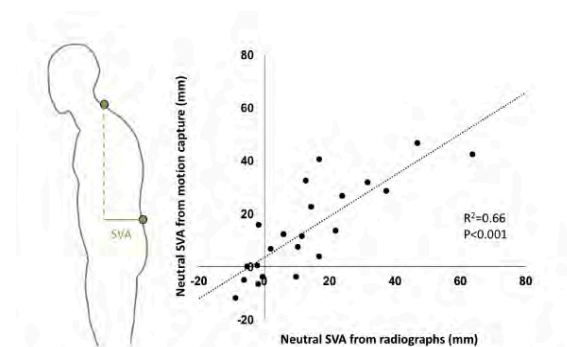
**Introduction:** Sagittal imbalance from adult spinal deformity (ASD) associates with poor patient-reported outcomes for disability and health-related quality of life. Sagittal balance is assessed using static standing radiography and quantitative measures of sagittal alignment from standing radiography guide realignment during multi-level fusion. To understand dynamic stability associated with sagittal imbalance and potential risk for Proximal Junction Kyphosis, we developed an in-clinic quantitative dynamic assessment of sagittal balance that reflects an individual's ability to actively stabilize their posture and maintain balance during movement. We measured the dynamic behavior of Sagittal Vertical Axis (SVA, the horizontal offset between C7 to S1) in patients moving, unassisted, from a seated to a standing position (Sit-to-Stand, STS). STS captures an individual's ability to stabilize their posture during a dynamic sagittal movement common in daily activity. We hypothesized that a dynamic measure of SVA reflective of postural stability would associate to patient-reported outcomes in ASD patients.

**Methods:** With IRB approval, 27 patients with ASD volunteered for an in-clinic motion analysis assessment using Microsoft Kinect technology. Patient and clinical demographics were collected from medical records. Retroreflective motion capture markers were placed at the C7 spinous process and sacrum (Figure 1). SVA was measured as the horizontal distance from the C7 marker to the sacral marker. The positions of the markers were recorded using the Kinect camera at 30 Hz as participants performed the STS task at their own pace. Standing, neutral SVA from the Kinect system was validated by comparison to traditional SVA radiographic measurements.

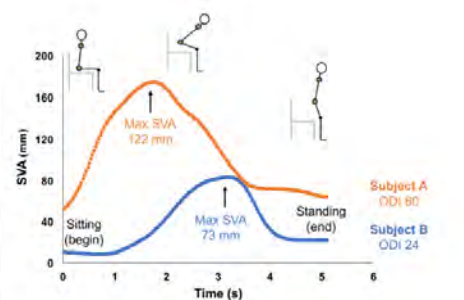
We have defined 'Dynamic SVA' as the maximum horizontal SVA (mm) a subject demonstrates when trying to stabilize their posture during the transition from a seated to a standing position (unassisted). Dynamic SVA was compared to patient-reported outcomes, including a numerical rating scale for pain (NRS; 0-10) and the Oswestry Disability Index for low back disability (ODI; 0-100). Statistical analysis included bivariate and multivariable linear regression analyses. Multivariable linear regression analyses included age and time required to complete the STS maneuver as covariates.

**Results:** Average age ( $\pm$  sd) for our patient population was  $61 \pm 14$  years. Our marker-based measurement of SVA positively correlated with radiographic measurement of SVA, both assessed in neutral standing posture ( $R^2=0.66$ ,  $p<0.001$ ; Figure 1). ODI positively associated with dynamic SVA ( $R^2=0.35$ ;  $p=0.01$ ; Figure 2). The positive association between ODI and dynamic SVA strengthened after adjusting for age and time required to complete the maneuver ( $R^2=0.51$ ;  $p=0.002$ ). NRS for pain, however, did not predict dynamic SVA with either bivariate or multivariable regression.

**Discussion:** This study suggests that a dynamic measure of SVA positively associates with ODI, a measure of patient-reported low back disability (Figure 2). This result linking dynamic SVA and ODI build upon the relationship previously established between SVA from standing radiographs and ODI. Although this sample is small and cross-sectional, this result supports utilizing a dynamic measure of sagittal balance to assess postural stability and post-surgical outcomes in ASD patients. Future studies will follow changes in dynamic SVA in deformity patients before and after sagittal realignment surgery.



**Figure 1:** The schematic on the left depicts how SVA (mm) is measured from the Kinect motion analysis markers. The plot on the right shows the association between the motion capture measurement of SVA and radiographic measurement of SVA.



**Figure 2:** Comparison of change in SVA over time during the dynamic STS task between two separate patient-subjects. Subject A demonstrated a larger anterior excursion of their trunk when rising out of the chair and had a greater maximum SVA during the STS maneuver compared to Subject B. In addition, Subject A had a greater ODI score than Subject B.

## Impact of paraspinal muscle degeneration on fatigue of spinopelvic compensatory mechanism in sagittal plane adult spinal deformity: quantitative assessment of MRI and sagittal parameters after 10 minutes walking

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**Introduction.** In adult spinal deformity, a spinal compensatory mechanism to maintain adequate sagittal balance is basically based on para-spinal muscles. Daily activity such as walking is often interrupted by progressive decompensation from fatigue causing sagittal malalignment. However, there is limited understanding of how sagittal parameters and compensatory changes due to fatigue are affected by para-spinal muscles. The purpose of this study is to assess the impact of para-spinal muscle on fatigue related change of sagittal compensatory mechanism evaluated with before and after walking for 10 minutes.

**Methods.** Consecutive adults with sagittal plane spinal deformity at a single institution were retrospectively reviewed. All patients were initially evaluated with full-length standing spinal radiographs and then asked to walk in clinic for 10 minutes. Subsequently, all were re-evaluated with a second full-length standing spinal radiograph. Spinal deformity sagittal parameters were measured on each radiograph and were compared before and after the timed walk for two groups: Compensated Sagittal Deformity (CSD: SVA $\leq$ 4cm and PT $>$ 20 $^{\circ}$ ) and Decompensated Sagittal Deformity (DSD: SVA $>$ 4cm and PT $>$ 20 $^{\circ}$ ). Area of psoas muscle at the L3 level, para-spinal muscle (PSM; multifidus and longissimus) at T12 and L4 low end-plate, the ratio of PSM and diameter of the L3 vertebral body (PSM/VB) and fatty infiltration (FI, %) into PSM that determined with pseudo-color mapping were measured with MRI. Student T-tests were used to assess changes in radiographic parameters and Pearson's correlation coefficients were used to evaluate correlations between muscle parameters and changes in the sagittal parameters after walking.

**Results.** 145 patients (135 females, 11 males; average age 68.1  $\pm$  5.9 years) met inclusion criteria. Initial average SVA was 1.8cm for CSD and 11cm for DSD ( $p<0.01$ ). Average initial PT was  $>30^{\circ}$  and TK was  $<12^{\circ}$  for both groups ( $p=0.517$  and  $p=0.326$ ). DSD patients had greater initial PI-LL mismatch than CSD patients ( $p=0.002$ ). After walking 10 minutes, significant deteriorations in SVA were observed by decreased PT and loss of LL ( $p<0.01$ ) in CSD without significant change in TK ( $p=0.828$ ), while SVA changes for DSD was correlated to worsening of all spinal parameters ( $p<0.01$ ).

DSD was more osteoporotic, and PSM degeneration was deteriorated such as decreased muscle volume at T12 and diverse muscle quality at the L4 level.

In CSD,  $\Delta$ LL was related with PSM/VB at L4 ( $r=-0.412$ ,  $p=0.046$ ) and  $\Delta$ TK was related with PSM/VB at L1 ( $r=0.477$ ,  $p=0.018$ ) and FI at T10 ( $r=-0.801$ ,  $p=0.017$ ).  $\Delta$ SVA was significantly related with FI at L4 ( $r=-0.577$ ,  $p=0.003$ ). In DSD,  $\Delta$ LL was related with PSM/VB at L1 and  $\Delta$ PT was negatively correlated with the mean signal intensity of PSM at L4 with low  $r$  value ( $-0.3<r<-0.1$ ).

**Conclusions.** After 10 minutes of walking, compensatory mechanisms to maintain sagittal balance are less pronounced than before walking in patients with ASD, which results in significant sagittal decompensation. DSD showed profound degeneration of PSM at both upper and lower lumbar spine. Influence of muscle mass and FI at PSM on fatigue of compensatory mechanism is more profound in CSD. Sagittal malalignment in DSD worsens less affected by muscle status.

## The relationship of spino-pelvic parameters between static radiograph and motion analysis in adult spinal deformity patients with positive sagittal imbalance

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### INTRODUCTION

A limitation for radiological assessment of ASD is a widely recognized discordance between natural standing posture and the posture during standing X-rays (hands on clavicle or hands on mandible/ fist on clavicle). We still don't know whether or how accurately radiological parameter measurement in the static radiograph can reflect the natural sagittal balance during the gait. Therefore, the purpose of this study was to compare the radiological pelvic parameter in static radiographs with the values in motion analysis during the gait. The second purpose was to analyze the correlation between the gait analysis and clinical outcomes about pain and disability.

### METHODS

A total of 20 consecutive patients diagnosed as ASD with severe positive sagittal balance were included for eligibility in this study at a single tertiary hospital between September 2016 and November 2017. All participants were scheduled to undergo corrective fusion surgery for sagittal imbalance. On the whole spine standing lateral x-ray, sagittal spino-pelvic parameters were measured, which included lumbar lordosis (LL), sagittal vertical axis (SVA), pelvic tilt (PT), sacral slope (SS), and pelvic incidence (PI). PI minus LL was also calculated. In addition, a 3-dimensional gait analysis was performed a few days before the surgery using a Motion Analysis system (Motion Analysis Corporation, CA, USA) that was equipped with 10 cameras and 2 force plates, by which pelvis rotation and knee flexion angle were measured in gait. For clinical outcome, VAS for back and leg pain, Oswestry Disability Index (ODI) scores and the EQ-5D (EuroQoL) were assessed. The correlation among parametric values of both x-ray and motion analysis were analyzed. In addition, the correlation between parametric values of motion analysis and clinical outcome variables were also analyzed.

### RESULTS

Mean age (standard deviation [SD]) was 72.3 (6.4). One participant was male, and 19 were female. On the standing X-ray, mean PI, PT, and SS (SD) were 59.4 (10.4), 45.7 (9.3), and 13.6 (7.9) degrees, respectively. In addition, LL and LL - PI were -5.9 (7.8) and 65.1 (10.5), respectively. On the motion analysis, mean pelvis rotation (SD) were 8.6 (10.7) and 8.5 (10.7) in right and left, respectively. For clinical outcomes, mean VAS for back and leg pain were 7.0 (2.6) and 4.8 (3.3), respectively. mean ODI were 59.8 (13.4). SS in the X-ray was significantly correlated with pelvic rotation in the motion analysis (right:  $r=0.521$ ,  $P=0.027$ , left:  $r=0.513$ ,  $P=0.030$ ). In addition, PI had significantly positive correlation with SS ( $r=0.512$ ,  $P=0.030$ ) and PT ( $r=0.582$ ,  $P=0.011$ ). Any clinical outcomes including VAS for back and leg pain, ODI, and EQ-5D were not correlated with parametric values from X-ray and motion analysis.

### DISCUSSION

The present results showed the sagittal balance on the plane X-ray can reflect the natural sagittal balance during the gait. In addition, positive correlation between PI and SS/PT indicates that high pelvic incidence means the capacity to compensate positive sagittal imbalance. In addition, in the patients with severe positive sagittal imbalance, the parameters from radiographic and motion analysis cannot predict clinical outcomes.

## The sex and age distribution of indices for muscle evaluation and their association with spinal sagittal alignment: The Wakayama Spine Study

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**Purpose:** A forward shift of the sagittal vertical axis (SVA) is reported to be a radiographic predictor of low back pain as well as disability for activities of daily living in the elderly. The relationship between postural change and sarcopenia remains unclear. This study considered the following questions. 1) Do the degeneration in limb skeletal muscles and paraspinal muscles proceed in parallel with age? 2) Among multiple muscle evaluation indices, what is most relevant to postural change?

**Methods:** This was a cross-sectional study using an established population-based cohort in Japan. Of the 952 subjects who participated in the second survey of the Wakayama Spine Study, 814 (247 men, 567 women, mean age 63.5±13.1 years) underwent sagittal whole-spine radiography in a standing position, whole-spine magnetic resonance imaging (MRI), and bioelectrical impedance analysis (BIA). The C7 SVA (mm) was measured in the radiograph. The fatty infiltration ratio (FIR, %) in the erector spinae and multifidus at L1 upper end-plate level was measured on axial MRI using Digital Imaging and Communications in Medicine software. Appendicular skeletal muscle mass index (ASMI) was calculated from the sum of the muscle masses of the four limbs after adjusting for height (kg/m<sup>2</sup>).

**Statistics:** 1) Participants were grouped into five classes based on age (years): <50, 50-59, 60-69, 70-79, and >80; the change in each measurement item based on sex and age was determined. 2) Multiple regression analysis with C7 SVA as the objective variable, and age, ASMI, and FIR of the erector spinae and multifidus as explanatory variables were conducted based on sex.

**Results:** In men, C7 SVA increased significantly starting at age 70 and ASMI significantly decreased starting at age 50. The multifidus FIR increased significantly starting at age 60 and the erector spinae FIR increased significantly starting at age 70. The erector spinae FIR at L1 alone was significantly associated with C7 SVA ( $p < 0.0001$ , standard  $\beta = 0.33$ ). In women, C7 SVA increased significantly starting at age 60 and ASMI decreased significantly starting at age 60. The multifidus FIR increased significantly starting at age 50 and the erector spinae FIR increased significantly starting at age 60. Factors significantly associated with C7 SVA were age ( $p < 0.0001$ , standard  $\beta = 0.32$ ), erector spinae FIR ( $p < 0.0001$ , standard  $\beta = 0.19$ ), and multifidus FIR ( $p < 0.01$ , standard  $\beta = 0.13$ ).

**Discussion:** The degeneration in limb skeletal muscles and paraspinal muscles did not proceed in parallel with age. ASMI, which is included in the criteria for sarcopenia, decreased starting at age 50 in men, i.e., 10 years earlier than in women. Paraspinal muscle degeneration began in women 10 years earlier than in men. Thus, significant multifidus changes began at age 50 and erector spinae changes at age 60 in women. The association with C7 SVA was not observed in ASMI, and changes in the erector spinae were found to be important. Although this study is limited by the cross-sectional design, it provides important data for use in preventing postural change in the elderly.

## Spinal alignment and additional surgery after short fusion for degenerative lumbar scoliosis

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[Introduction] Surgical methods for degenerative lumbar scoliosis (DLS) range from decompression alone to long corrective fusion. Short fusion is frequently indicated in case that neurological symptoms are predominant rather than those related to spinal deformity. However, there are controversies regarding the postoperative curve progression and additional surgery. The aim of this study was to evaluate the change of spinal alignment and the rate of additional surgery after short fusion for DLS.

[Methods] Sixty-nine patients who had undergone a short fusion for DLS from 2009 to 2015 were included in this study. DLS was defined as more than 10 degrees of scoliosis in this study. They were 16 men and 53 women with a mean age of 71 years. Mean follow-up period was 3.7 years. Number of fusion segments were one segment in 35, two in 26, and three in 8 patients. Radiographic parameters included coronal Cobb angle, coronal upper and lower intervertebral angle, lumbar lordosis (LL), sacral slope (SS), pelvic tilt (PT), pelvic incidence (PI), sagittal vertical axis (SVA), and T1 pelvic angle (TPA). These parameters were evaluated using standing whole spine radiographs preoperatively (pre), immediately after surgery (post), and at the final follow-up (final). The pathologies for additional surgery were also reviewed.

[Results] Mean coronal Cobb angle was 20 degrees preoperatively. Fifty-eight patients (89%) had less than 30 degrees of scoliosis. Coronal Cobb angle was improved to 13 degrees immediately after surgery, and 17 degrees at the final follow-up. Only five patients (7%) developed more than 10 degrees of coronal curve progression. No patients developed more than 10 degrees of coronal upper and lower intervertebral angle. Also, no remarkable changes were observed in the other angular parameters (pre/post/final): LL (31/35/30 degrees), SS (25/28/25 degrees), PT (22/21/24 degrees), PI (48/49/49 degrees), and TPA (22/20/24 degrees). SVA was 6.3 cm before surgery, 5.1 cm immediately after surgery, and 7.2 cm at the final follow-up. Additional surgeries were required in 12 patients (17%). The pathologies were adjacent segmental disease (ASD) in eight patients (12%), subsequent vertebral fracture in two patients (2.9%), pseudarthrosis and aggravation of spinal alignment in one each (1.4%). In six of eight patients (75%) who needed additional surgery for ASD, the pathology was radiculopathy due to foraminal stenosis at concave side.

[Discussion] The current results showed that residual coronal curve and global sagittal alignment were unlikely to deteriorate after short fusion for DLS. Additional surgery for aggravation of spinal alignment was required in only one patient (1.4% of entire cohort). Neurological deterioration at adjacent segment (12% of entire cohort) predominantly occurred at concave-side neuroforamen. Although neurological deterioration after short fusion for DLS did not frequently occur, concave-side foraminal stenosis adjacent to fusion might be a potential risk for additional surgery. Careful observation of postoperative clinical and radiographic changes might be required.

## **Clinical outcomes of minimally invasive spinal decompression surgery for lumbar spinal stenosis with I grade degenerative spondylolisthesis: A 4-year Follow-up Study**

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**Introduction:** Recently, as a surgical treatment for patients with lumbar spinal stenosis (LSS) with or without degenerative spondylolisthesis (DS), a random prospective control trial reported that decompression with fusion did not result in clinical outcomes that were superior to those with decompression surgery alone (N Engl J Med 2016). The purpose of this study was to prospectively investigate the long-term clinical outcomes of minimally invasive decompression surgery (MIS) for patients of LSS with or without DS. The authors have developed the novel microendoscopic laminotomy (MEL) technique as a MIS to lumbar spinal disorders.

**Methods:** A total of 486 patients (mean age, 68 years) who underwent MEL for one or two adjacent vertebral level(s) LSS at the authors' institute were recruited. Patients with I grade DS were included into the DS group (n=181) and those without DS into the control group (n=231). In addition to slippage rate, Japanese Orthopaedic Association (JOA) score, recovery rate, Short-Form 36 (SF-36), and Roland-Morris Disability Questionnaire (RDQ) were evaluated preoperatively and at 2 years and 4 years postoperatively. All parameters were statistically analyzed by Student's t-test. P values < 0.05 were statistically significant.

**Results:** Of the 340 patients, the 2 years follow-up rate was 70.0%. The primary analysis, which was a per-protocol analysis, did not include the patients who did not receive the assigned treatment and who were lost to follow-up. There was no significant difference between the groups in the JOA recovery rates at 2 years (DS: 60.2%, control 58.1%, P>0.05), RDQ, and each subscale of SF-36. Results were similar between patients with and those without DS. Among the patients who had 4 years of follow-up and were eligible for inclusion in the 4-year analysis, there were no significant differences between the groups in clinical outcomes at 4 years. The slippage rate in the DS group was 14.5% preoperatively and 15.8% at 4 years postoperatively (p>0.05). Spinal re-stabilization was demonstrated in 31% of patients with DS. The success rate of MEL was good/excellent in 70%, fair in 20%, and poor in 10% of patients in both groups.

**Conclusion.** The clinical outcomes of MEL were similar in LSS patients with DS and those without DS.



## Distribution and determinants of 90-day payments for multi-level posterior lumbar fusion: a medicare analysis

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### INTRODUCTION

Bundled payments represent a single payment system to cover all costs associated with a single episode of care, typically over 90-days. The dollar amount spent on different health service providers and the variation in payments for ≥3 level posterior lumbar fusion (PLF) have not been analyzed from a bundled perspective. The objective of the study was to analyze the distribution of 90-day payments, sources of variation, and reimbursement for complications/readmissions for primary ≥3 level PLF from Medicare data. A secondary objective was to identify risk factors for complications.

### METHODS

5% Medicare data was used to study 90-day reimbursements for primary ≥3 level PLF for deformity and degenerative conditions of the lumbar spine. Distribution of payments, sources of variation, and reimbursements for managing complications were studied using linear regression models. Risk factors for complications was studied by backward stepwise multiple-variable logistic regression analysis.

### RESULTS

Hospital payments comprised 73.8% share of total 90-day payment (Fig 1). Adjusted analysis identified several factors for variation in index hospital payments (Fig 2). The average 90-day Medicare payment for all multi-level PLFs without complications was \$35,878 per patient. The incidence of intra-operative complications was 1017/2759 (36.9%) while the incidence of post-operative complications was 874/2759 (31.7%). The additional average cost of treating complications with/without revision surgery within the 90-day period ranged from \$17,284 to \$68,963 (Fig 3). A 90-day bundle for ≥3 level PLF with readmission ranges from \$88,648 (3-level) to \$117,215 (8+ level). Significant risk factors for development of any complication are given in Fig 4.

### DISCUSSION

The average 90-day payment per patient from Medicare was \$35,878 with several factors such as levels of surgery, comorbidities, and development of complications influencing the cost. Our adjusted analysis of hospital LOS showed that 8+ level surgery, diabetes, congestive heart failure, chronic kidney disease, malnutrition, anemia, and coagulopathy increased hospital stay significantly. Whereas fusion in the West, increasing levels of fusion, chronic liver and kidney disease, and malnutrition were independent risk factors for higher hospital payments, age or other comorbidities such as obesity, diabetes, cardiac or pulmonary disease were not found to influence hospital payment significantly. We also postulate three specific independent risk factors that resulted in maximum escalation of costs from our data; 8+ level fusion, chronic kidney disease and malnutrition. This is by virtue of added hospital cost and LOS for index procedure, and being independent risk factors for development of complications, which were shown to add substantially to costs. Readmission can cost as much as 192% the average amount Medicare pays for an uncomplicated multi-level lumbar fusion over 90-days.

Fig 1. 90-day reimbursement for multi-level posterior lumbar fusion - Region wise (Medicare 2005 - 2012)

	NE	SW	SO	WE	OVERALL
No. of Patients (%)	200 (20%)	408 (27%)	476 (18%)	476 (18%)	1562 (100%)
90 Day payment					
Average Payment ± SE					
Facility	\$6,827,740 (\$73,294)	\$6,975,402 (\$74,294)	\$3,209,084 (\$72,294)	\$7,148,824 (\$74,294)	\$73,088,433 (\$74,294)
Index Facility	\$20,847 (\$2,894)	\$19,628 (\$2,894)	\$1,216,627 (\$2,894)	\$8,212,715 (\$2,894)	\$2,288,977 (\$2,894)
Index Facility	\$1,022 (\$1,994)	\$24,777 (\$1,994)	\$79,436 (\$1,994)	\$86,740 (\$1,994)	\$11,439 (\$1,994)
Index Facility	\$22,760 (\$2,994)	\$30,813 (\$2,994)	\$81,181 (\$2,994)	\$20,418 (\$2,994)	\$1,514,548 (\$2,994)
Index Facility	\$1,118,384 (\$2,994)	\$2,098,439 (\$2,994)	\$5,081,843 (\$2,994)	\$2,766,896 (\$2,994)	\$12,766,421 (\$2,994)
Emergency Department	\$24,406 (\$2,994)	\$76,719 (\$2,994)	\$12,522 (\$2,994)	\$6,849 (\$2,994)	\$229,396 (\$2,994)
Index Facility	\$16,487 (\$2,994)	\$1,471,118 (\$2,994)	\$1,418,220 (\$2,994)	\$1,052,718 (\$2,994)	\$7,171,081 (\$2,994)
Index Facility	\$14,433 (\$2,994)	\$106,064 (\$2,994)	\$32,094 (\$2,994)	\$24,861 (\$2,994)	\$1,248,829 (\$2,994)
Index Facility	\$6,416 (\$2,994)	\$11,642 (\$2,994)	\$49,994 (\$2,994)	\$17,491 (\$2,994)	\$68,439 (\$2,994)
Index Facility	\$1,017,112 (\$2,994)	\$2,122,736 (\$2,994)	\$46,406 (\$2,994)	\$2,022,126 (\$2,994)	\$9,088,122 (\$2,994)
Average Per Patient	\$37,545	\$34,889	\$14,437	\$39,395	\$35,878

Fig 2. Adjusted analysis of variation in mean hospital payment for index surgery

	Hospital payment (mean ± SE)
<b>Region</b>	
Northwest	\$27,827 ± \$1,804
Midwest	\$27,421 ± \$1,669
South	\$26,156 ± \$1,628
West	\$31,673 ± 1,664*
<b>Levels of Surgery</b>	
3	\$25,171 ± \$820
4-5	\$28,938 ± \$865*
8+	\$50,507 ± \$1,996*
<b>Comorbidities*</b>	
Chronic Liver Disease	† \$4,905 ± \$1,152*
Chronic Kidney Disease	† \$4,129 ± \$848*
Malnutrition	† \$7,236 ± \$1,859*

\* p<0.05  
† Incremental cost, only significant values given.

Fig 3. Incidence and associated reimbursement for management of intra-operative complications, and complications in readmitted patients

Complications	Incidence N (%)	Total Reimbursement	Length of stay Average (Range)	Average Reimbursement
<b>Intra-operative, in all patients (n=2759)</b>				
Acute post-hemorrhagic anemia	853 (30.9%)	-	-	-
Cauda equina syndrome	35 (1.3%)	-	-	-
Dural tear	113 (4.1%)	-	-	-
Accidental cut/puncture/hemorrhage	91 (3.3%)	-	-	-
<b>Overall</b>	<b>1017 (36.9%)</b>	-	<b>† 6.77 ± 0.63*</b>	<b>† \$3,822 ± \$533*</b>
<b>In readmitted patients (n=165)</b>				
Surgical Site Infection (SSI)	55 (33.3%)	\$2,281,054	6 (5-7) days	\$41,474
Respiratory	49 (29.7%)	\$1,027,118	4 (2-6) days	\$20,962
Cardiac	38 (23%)	\$725,293	3.5 (3-6) days	\$19,087
Abdominal	48 (29.1%)	\$629,625	4.3 (3-12) days	\$13,284
DVT and/or PE	22 (13.3%)	\$588,004	7 (3-27) days	\$26,731
Sepsis	16 (9.7%)	\$1,103,412	7.8 (3-12) days	\$68,963
Renal	61 (37%)	\$1,464,052	6 (1-40) days	\$24,001
Pain/analgesic related	62 (37.6%)	\$1,333,663	3.7 (1-9) days	\$21,511
<b>Overall</b>	<b>59,349,221</b>	<b>4.7 (1-27) days</b>	<b>\$56,662</b>	

\* Incremental value compared to patients without intra-operative complications, p<0.001

Fig 4. Risk Factors for development of complications

Risk Factor	Odds Ratio (OR)	95 % Confidence Interval (CI)	P-value
<b>Multiple Variable Analysis*</b>			
Ischemic Heart Disease	1.2	1.02- 1.4	0.02
Chronic Kidney Disease	1.6	1.2 – 2.1	<0.001
Malnutrition	1.9	1.04 – 3.4	0.03
8+ level fusion	2.3	1.2 – 4.5	0.009
Depression	1.2	1.01 – 1.5	0.03
Inflammatory Arthritis	1.4	1.1 – 1.7	0.005
Tobacco Use	0.6	0.5 – 0.8	<0.001

\*Only significant values given

## Recovery rate of sensory symptoms following decompression of nerve root in cervical vs lumbar radiculopathy – a prospective, self-reported, computerized pain drawing study

Dilip Sengupta

### INTRODUCTION:

**Study Design.** A single-center, retrospective study on prospective, self-reported data.

**Objective.** To compare the speed of recovery of the sensory symptoms, pain, numbness and paraesthesia, following surgical decompression of nerve root in cervical and lumbar radiculopathy.

**METHODS:** This study included 139 lumbar and cervical disorder patients. In lumbar group, there were 95 cases (M 44, F 51, mean age 51.6 yr, range 18-78) with predominant lumbar radiculopathy undergoing discectomy/laminectomy with or without fusion surgery. In cervical group, there were 64 cervical spondylosis patients (M 28, F 36, mean age 51.6 yr, range 33-74) undergoing ACDF/ACF surgery. The patients' self-recorded data including ODI score, SF-36 scores (PCS and MCS), and pain drawing during the preoperative and postoperative visits at 6 weeks, 3 months, 6 months and at 1 year were reviewed. Statistical analysis was performed to compare the recovery speed between different sensory symptoms like pain, numbness and paresthesia in cervical and lumbar groups.

**RESULTS:** In lumbar radiculopathy patients, 86.3% had pain, 75.8% had numbness, 44.2% had paresthesia, and 32.6% had all these three symptoms at baseline. In cervical patients, more patients had pain (87.5%), numbness (85.9%) and paresthesia(62.5%), and 54.6% had all these three symptoms. Pain component improved fastest both in lumbar (56.9% resolved, P=0.000) and cervical (74.6% resolved, P=0.000) at 6 wks after surgery. In lumbar radiculopathy patients, numbness showed a gradual recovery, but in cervical radiculopathy numbness recovered faster, 24.8% resolved during the initial 6 weeks period, 44.5% resolved (P=0.001) between 6 weeks to 3 months. In lumbar group, paresthesia showed a trend of gradual recovery, but in cervical group showed a sharp improvement (60% resolved, p=0.002) during the initial 6 weeks period. In lumbar group, the largest improvement in the ODI score was observed during the initial 3 months following surgery. Similar tendency had been found in cervical group. PCS score and the MCS scores showed the similar trend in cervical and lumbar groups.

**CONCLUSION:** In cervical radiculopathy patients, more patients reported pain, numbness and paresthesia before surgery than lumbar group. Following surgical decompression, pain improved faster than numbness or paresthesia both in lumbar and cervical patients, but decreased faster in cervical group. Numbness and paresthesia had a slower recovery than pain in both groups, but faster was noted in the cervical group. ODI, PCS and MCS showed the similar recovery trend after surgery in both groups.

**REF:** [Huang P, Sengupta DK](#) How fast pain, numbness, and paresthesia resolves after lumbar nerve root decompression: a retrospective study of patient's self-reported computerized pain drawing; [Spine](#) 2014 Apr 15;39(8):E529-36

## Patients' expectations for spine surgery: what are they, are we meeting them and does it correlate to one year postoperative satisfaction

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**Objectives:** The objectives of this national study were to examine the most important change patients expected from their spine surgery, the extent to which patient expectations of spine surgery were fulfilled and to examine the association between unmet expectations and post-operative satisfaction after accounting for socio-demographic and clinical characteristics.

**Methods:** Data from the Canadian Spine Outcomes and Research Network (CSORN) Registry with a primary degenerative spinal diagnosis and 1-year follow-up data were used for analysis (n=1985). Patients indicated on a questionnaire their level of expectation as it related to seven separate dimensions as: no change (0), somewhat better (1), better (2), and much better (3). Patients also indicated which of the seven areas was most important to them. For each dimension, patients reported their overall satisfaction with surgery and whether their expectations were fulfilled at 1 year follow-up. Socio-demographic and clinical variables including pain and back/neck disability scores were also collected. Logistic regression models were fit to examine a) the association between expectations being met and baseline socio-demographic and clinical variables including pre- and post-surgical changes in pain and disability scores, and b) the association between expectations being met with overall satisfaction with surgery (Extremely/Somewhat satisfied vs. Neither/Somewhat/ Extremely dissatisfied) after accounting for socio-demographic, clinical and patient reported outcome variables.

**Results:** 29.5% ranked "improve leg/arm pain", 26.3% ranked "back/neck pain", 21.4% ranked "general physical capacity", and 15.3% ranked "independence in everyday activities" as the most important expected change. No differences were found in the ranking of expectations by demographic or clinical variables. Overall 88.8% of patients reported that their most important expected change was met: 95.8% among those expecting improvement in independence in everyday activities, 94.5% for improvements in sporting activities/recreation, 89.0% and 87.3% for improvements in leg/arm pain and back/neck pain respectively, 85.4% for improvements in general physical capacity, and 82.7% of those expecting improvements in mental well-being. Factors associated with expectations being met were spondylolisthesis diagnosis vs. stenosis and improvements in pre- to post-surgical pain and disability scores (p<0.0001 for all variables). In addition, about 93% of patients who had their most important expectations met were extremely/somewhat satisfied with their surgery vs. 52.2% among those with unmet expectations. Similar trends were seen for each of the expectation dimensions examined. In multivariate analysis, meeting the most important expected change was independently associated with being extremely/somewhat satisfied with the surgery (OR=4.5, 95% CI: 3.2-6.3). In addition, post-operative pain and disability were significantly associated with satisfaction, such that reporting worse post-operative ODI/NDI and/or pain was associated with not being satisfied with surgery.

**Conclusions:** The most important expected change from spine surgery is highly variable across patients. The vast majority of patients reported their most important surgical expectation as being met. While met/unmet expectations were strongly associated with satisfaction/dissatisfaction, this must be considered against a backdrop of 'most important expected change' being highly variable across patients. Preoperative inquiry and education regarding realistic individual patient expectations may be paramount in determining the drivers of individual patient satisfaction with spine surgery.

## Adapting a deep learning model to a different grading system in a new dataset

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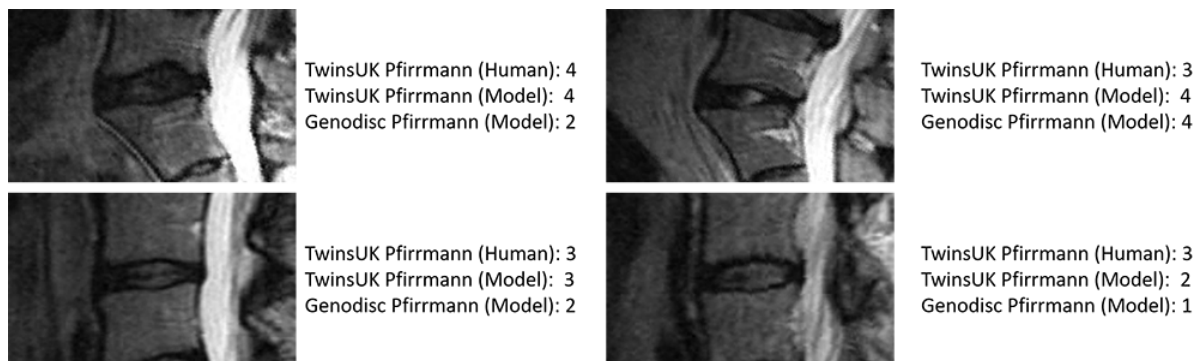
**INTRODUCTION.** Automated radiological grading of the intervertebral discs and the vertebral bodies in lumbar MRIs using deep learning has been proven to be near human performance. However, radiological gradings produced by models trained on one dataset would normally be incomparable to different gradings assessed in a different dataset. In this study, we investigated the possibility of extending a deep learning model trained on the Genodisc dataset by teaching it to read and assess a different grading system in the TwinsUK dataset.

**METHODS.** There are two different study populations: (1) Genodisc consisted of 2009 subjects (mean age  $50.2 \pm 14.6$ , 54.4% female), 12018 discs, with back pain, and (2) TwinsUK consisted of 920 volunteers (mean age  $53.1 \pm 8.5$ , 96.2% female), 6327 discs. Only T2-weighted sagittal scans were used; scans in Genodisc vary in terms of acquisition and protocol unlike scans in TwinsUK. Subjects in the Genodisc dataset were graded with multiple radiological gradings by an experienced radiologist, of which we trained a deep learning model on six: (1) Pfirrmann grading, (2) disc narrowing, (3) spondylolisthesis, (4) central canal stenosis, (5) endplate defects, and (6) marrow signal variations (Modic changes). This learnt model was then trained to read the TwinsUK's definition of Pfirrmann grading (assessed by a different radiologist who assessed the Genodisc dataset) where we used 720 subjects for training and tested our performance on a withheld test set of 200 subjects.

**RESULTS.** For each one out of 200 subjects or 999 discs, in the test set, the model was able to produce not only the TwinsUK definition of Pfirrmann but also the Genodisc equivalent. There was a weighted agreement of 49.0% and a Lin's concordance correlation coefficient of 0.55 between the Genodisc Pfirrmann grading (produced by the model) and the TwinsUK Pfirrmann grading (assessed by a human). We achieved a weighted agreement of 75.6% and a correlation coefficient of 0.74, when comparing TwinsUK Pfirrmann grading produced by the model against human readings which suggests an agreement between the two readings ( $p < 0.005$ ) on the withheld test set. Figure 1 shows several examples of the discs and their gradings in the test set.

**DISCUSSION.** This study has shown that it is possible for a model to adapt and learn a different grading system in a different dataset than it was originally trained for. Hence, we can now compare multiple grading systems across multiple datasets which is extremely beneficial for cross-population studies.

**Figure 1.** Discs in the test set with the corresponding gradings; TwinsUK's definition of Pfirrmann grading assessed by a human, TwinsUK's definition of Pfirrmann grading predicted with model and Genodisc's definition of Pfirrmann grading predicted with the model.



## **A possible mechanism underlying pain-related behavior induced by lumbar facetectomy and repeated cold stress in rats — DNA microarray analysis**

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**INTRODUCTION:** For future effective treatments of discogenic low back pain, a cause of nonspecific low back pain, it is important to evaluate the pathogenesis. However, there are no optimal animal models of nonspecific low back pain caused by intervertebral disc degeneration. We have developed a rat model of low back pain induced by lumbar facetectomy, in which repeated cold stress increases the magnitude of pain-related behavior. This model may be useful for elucidating the pathophysiological mechanisms responsible for nonspecific low back pain. In the present study, we performed DNA microarray analysis to examine the mechanisms underlying the behavioral changes associated with low back pain in this model.

**METHODS:** Rats were divided into four groups: (1) sham group, which received sham surgery (control group), (2) repeated cold stress loading group, which received this stress for 8 weeks postoperatively (S group), (3) facetectomy group, which received L4/5 facetectomy (F group), and (4) L4/5 facetectomy with repeated cold stress loading group, which received L4/5 facetectomy and loaded stress for 8 weeks postoperatively (FS group). The dorsal root ganglion (DRG) at the L4/5 level was harvested in control group at 2 weeks postoperatively and the other groups at 8 weeks postoperatively. Gene expression levels in the DRG were evaluated using DNA microarray analysis. Genes whose expression decreased to less than half or increased by more than double in the DNA microarray analysis relative to the control group were extracted. We made Venn diagrams to compare these factors between the S, F, and FS groups, and evaluated in detail genes expressed specifically in the FS group. Pathway analysis was performed for genes expressed specifically in the FS group using the WikiPathways pathway database.

**RESULTS:** In the S, F, and FS groups, expression of 1295, 1187, and 1497 genes decreased or increased relative to the control group, respectively; 642 were specific to the FS group. Pathway analysis showed that these 642 genes were significantly related to the inflammatory response pathway, G-protein-coupled receptor (GPCR; peptide, class A, rhodopsin-like, monoamine, others), and  $\alpha 6\beta 4$  integrin signaling. These pathways included genes for galanin receptor 1 (GalR1), 5-HT7, 5-HT4, GPCR 84 (GPR84), and GPR44. GalR1, 5-HT7, 5-HT4, and GPR44 expression decreased and GPR84 expression increased relative to the control group.

**DISCUSSION:** These results suggest the involvement of the inflammatory pathway, GPCR, and  $\alpha 6\beta 4$  integrin signaling in pain-related behavior in this model. We focused on the genes for GalR1, GPR84, 5-HT7, 5-HT4, and GPR44, which have been reported to be related to pain or inflammation. Data from previous studies suggest that downregulation of GalR1, 5-HT7, and 5-HT4 might cause reinforcement of pain. Suzuki reported that GPR84 plays a proinflammatory role. Knockdown of glial GPR44 impairs myelination. Collectively, these results suggest that intervertebral disc degeneration induced by facetectomy and stress loading causes inflammation and disordered myelination in the DRG and that the pain is increased under the influence of GalR1, 5-HT7, and 5-HT4. Control of the expression of these genes may have potential for managing pain induced by degenerative disc disease.

SP03

**Melatonin breakdown the vicious circle of IL-1  $\beta$  induced intervertebral disc degeneration by NLRP3 inflammasome inhibition.**

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**Introduction:**

Intervertebral disc degeneration (IVDD) is strongly associated with spinal degenerative diseases, and is the main reason of low back pain (LBP) and leading to disability. Melatonin (N-acetyl-5-methoxytryptamine), a hormone is a hormone with complex roles in the pathogenesis of different disorders, has been confirmed that melatonin exerts anti-inflammatory, anti-degeneration, anti-oxidant and immune-enhancing effects in vitro and in vivo. NLRP3 inflammasome, the unique family member of NLRs, composed with other intracellular molecules such as inflammatory caspases and apoptosis-associated speck-like protein containing a CARD (ASC), generated cytokines, such as IL-1  $\beta$  and IL-18. This report is the first time study melatonin and the cytokines – NLRP3 inflammasome – cytokines axle in IVDD. The objective of the study is to investigate melatonin attenuate intervertebral disc degeneration through suppressing NLRP3 inflammasome activation in vivo and vitro.

**Methods:**

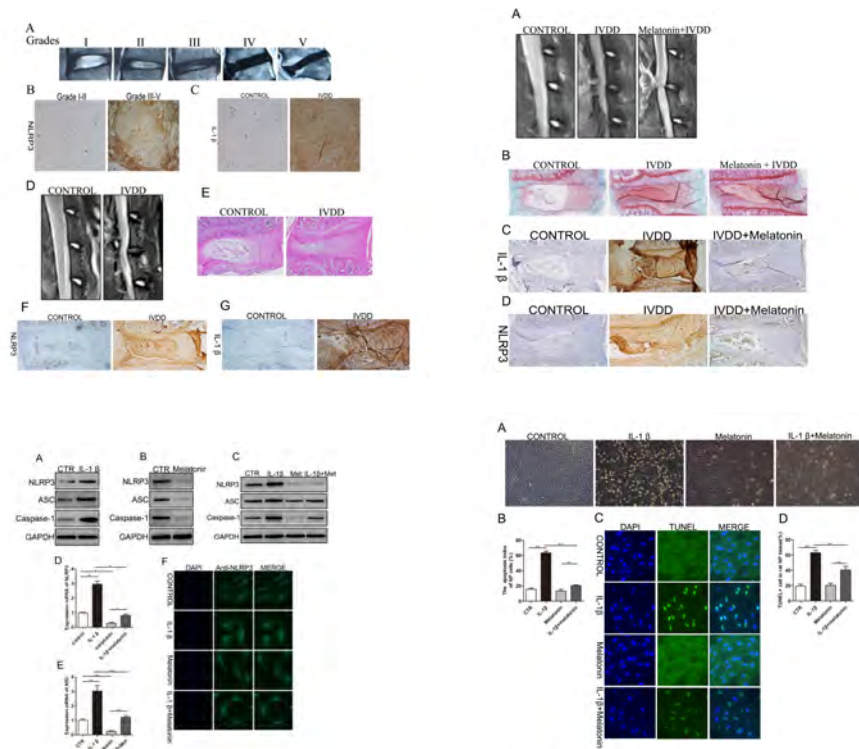
A rat IVDD model was established to confirm the effect of melatonin on IVDD. MRIs, H&E staining, safranin O and fast green and immunohistochemistry staining were used to detect the role of melatonin and NLRP3 inflammasome in disc degeneration. Western blot was used to confirm the role of NLRP3 inflammasome in IL-1 $\beta$  induced IVDD cellular model. The role of melatonin attenuated the NLRP3 inflammasome activity on IVDD was revealed by Western blots, RT-qPCR and immunofluorescence staining. The mechanism of melatonin prevents disc degeneration through suppressing NLRP3 inflammasome activation by cellular morphology observing and TUNEL staining.

**Result:**

In human and rat disc samples, the expression of the specific markers NLRP3 and IL-1 $\beta$  provide the first demonstration that NLRP3 inflammasome was activated in IVDD. Furthermore, in a needle puncture-induced rat IVDD model, the application of melatonin prevented IVDD development in vivo. Melatonin application attenuated IVDD by inhibiting NLRP3 inflammasome activation in vivo. NLRP3 inflammasome was significantly activated in an IL-1 $\beta$ -induced IVDD cellular model, and melatonin antagonized this effect in IVDD cellular model. Following melatonin attenuated IVDD cellular model induced NP cells apoptosis.

**Discussion:**

This study first confirmed that melatonin prevented IVDD by inhibiting NLRP3 inflammasome activation both in vitro and in vivo. Another major finding of our research was that melatonin attenuated IVDD cellular model induced NP cells apoptosis. Our study might provide a possible therapeutic target for controlling the development or progression of IVDD.



## **Temsirolimus is a candidate of the optimal mTOR inhibitor to protect human disc cells depending on Akt and autophagy induction**

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**INTRODUCTION:** The mammalian target of rapamycin (mTOR) is a serine/threonine kinase that plays a central role in cell growth and protein synthesis. We previously reported protective effects of RNA interference mTOR on human disc cells. However, in clinical use, pharmacological intracellular signal modulation is favorable compared to gene therapy because of the safety issue. More importantly, it remains unknown which signal(s) substantially provides beneficial effects of mTOR suppression. Therefore, a human disc-cell study was designed to identify the most suitable mTOR inhibitor and its plausible mechanistic explanation to treat disc disease.

**METHODS:** Human disc nucleus pulposus cells were isolated from 28 patient specimens undertaking lumbar surgery (65.0±13.8 years; male:female=12:16; Pfirrmann degeneration grade, 3.4±0.5). Cells were cultured in DMEM with or without serum to simulate nutrient deprivation. Also, 10-ng/ml IL-1β was applied to simulate inflammation. Four mTOR inhibitors—rapamycin, temsirolimus, everolimus, and curcumin—and an allosteric Akt inhibitor, MK-2206, were applied. Cell viability was investigated by using the Cell Counting Kit-8 (CCK-8). Expression and phosphorylation of mTOR and its down-stream effector p70/S6K and upstream regulator Akt were assessed by Western blotting. Autophagy marker LC3-II and substrate p62/SQSTM1 were also evaluated. Apoptotic cleaved PARP, cleaved caspase-9, and senescent p16/INK4A in cell lysates and catabolic MMPs and anti-catabolic TIMPs in culture supernatants were analyzed similarly. TUNEL and senescence-associated beta-galactosidase (SA-β-gal) staining was performed to determine apoptosis and senescence levels. Anabolic *aggrecan* and *collagen* gene expression relative to *GAPDH* was assessed.

**RESULTS:** Rapamycin, temsirolimus, and everolimus showed dose-dependent decreases in CCK-8 dehydrogenase activity ( $P<0.01$  in  $>1 \mu\text{M}$ ). Based on the CCK-8 findings, 100 nM in every agent was selected as an effective but non-toxic concentration. Western blotting showed that rapamycin, temsirolimus, and everolimus decreased mTOR and p70/S6K but increased Akt phosphorylation ( $P<0.05$ ). Rapamycin, temsirolimus, and everolimus increased LC3-II and decreased p62/SQSTM1 ( $P<0.05$ ), consistent with autophagy induction. The degree of autophagy induction was more evident by temsirolimus ( $P<0.05$ ). Western blotting showed that all the agents suppressed IL-1β-induced increases in apoptotic cleaved PARP and caspase-9 and senescent p16/INK4A expression ( $P<0.05$ ). This trend was more distinct in rapamycin, temsirolimus, and everolimus than curcumin. Similar findings were observed in TUNEL and SA-β-gal staining ( $P<0.05$ ). Furthermore, all these agents suppressed IL-1β-induced release in MMPs and TIMPs ( $P<0.05$ ). In real-time RT-PCR, IL-1β-induced down-regulation of *aggrecan* and type-II collagen was rescued by rapamycin, temsirolimus, and everolimus ( $P<0.05$ ). These findings suggest temsirolimus as the optimal mTOR inhibitor. Then, in mechanistic examination, administration of MK-2206 increased Akt phosphorylation by temsirolimus ( $P<0.05$ ). Unlike temsirolimus, combined temsirolimus and MK-2206 developed additional increases in IL-1β-induced apoptosis and senescence ( $P<0.05$ ). Moreover, IL-1β-induced MMP production was suppressed by temsirolimus but enhanced by combined MK-2206. These findings highlighted the importance of Akt in this signaling pathway.

**DISCUSSION:** Protective effects of mTOR inhibitors against apoptosis, senescence, and matrix catabolism in human disc cells is the most remarkable in temsirolimus. These actions are primarily through Akt induction. Pharmacologically, temsirolimus has an improved water solubility, allowing intravenous/local administration. Thus, temsirolimus is a potential therapeutic application to human disc disease.

## Validation of anti-inflammatory and regenerative drug therapy in a bioreactor-guided intervertebral disc organ culture model

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**Introduction:** Low back pain (LBP) is the leading cause of disability worldwide, exerting a substantial health care problem and socioeconomic impact. LBP is frequently attributed to intervertebral disc (IVD) degeneration; while there is increasing evidence that inflammatory mediators, such as tumor necrosis factor alpha (TNF- $\alpha$ ) play a key role in the progression of painful IVD degeneration. The aims of this study were (I) to investigate the interplay between inflammation and degeneration within a loaded whole IVD organ culture system; (II) to investigate the anti-inflammatory and anti-catabolic effect of the TNF- $\alpha$  antagonist Etanercept in the organ culture model.

**Methods:** Part I: Bovine caudal IVDs were cultured within a bioreactor for 4 or 11 days. The control group (Phy) was cultured under physiological loading (0.02-0.2 MPa; 0.2 Hz; 2h/day) and high glucose (4.5 g/L) medium. In the degenerative group (Deg), detrimental loading (0.32-0.5 MPa; 5 Hz; 2h/day) and low glucose (2 g/L) medium was applied to mimic the condition of abnormal mechanical stress and limited nutrition. TNF- $\alpha$  was injected into the nucleus pulposus (NP) (100 ng/IVD) as proinflammatory trigger. Expression of inflammatory, anabolic and catabolic genes, release of nitric oxide (NO), cytokines and glycosaminoglycan (GAG), and cell viability were assessed. Part II: Etanercept (3.5 mg/70  $\mu$ L/IVD) or phosphate buffered saline (PBS) (70  $\mu$ L/IVD) were injected into the IVD cultured under Deg+TNF- $\alpha$  conditions. After 4 days, the effect of Etanercept on gene expression and molecule release from IVD cells was analyzed. One-way ANOVA or Kruskal-Wallis tests were used to determine statistical differences.

**Results:** Part I: TNF- $\alpha$  injection combined with detrimental loading and low glucose medium significantly upregulated the expression of interleukin (IL)-1 $\beta$ , IL-6 and IL-8 genes in cells of the organ cultured IVD; moreover, NO and IL-8 release from IVD was increased, indicating a proinflammatory effect (all  $p < 0.05$  vs. Phy). The combined initiators also significantly up-regulated matrix metalloproteinase 1 (MMP-1) gene expression, downregulated gene expression of type I collagen in annulus fibrosus and type II collagen in NP ( $p < 0.05$  vs. Phy). Furthermore, the combined treatment induced a degradative reaction, as indicated by markedly higher GAG release into conditioned medium. Deg culture condition with/without TNF- $\alpha$  reduced cell viability to around 40% in AF and 60% in NP ( $p < 0.05$  vs. Phy).

Part II: Compared with the Deg+TNF- $\alpha$  group, injection of Etanercept partially reduced the release of GAG and NO from disc tissue. Degenerative culture conditions and TNF- $\alpha$  injection upregulated the expression of catabolic enzyme MMP-1, proinflammatory cytokines IL-1 $\beta$ , IL-6, and IL-8, cyclooxygenase-2 (COX-2), and nerve growth factor (NGF); whereas Etanercept injection partially reduced these effects.

**Discussion:** The combination of detrimental dynamic loading, nutrient deficiency and intradiscal TNF- $\alpha$  injection could synergistically simulate the proinflammatory and degenerative condition within a degenerative IVD, demonstrating the potential of our whole IVD organ culture model for testing of anti-inflammatory or regenerative therapies. Etanercept showed the ability to slow down the degenerative response and reduce inflammation in the organ culture model, though combined anti-inflammatory and anabolic treatment may be required to completely halt or reverse the degenerative process.



## Role of PHLPP1 in cell proliferation and apoptosis in intervertebral disc and vertebrae

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### INTRODUCTION:

Back pain is a major socioeconomic burden and often related to intervertebral disc (IVD) degeneration (IDD)<sup>1</sup>. Hallmarks of advanced IDD include cell loss and fissure formation. The Akt pathway plays essential roles in IVD cell survival<sup>2</sup>. The recently discovered phosphatase PH-domain leucine rich repeat protein phosphatase-1 (Phlpp1) plays an important role in cell proliferation by dephosphorylating Akt thereby inducing cell-death, and contributing to pathologies like osteoarthritis<sup>3</sup>. Nothing is known about its role in IDD. We hypothesize that Phlpp1 is a key factor in IVD cell proliferation and apoptosis. This study investigated a relationship between Phlpp1 expression with degeneration grade in human IVDs and mechanistically evaluated its effect on IVD cellularity during growth and maturation using Phlpp1-knockout (KO) mice.

### METHODS:

Histological sections of Human IVDs (Thompson grades 1-4; Fig.1) were assessed immunohistochemically for Phlpp1 and active-Caspase-3 (apoptosis). Lumbar spines of C57BL/6J wild-type (WT) and Phlpp1-KO mice were harvested with approval of the IACUC at Mount Sinai. Spinal morphology of adolescent (1-month) WT and Phlpp1-KO mice was assessed histologically for IVD morphology (Picrosirius-Red/Alcian-Blue), skeletally mature (6-months) lumbar (L4-5) vertebrae were assessed for Bone mineral density (BMD; DEXA; n=2/group), disc height index (DHI; n=6/group) and vertebral length (x-ray; n=6/group). Differences in human Phlpp1 expression were evaluated using linear regression analysis, Spinal morphology in mice was analyzed via Student's t-test.  $p < 0.05$  determined statistical significance

### RESULTS:

In human IVDs, Phlpp1 expression was positively and strongly correlated with degeneration (Fig.1) and often localized close to fissures and injured areas of degenerated IVDs (n=8, Fig.2). Expression of active-Caspase-3 (n=2) was often observed in areas that were also Phlpp1 positive (Fig.2). Compared to adolescent WT mice, Phlpp1-KO mice had an increased notochordal-band area (n=6/group; Fig.3) and increased cellularity in the proliferative zone of the vertebral growth plate ( $p=0.049$ ). Skeletally mature Phlpp1-KO mice had increased BMD (14%, n=2) and increased lumbar (L4) vertebrae length (WT:  $3.05 \pm 0.1$ , KO:  $3.34 \pm 0.06$ ;  $p=0.045$ ). No differences were observed between DHI ( $p=0.575$ ).

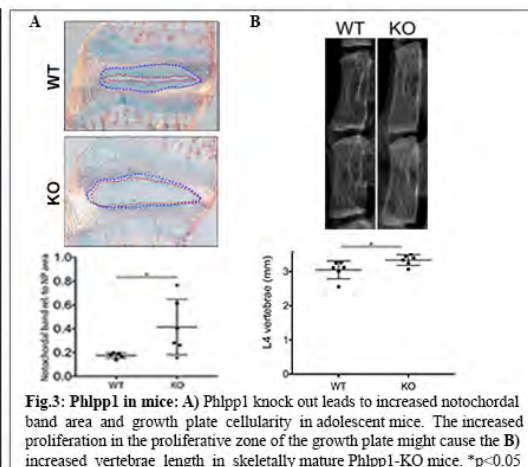
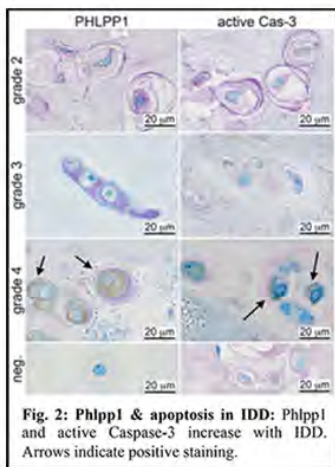
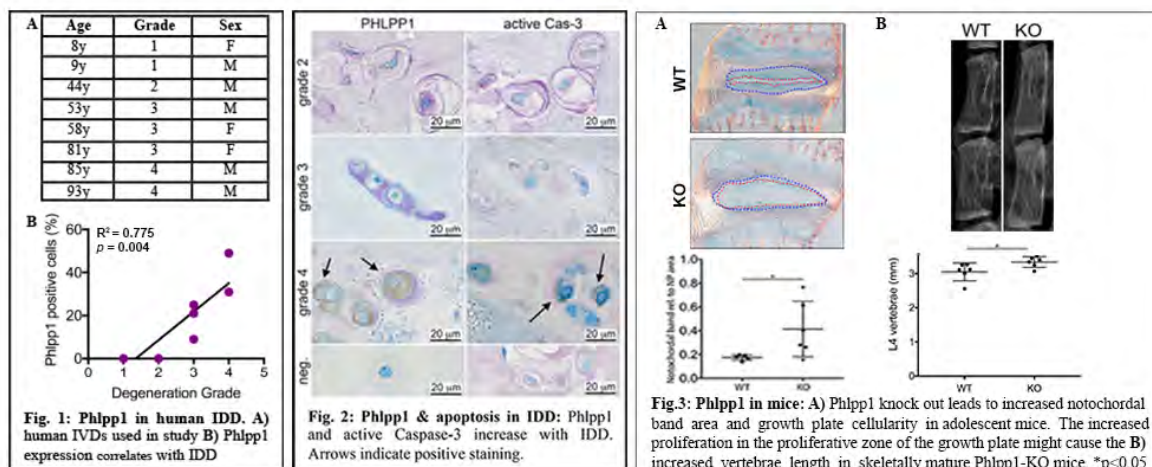
### DISCUSSION:

Phlpp1 expression strongly correlated with IDD in human IVDs, suggesting a role of Phlpp1 in regulating apoptosis during advanced IDD, while cell proliferation during attempted healing might not be regulated by Phlpp1. Increased proliferation in Phlpp1-KO IVDs strongly suggests a role of Phlpp1 in regulating proliferating cells during IVD growth and likely explains the increased BMD and vertebrae length; while the lack of phenotypic differences in IVDs of skeletally mature Phlpp1-KO and WT mice is likely due to the quiescent nature of healthy NP cells at this age. We conclude that Phlpp1 plays a key role in controlling cell proliferation and apoptosis during IVD growth and degeneration. Future studies will better understand roles that Phlpp1 plays in regulating cell proliferation and apoptosis at varying ages and degeneration levels. Investigations of Phlpp1 will provide insights into cellular processes of IDD-progression and may provide a novel target for pharmacological intervention.

### REFERENCES:

<sup>1</sup>Vos+ Lancet 2012, <sup>2</sup>Wang+ Exp.Cell.Res. 2016, <sup>3</sup>Bradley+ J.Biol.Chem 2013

**ACKNOWLEDGEMENTS:** Funded by NIH/NIAM R01 AR069315, AR68103, and Dept. of Orthopaedics at Mount Sinai. Phlpp1-KO mice originated from Dr. Newton, UC, San Diego.



## How does transition zone structure influence the herniation process?

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### INTRODUCTION

Our recent investigation found that defects in the posterior mid and inner annulus (visualised with 11.7T micro-MRI) were associated with herniations when discs were subjected to complex loading, implying that this region plays an important role in the herniation process. Exposure to complex loading also created similar defects in previously intact discs. The present study aimed to investigate whether these defects influenced the resulting herniation at the microstructural level. A parallel aim was to use a multi-scalar approach to explore the transition zone (inner annulus and nucleus) of healthy discs to better characterise its architecture and identify potential reasons for failure.

### METHODS

Microstructural examination was performed on 30 mature (3-5 year old) ovine lumbar motion segments exposed to complex loading conditions which had caused 11 to suffer nucleus migration or herniation apparent under 11.7T micro-MRI. Fixation and decalcification enabled discs to be cryosectioned and imaged with standard light microscopy. A further 15 healthy lumbar discs were imaged with micro-MRI, after which the transition zone of the disc was isolated from the endplates and fixed under load to capture detail in a single imaging plane. They were then cryosectioned and examined using light microscopy. From these samples, 18 sections were selected for detailed investigation with scanning electron microscopy.

### RESULTS

All but one of the tested discs suffered outer annulus failure visible at the microstructural level. Those discs that suffered herniation or migration of the nucleus exhibited failure of alternate lamellae in the mid and outer annulus (Figure 1). Those discs which had not suffered migration exhibited delamination and disruption of the lamellae visible at the microstructural level (Figure 2). Micro-MRI imaging of the healthy, untested discs revealed bundles of radially oriented fibres penetrating the inner annulus around the periphery of the nucleus. Ultrastructural investigation revealed that these bundles consist of nucleus fibrils branching out at multiple radial depths and interweaving with the lamellae of the inner annulus.

### DISCUSSION

Microstructural analysis showing the mid and inner annulus lamellae remaining continuous following testing indicate that this region was able to contain the pressure generated within the nucleus. That discs failed when it was compromised shows that it plays an important role in redistributing loads within the disc, thus preventing immediate herniation under the acute loading. However, the observation of disruption and delamination of the lamellae following testing indicates that it is vulnerable to fatigue type damage.

Ultrastructural investigation of the transition zone of intact discs shows for the first time how the three-dimensional network of the nucleus is interwoven with the lamellae of the annulus. When correlated with micro-MRI images it is apparent that this integration occurs at multiple radial depths across the annular wall. This illustrates both how this network facilitates load transfer within the disc and how it could be vulnerable to repetitive loading regimes causing relative motion between lamellae.

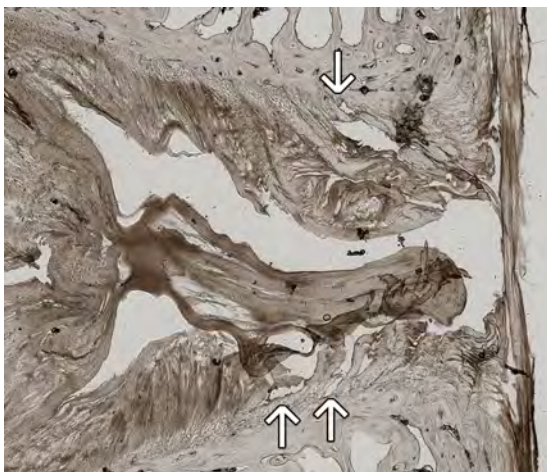


Figure 1: Subligamentous herniation with alternate lamella failure in mid annulus-endplate region indicated with arrows



Figure 2: Disc without nucleus migration but mid and inner annulus disruption highlighted in red.

## Incidence of intervertebral vacuum phenomenon in the general population and in patients with lumbar spondylolysis.

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**Introduction:** The vacuum phenomenon, a collection of gas within the intervertebral disc, is considered to be the end stage of disc degeneration. Vacuum phenomenon is uncommon in young patients, however, is commonly observed in the elderly, low back pain patients, and the discs adjacent to fractured vertebrae. Disc degeneration is commonly observed in patients with lumbar spondylolysis, thus, we hypothesized that vacuum phenomenon is more frequently observed in the discs adjacent to spondylolysis. At this moment, there is no detailed information about age-specific incidence of vacuum phenomenon. First, we investigated the incidence of vacuum phenomenon in the general population. Second, we examined the incidence of vacuum phenomenon in the discs adjacent (cranial and caudal) to the spondylolysis, and comparison with the general population was performed.

**Methods:** Patients undergoing computed tomography (CT) scans of abdominal or lumbar regions for reasons other than low back disorders were included (n=566). Patients whose ethnicity was not Japanese were excluded. Sagittal multiplanar reconstruction CT images were obtained and the lumbar intervertebral discs (L1-L2 to L5-S1) were evaluated. First, the incidence of vacuum phenomenon in all the patients (regarded as general population) was examined. Second, the incidence of vacuum phenomenon in patients with spondylolysis was examined and compared with that of general population.

**Results:** Of the 2830 discs from 566 patients (mean age: 64.3  $\pm$  18.9 years-old; 327 men/239 women), 641 discs (22.7%) showed vacuum phenomenon. Percentage of discs showing vacuum phenomenon at each disc level was as follows; L1-L2, 17.3%; L2-L3, 20.3%; L3-L4, 20.3%; L4-L5, 28.9%; L5-S1, 26.3%. The age-specific incidence of vacuum phenomenon within the lumbar spine is as follows; 20-29 years-old, 0%; 30-39, 2.8%; 40-49, 16.0%; 50-59, 30.4%; 60-69, 57.8%; 70-79, 66.4%, and 80-89, 80.6%. Of the 566 patients, 37 patients (mean age: 63.8  $\pm$  22.2 years-old; 26 men/11 women) had spondylolysis. The percentages of vacuum phenomenon in the discs adjacent to the spondylolysis were 21.6% at the cranial discs and 40.5% at the caudal discs. The caudal discs showed a tendency toward higher incidence of vacuum phenomenon as compared with cranial discs (p=0.078) and the general population (p<0.05).

**Discussion:** Our study revealed the age-specific incidence of intervertebral vacuum phenomenon in the general population. The results suggest that the incidence increased in the lower lumbar levels, and intervertebral vacuum phenomenon is rarely present in patients younger than 40 years-old, however, over half of patients over 60 years-old showed vacuum phenomenon at least one level. Increased incidence at the level caudal to the spondylolysis suggests that increased mechanical stress due to spondylolysis causes severe degeneration at the disc caudal to the spondylolysis.

## Follow-up study of condoliase treatment in patients with lumbar disc herniation

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### INTRODUCTION

We previously conducted two multicenter, randomized, double-blind, placebo-controlled trials that demonstrated the efficacy and safety of condoliase for up to 12 months after single-dose administration in patients with lumbar disc herniation (LDH). Here, we report results of additional follow-up study to evaluate long-term safety and efficacy of condoliase.

### METHODS

This study was conducted at 44 sites in Japan. All subjects of Phase II/III or Phase III studies conducted in Japan who received the investigational drug (condoliase or placebo) were asked to participate. Subjects were either interviewed by telephone or asked in person at the study site whether they underwent any lumbar spine surgery after administration of the investigational drug. The following variables were investigated in the subjects who could visit the study sites: (1) presence/absence of lumbar spine instability and (2) clinical symptoms and dysfunction at the time of this follow-up study. Lumbar spine instability was evaluated by the investigator in each study site based on X-ray or magnetic resonance imaging findings obtained in accordance with the predetermined imaging protocol. The acquired images were sent to a central imaging facility, where they were processed and evaluated independently. Disc height, posterior intervertebral angle, vertebral translation, and Modic change were assessed following the same procedures as in our previous studies. The investigators assessed clinical symptoms and dysfunction. In addition, subjects performed self-evaluations using the Oswestry Disability Index (ODI).

### RESULTS

Among 356 patients who participated in either of the previous two trials (combined: 228 in the condoliase and 128 in the placebo group), 176 (108 in condoliase and 68 in placebo group), were available for the present study (follow-up rate: 49.4%). The mean follow-up period was  $43.9 \pm 22.5$  (maximum 80.7) months after administration of the investigational drug. In both the condoliase and placebo groups, 24 patients each underwent surgery mostly due to insufficient improvement of leg symptoms, and most surgeries (>70%) were performed within 6 months of administration in both groups. The rate of salvage surgery was significantly lower in the condoliase than in the placebo group (13.4% vs. 20.7%; log-rank test,  $p=0.0206$ ). The mean decrease of disc height in the condoliase group was  $17.14 \pm 13.00\%$  at the follow-up evaluation. There was no significant progression of disc space narrowing after 1 year. In addition, no significant time interval changes in posterior intervertebral angle or vertebral body translation were observed, and there were no patients who underwent surgery for spinal instability in either group. The mean changes in ODI scores from the time of initial trials to that of this follow-up evaluation were greater in the condoliase than placebo group ( $-32.7 \pm 18.6\%$  vs  $-24.7 \pm 15.0\%$ ,  $p=0.003$ ).

### DISCUSSION

No significant differences in long-term imaging findings between the condoliase and the placebo group were observed. There was no aggravation in clinical symptoms that affected long-term outcomes. Furthermore, greater improvements of ODI scores were maintained in condoliase group over the long-term follow-up period. The results of present study revealed that there were no significant long-term safety issues after single administration of condoliase.

SP10

**A small molecule inhibitor of the Wnt pathway (SM04690) as a potential treatment for degenerative disc disease**

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**Introduction:**

Degenerative Disc Disease (DDD) involves degeneration of intervertebral disc structure, including the nucleus pulposus (NP), annulus fibrosus (AF), and cartilage matrix. Wnt signaling plays an important role in DDD, regulating the proliferation and differentiation of resident NP cells. SM04690, a novel, small-molecule, Wnt pathway inhibitor was evaluated in preclinical studies to determine its potential to induce proliferation and differentiation of NP cells, thereby promoting disc healing.

**Methods:**

Wnt pathway inhibition was measured using a cell-based reporter assay. *In vitro* proliferation of rat NP cells was measured by cell doubling index (CDI= cell number/initial cell number/days). Differentiation of NP cells into 'chondrocyte-like' NP cells was measured by Alcian blue absorbance based quantification. The effect on myofibroblast differentiation was assessed in TGF-β stimulated human dermal fibroblasts by measuring smooth muscle actin (αSMA) using immunocytochemistry. Pharmacokinetics were evaluated by intradiscal injection in rats, followed by analysis of compound concentrations in the disc and plasma. *In vivo* efficacy following a single intradiscal injection of SM04690 was evaluated in a rat coccygeal intervertebral disc needle puncture model of DDD<sup>1</sup> using radiographic measurement of disc height index (DHI = disc height/vertebral height), and histological scoring (total 4-16) of Safranin O- stained sections for AF integrity, AF and NP border, cellularity, and NP matrix.

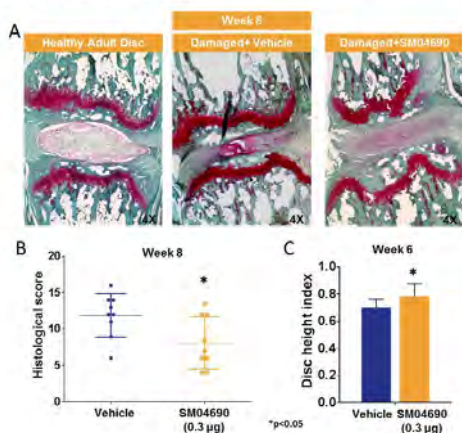
**Results:**

SM04690 was a potent (EC<sub>50</sub>=11nM) inhibitor of Wnt signaling. *In vitro*, SM4690 induced dose-dependent proliferation of NP cells with CDI ~2-fold greater than vehicle (p<0.05). Cells treated with SM04690 also showed significantly increased Alcian blue absorbance vs. vehicle (P<0.01), indicating differentiation to "chondrocyte-like" cells and production of proteoglycan components of the extracellular matrix (ECM). SM04690 inhibited TGF-β1-induced expression of α-SMA (EC<sub>50</sub>=16.7 nM). Single intradiscal injection of SM04690 resulted in disc concentrations >EC<sub>50</sub> for >180 days, with minimal systemic exposure or toxicity, measured as behavioral health, morphology and microscopic changes. In the rat DDD model, a single intradiscal injection of SM04690 (0.33µg/disc) increased Safranin O/Fast Green stained cartilage matrix (Figure A), and decreased histology scores at 8 weeks (P<0.05; Figure B), indicating reduced AF lamellar disorganization and fragmentation, larger NP area, increased cellularity of NP and increased ECM vs. vehicle control. Radiographic measurement of disc height demonstrated significantly increased DHI at 6 weeks (P<0.05; Figure C) in SM04690-treated rats as compared to vehicle.

**Discussion:**

Wnt signaling plays a critical role in the progression of DDD as well as NP cell differentiation and disc regeneration. SM04690, a small molecule Wnt pathway inhibitor, promoted proliferation and differentiation of NP cells and prevented myofibroblast differentiation *in vitro*. In a rat model of DDD, single intradiscal injection of SM04690 partially reversed disc degeneration with regenerated NP cells and cartilage matrix, and improved disc height, health and shape compared to vehicle, with minimal exposure in the plasma and systemic toxicity. These results suggested that SM04690 has potential as a treatment for DDD. A phase 1 clinical trial is ongoing.

Figure: SM04690 stimulated differentiation of NP cells and improved disc height and health in a rat model of DDD



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## Detailed T2-mapping analysis reveal differences in IVD characteristics between low back patients and controls

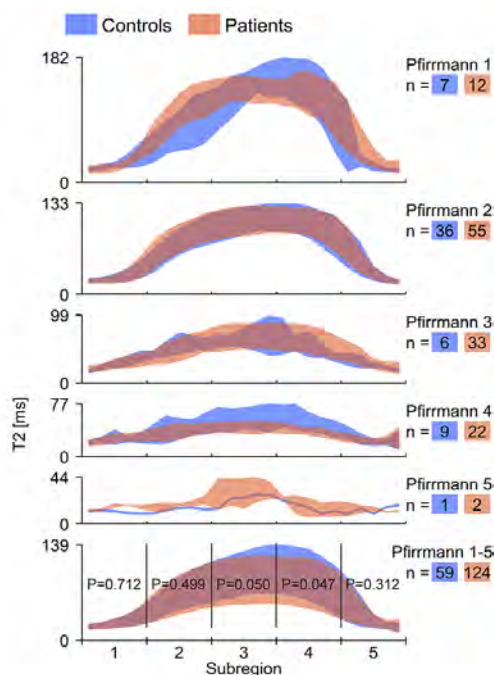
Christian Waldenberg, Hanna Hebelka, Helena Brisby, Kerstin Lagerstrand

**Introduction** T2-mapping based on MRI can provide objective continuous intervertebral disc (IVD) measures in patients with low back pain (LBP). However, there are limited studies comparing such quantitative IVD measures of symptomatic and asymptomatic individuals. Accordingly, the aim was to analyse T2-maps in detail to seek for possible differences in IVD functionality between LBP-patients and asymptomatic individuals.

**Methods** Twenty-five LBP-patients (25-69y, mean 38y, 11 males, 124 IVDs, 20 of which have HIZ) and 12 matched controls (25-59y, mean 38y, 7 males 59 IVDs, 4 of which have HIZ) were examined with T2-mapping on a 1.5T MRI scanner (Siemens Magnetom Aera, Erlangen, Germany). All IVDs were Pfirrmann graded by an experienced radiologist. The mean T2-value and standard deviation (SD) were determined for the entire IVD and for five sub-regions dividing each IVD into equal parts in the sagittal plane. Histogram analysis, proposed by Waldenberg et al. [1], was also performed to provide additional quantitative metric ( $\Delta\mu$ ) describing the IVD tissue structure.

**Results** For the entire IVD, the T2-value, SD and  $\Delta\mu$  decreased with increasing degeneration in both cohorts. Significant difference in T2-value was found between the cohorts regarding Pfirrmann grade 4 ( $P=0.007$ ). On a group level, patient IVDs reached lower mean values for all metrics when compared to controls, with significant differences for SD ( $P=0.026$ ) and  $\Delta\mu$  ( $P=0.048$ ), but no significant difference for the T2-value ( $P=0.115$ ). Significantly different T2-value was found between the cohorts in sub-region 4 ( $P=0.047$ ) and was close to significant in sub-region 3 ( $P=0.050$ ) (Figure 1). When excluding IVDs with HIZ from the analysis, no significant differences between the two cohorts could no longer be found for any of the analysed metrics ( $P=0.053-0.995$ ).

**Discussion** In this study, detailed T2-mapping analysis revealed relevant differences in the T2-value between LBP-patients and matched controls within the sub-regions occupied foremost by nucleus pulposus. However, no significant difference was found between the cohorts when HIZ IVDs were excluded in the analysis. Thus, also detailed T2-mapping analysis mainly reflect IVD degeneration. The relation between presence of HIZ and T2-differences found between the cohorts regarding the nucleus pulposus region may reflect altered function of the IVD. Future studies are recommended to further explore detailed MRI analysis for assessment of IVD functionality and to further investigate the relation between HIZ and LBP.



**Figure 1.** Distribution of T2-relaxation time in different volumes of the IVD. Controls (blue) and patients (red) are sorted and compared by Pfirrmann grades ranging from 1 (anterior) to 5 (posterior) and also grouped in Pfirrmann grades 1-5. The height of each patch represents mean data  $\pm$  one standard deviation. The number of IVDs in each group is denoted with n. In the bottom graph (Pfirrmann 1-5), significance was tested between patient and control data for each sub-region.

1. Waldenberg, C., et al., MRI histogram analysis enables objective and continuous classification of intervertebral disc degeneration. *European Spine Journal*, 2017.

## MicroRNA-19b with special expression profile in osteoporotic patients regulates osteogenic differentiation

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### INTRODUCTION

MicroRNAs (MiRNAs), small non-coding RNA ~22 nucleotides found in plants, animals, and certain viruses, regulate gene post-transcriptional expression by curbing mRNA translation and promoting mRNA deterioration. Recent years, the roles of miRNAs in bone homeostasis have attracted extensive attention and showed significant promise for the rescue of bone disorders. Here we investigated miRNA-19b in the plasma of osteoporotic patients with/without vertebral fractures compared to the non-osteoporotic control group and acquired distinct serum miRNA profile. The functional role of miR-19b in osteoblast differentiation was determined using miR-19b mimic/inhibitor and the expression of osteoblast differentiation marker genes including ALP, OCN and Runx2. We further identified that the PTEN 3'UTR is directly targeted by miR-19b using the luciferase reporter gene system. The expression of PTEN was decreased at mRNA and protein levels by miR-19b mimic. Hence, based on the research, we suggest that miR-19b can act as a positive regulator for osteogenesis.

### METHODS

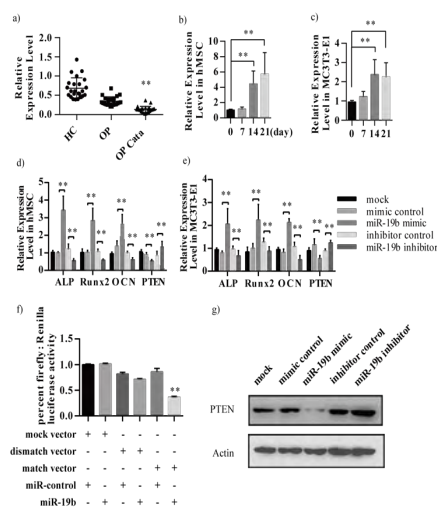
QRT-PCR was established on an independent sample set, which was consisted of plasma samples from 24 osteoporotic patients with vertebral fractures, 24 osteoporotic patients without fracture and 24 non-osteoporotic patients to compare the expression level of miR-19b. The Clinical Research Ethics Committee approved this study, and the candidates read and signed an informed consent according to the regulations of the Institute of Health Research, Shenzhen People's hospital. We next examined the changes in the expression of miR-19b during different stages of human MSCs (hMSCs) and MC3T3-E1 cells osteoblastic differentiation, namely at day 0, 7, 14 and 21. We further analyzed the functional role of miR-19b during osteoblast differentiation by overexpression and knockdown of miR-19b in the hMSCs and MC3T3-E1. The transfected cells were collected at day 6 in osteogenic medium followed by QRT-PCR analysis for OCN, ALP, Runx2 and PTEN. Dual-luciferase reporter system were used to identify the target gene of PTEN. Finally, we observed the change of PTEN protein by western blot.

### RESULTS

The overall relative expression levels of miR-19b between samples of osteoporotic patients and non-osteoporotic samples are shown in Fig. 1 a. The result (Fig.1 b&c) showed that the expression level of miR-19b was 4–9 fold and 2-4 fold up-regulated during osteogenic differentiation of hMSCs and MC3T3-E1 cells, respectively. When cells were transfected with miR-19b mimic, mRNA expression of OCN, ALP and Runx2 were increased. On the contrary, the transfection of miR-19b inhibitor resulted in the decreased mRNA level of OCN, ALP and Runx2 (Fig 1 d&e). PTEN was identified as a target gene for miR-19b (Fig 1 f). The level of PTEN protein was also proved to be regulated by miR-19b treatment (Fig 1 g).

### DISCUSSION

The role of miR-19b in bone remodeling process has not been investigated. In this study, miR-19b presented an osteogenesis-stimulating effect with a special expression profile in patients. Hence, we demonstrated the positive role of miR-19b in the process of osteogenesis.



## Clinical and radiographic features of subtypes of proximal junctional failures following correction surgery for degenerative adult spinal deformity

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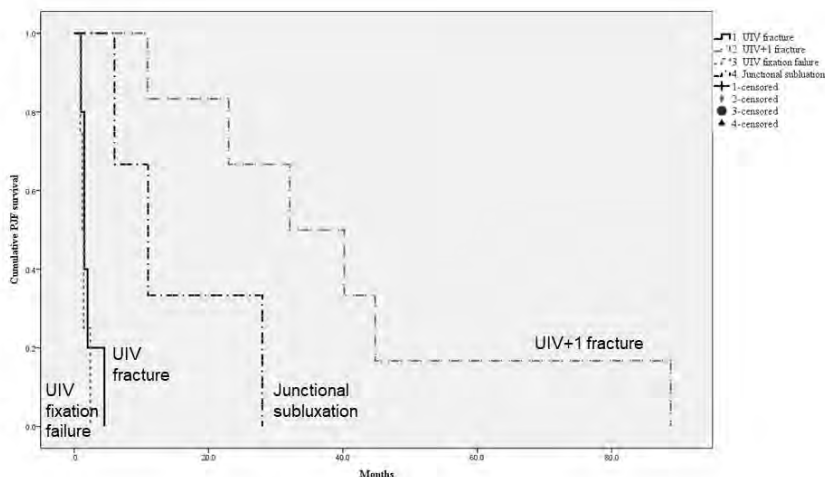
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**Introduction:** Proximal junctional failures (PJFs) following correction surgery for degenerative adult spinal deformity (ASD) may cause catastrophic results.<sup>1</sup> To avoid PJFs, risk factors have been investigated.<sup>2-4</sup> However, there is a paucity of reports on clinical features of each form of PJFs.<sup>5</sup> The purpose of this study is to identify clinical and radiographic features of each subtype of PJFs following correction surgery for degenerative ASD

**Methods:** A total of 157 patients with an average age of 68.0±6.3 years (range, 60-84) who underwent correction surgery for ASD were evaluated retrospectively. PJFs were investigated in four different forms based on morphologic features: fracture at upper instrumented vertebra (UIV), fracture at UIV+1, fixation failure at UIV, and junctional subluxation. Demographic, clinical and radiographic data were analyzed.

**Results:** Eighteen (11.5%) of 157 patients presented PJFs. The PJF group had significantly lower T-score (-3.3±1.1 versus -1.9±1.5) and lower body mass index (BMI) (23.0±3.9 kg/m<sup>2</sup> versus 25.6±3.7) than the non-PJF group. However, radiographic parameters exhibited no significant differences between the two groups. UIV fracture, UIV+1 fracture, UIV fixation failure, and junctional subluxation were observed in 5, 6, 4, and 3 patients, respectively. Fixation failure developed the earliest (occurred within a median of 1.3 month after the index surgery), followed by UIV fracture (median 1.5 months). Figure shows the development of each form of PJFs. UIV fracture occurred earlier than UIV+1 fracture (median, 1.5 versus 36 months). Patients with UIV and UIV+1 fractures had significantly lower T-scores than others. On risk factor analysis, BMI and T-score showed significant association for overall PJF ( $P=0.043$  and  $0.021$ , respectively). When each form of PJF was analyzed separately, different risk factors for each form were identified.

**Conclusions:** Each form of PJFs had different clinical and radiographic features. Risk factor analysis suggested that each subtype had different risk factors. Identifying specific risk factors for each form of PJF might help avoid it.



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## Relationship between spinopelvic parameters and baseline pain, function, or health related quality of life in degenerative lumbar spondylolisthesis.

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**Introduction.** The importance of sagittal balance and spinopelvic parameters are recognized in the management and outcomes of adult spinal deformity and isthmic spondylolisthesis, but less is known regarding their role in degenerative lumbar spondylolisthesis (DLS). The purpose of this study is to determine the influence of baseline sagittal balance and spinopelvic parameters on pain, function, and health-related quality of life (HRQOL) of patients presenting with degenerative lumbar spondylolisthesis.

**Methods.** Patients with degenerative lumbar spondylolisthesis were enrolled in a prospective, multi-centre study. Baseline patient demographics, radiographic spinopelvic parameters, and sagittal alignment were analyzed for possible correlation to HRQOL outcomes (numeric rating scale back or leg pain, disability score, SF12, EQ-5D) using Pearson correlations.

**Results.** There were 154 patients who were analyzed (mean age: 65.8, BMI: 29.1) with grade I (72%) or II (28%) DLS, of which 95 were female. Primary symptoms were related to neurogenic claudication (80%), radiculopathy (15.3%) or back pain (4.7%). On average, symptom duration was greater than 2 years in 71% of patients.

Patients had moderate to severe symptoms and disability (mean numeric rating scale back: 7.2, numeric rating scale leg: 7.3, disability score: 45.6, Physical Component Score of SF12: 33.2, Mental Component Score of SF12: 49.6, EQ-5D: 0.54). Baseline measurements of radiographic alignment included sacral slope= $34.9 \pm 16.7^\circ$ , pelvic tilt= $24.8 \pm 9.5^\circ$ , pelvic incidence= $57.4 \pm 13.8^\circ$ , sagittal vertical axis= $35.8 \pm 40.8\text{mm}$ , lumbar lordosis= $45.7 \pm 13.6^\circ$ , thoracic kyphosis= $36.8 \pm 13.0^\circ$ , T9-spinopelvic inclination= $9.62 \pm 4.0^\circ$ , and T1-spinopelvic inclination= $4.43 \pm 10.4^\circ$ .

There were 54% of patients who had an insufficient lumbar lordosis based on the relationship between pelvic incidence and lumbar lordosis ( $LL < PI - 9^\circ$ ). Sagittal vertical axis correlated with T9-spinopelvic inclination, pelvic incidence, lumbar lordosis and pelvic tilt. T9-spinopelvic inclination correlated with sagittal vertical axis SVA, lumbar lordosis, thoracic kyphosis and T1-spinopelvic inclination. There was no correlation between baseline patient outcomes and spinopelvic parameters and alignment.

**Discussion.** Patients with degenerative lumbar spondylolisthesis have global sagittal misalignment compared to published normative controls, highlighted by less lumbar lordosis, a pelvic incidence to lumbar lordosis mismatch, and increased pelvic tilt. Spinopelvic alignment was not associated with patient outcomes, although positive sagittal balance may also be influenced by spinal stenosis.

## Surgical realignment in adult deformity patients increased balance within the cone of economy

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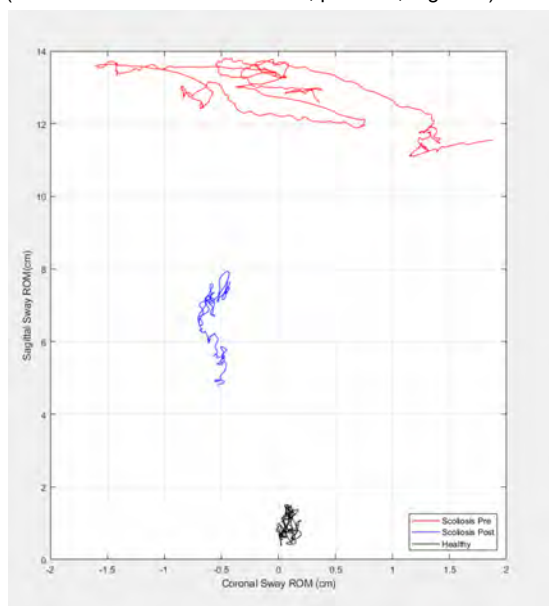
**Objective:** To quantify the extent of change in sway associated with maintaining a balanced posture within the cone of economy (COE), in adult degenerative scoliosis (ADS) patients' pre and post-surgery and compare them to matched non-scoliotic controls.

**Introduction:** Balance is defined as the ability of the human body to maintain its center of mass (COM) within the base of support with minimal postural sway. In spinal deformity patients a variety of postural changes in the spine, pelvis and lower extremities are observed in their effort to compensate for the anterior shift in the gravity line. Spinal alignment surgery was found to improve SVA and balance. ADS patients exhibit an increase in both the sagittal and coronal sway, and expend more energy while simply standing when compared to healthy controls.

**Methods:** Twenty ADS patients performed a series of functional balance tests a week before and 3 months after surgery. Twenty non scoliotic controls performed a similar balance test. The functional balance test was essentially a Romberg's test. All test subjects were fitted to a full body reflective markers set and surface EMG. Repeated measurements and one way ANOVAs were used.

**Outcome Measures:** COM and head sway in the sagittal and coronal planes, total sway amount and spine and lower extremity neuromuscular energy expenditure.

**Results:** ADS patients presented with less COM (Pre: 36.10 cm vs. Post: 25.71 cm,  $p=0.032$ , Figure 1) and head(Pre: 39.85 cm vs. Post: 28.11 cm,  $p=0.048$ ) displacements, less COM sway (Pre: 1.73 cm vs. Post: 1.12 cm,  $p=0.043$ ) and head sway (Pre: 1.24 cm vs. Post: 0.77 cm,  $p=0.050$ ), less right Multifidus muscle (Pre: 31.26 mV vs. Post: 16.15 mV,  $p=0.035$ ) but more Rectus Femoris muscle(Pre: 20.29 mV vs. Post: 29.98 mV,  $p=0.026$ ) activity after surgical re-alignment in comparison to their pre-surgery state. ADS patients demonstrated more initial COM (Pre: 36.10 cm vs. C: 19.26 cm,  $p=0.001$ , Figure 1) and head (Pre: 39.85 cm vs. C: 19.93 cm,  $p=0.011$ ) displacements, more COM sway (Pre: 1.73 cm vs. C: 1.11 cm,  $p=0.042$ ) in the sagittal direction, and increased muscle activity in their right Erector Spinae(Pre: 30.08 mV vs. C: 14.40 mV,  $p=0.003$ ), left Gluteus Maximus(Pre: 18.26 mV vs. C: 10.37 mV,  $p=0.045$ ), and bilateral Tibialis Anterior(Right: Pre: 24.64 mV vs. C: 14.49 mV,  $p=0.023$ ; Left:Pre: 25.01 mV vs. C: 13.97 mV,  $p=0.038$ ) muscles in comparison to non-scoliotic controls. Post-surgical ADS patients demonstrated more COM (Post: 25.71 cm vs. C: 19.26 cm,  $p=0.004$ , Figure 1) and head (Post: 28.11 cm vs. C: 19.93 cm,  $p=0.025$ ) displacements.



**Conclusions:** Surgical alignment reduced the amount of sway and overall displacement and reduced spine and lower extremity energy expenditure in ADS' patients 3 months after surgical intervention. In symptomatic ADS patients, sway increased with the sagittal sway increasing along with higher lumbar spine and lower extremity neuromuscular activity in comparison to a non-scoliotic control. Although surgical re-alignment improved ADS patients' functional parameters during a dynamic balance test, these parameters approached but did not fully achieve non-scoliotic control parameters when measured 3 months after surgery.

## Narcotic use trends in elective thoracolumbar spinal surgery patients

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**Introduction.** Narcotic use has increased rapidly in the North America in recent years. There is an association between pre-operative narcotic use and increased length of stay, inadequate peri-operative pain control and poor spinal surgery outcomes. Our aim was to investigate patterns of narcotic use in Canadian spinal surgery patients, examine trends over time, and determine the effect of spinal surgery on post-operative narcotic use.

**Methods.** Retrospective analysis of prospectively collected data on elective thoracolumbar surgery patients in the Canadian Spine Outcomes and Research Network (CSORN) database. Self-reported narcotic use at baseline, pre-surgery and one year post-operative were compared. Baseline narcotic use by age, gender and presenting complaint was also compared. All consecutive patients meeting eligibility criteria from database inception (2008) to 2017 were included.

**Results.** There were 3,511 patients that met inclusion criteria.

Over time (<2014 to 2017), there was no statistically significant change in the proportion of patients taking narcotics on a daily (range: 36.9% - 46.5%) or intermittent (range: 16.2% - 24.7%) basis.

There was no difference in the frequency of narcotic use at baseline and pre-surgery in patients who waited longer than six weeks for surgery.

There were significantly more patients using narcotics with a chief complaint of back pain or radiculopathy than neurogenic claudication ( $p<0.001$ ), and who were younger (<65 years old) than older ( $p<0.001$ ).

At one year post-operatively, daily narcotic use decreased significantly from baseline (44.4% to 22.9% ( $p<0.01$ )).

**Discussion.** Narcotic use in spinal surgery patients in Canada is widespread. While narcotic use might decrease post-operatively, surgeons are having little to no impact on patient narcotic use while on wait-lists for surgery. An opportunity may exist to intervene in this critical pre-operative stage to optimize surgical outcomes. Continued efforts to decrease narcotic use should be focused on <65 year old radiculopathy and back pain patients.

## Risk factors and clinical outcomes of proximal junctional kyphosis following iliac screw fixation for degenerative adult spinal deformity

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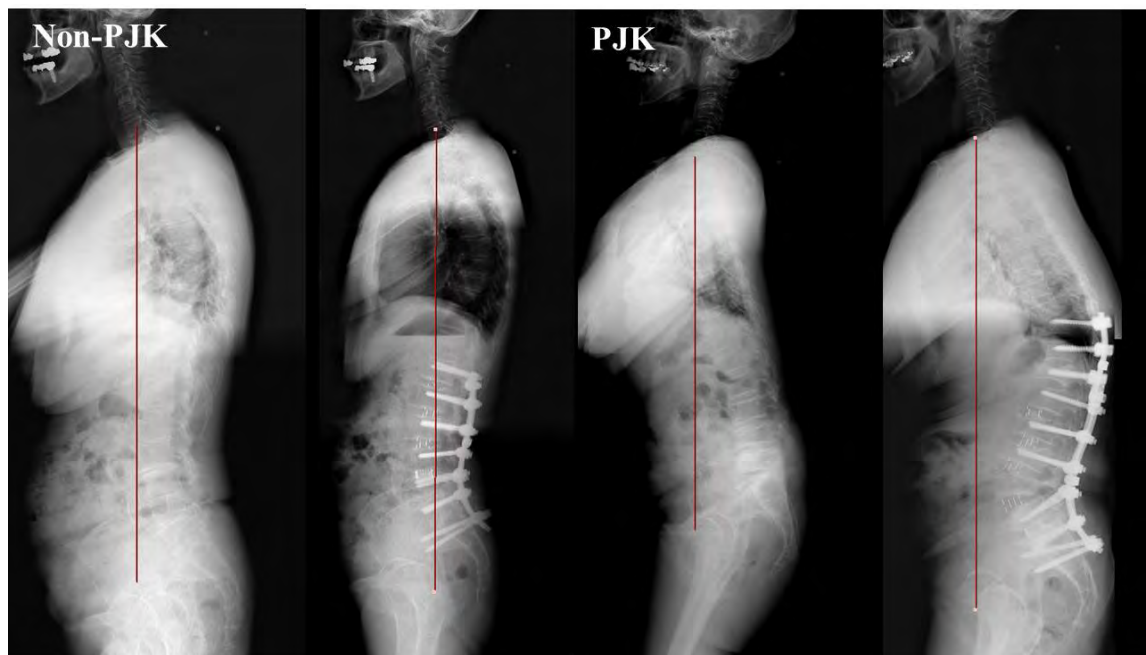
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**Introduction** Sacropelvic fixation using iliac screws have been increasingly applied for restoration of global alignment in degenerative adult spinal deformity (ASD). However, few reports on proximal junctional kyphosis (PJK) after long instrumented fusion with iliac screw fixation have been reported. The objective is to evaluate risk factors and clinical outcomes of PJK after iliac screw fixation for degenerative adult spinal deformity.

**Methods** 93 patients who had undergone sacropelvic fixation for degenerative ASD were retrospectively reviewed. Patients who were more than 60 years old at the time of index surgery were included for homogeneity. All patients had degenerative sagittal imbalance preoperatively, who had more 5 levels fusion from upper instrumented vertebra (UIV) of L1 and above. Univariate and multivariate analysis for clinical, surgical and radiological factors including paravertebral muscles were conducted for risk factors for PJK compared to non-PJK group. Clinical outcomes were compared between two groups and within each group.

**Results** 69 patients without PJK were compared with patients who had PJK (n=24). The median time to development of PJK was 10.3 months [1-72 months] and the most common mechanism of PJK was the disc degeneration (11 patients, 54.1%) followed by fracture above UIV (17%), fracture at UIV (12.5%), subluxation and hardware failure (8.3%, respectively). In univariate analysis for PJK, higher body mass index (BMI, 24.1 vs. 26.5, p=0.011), pre-operative pelvic incidence (PI) and lumbar lordosis (LL) mismatch (37.2° vs. 47.1°, p=0.027), pre-operative sagittal vertical axis (SVA, 73.0mm vs. 119.5mm, p=0.05), post-operative of SVA (28.6mm vs. 54.4mm, p=0.008) were significant risk factor. Moreover, paravertebral muscles including cross sectional area (CSA, 1706mm<sup>2</sup> vs. 1477mm<sup>2</sup>, p=0.021), and ratio of CSA of paravertebral muscle to disc (0.91 vs. 0.76, p=0.020) were also significant risk factor in univariate analysis. Higher BMI (odds ratio (OR)=1.347, p=0.005), pre-operative PI and LL mismatch (OR=1.061, p=0.017), pre-operative SVA (OR=1.015, p=0.044), and lower ratio of CSA of paravertebral muscle to disc (OR=1.052, p=0.005) were the independent risk factors for PJK in multivariate analysis. Regarding the clinical outcomes, there was a significant difference in VAS for back pain (4.3 vs. 6.5, p=0.001) and ODI (41.3 vs. 54.4, p=0.015) between two groups at last follow-up. In addition, patients in non- PJK group reported significant improvement of VAS for back and leg pain, and ODI while there was no significant improvement of VAS and ODI in PJK group.

**Discussion/Conclusion** Greater post-operative SVA and weakness of paravertebral muscles including CSA were the significant risk factors for PJK after iliac screw fixation for degenerative ASD in this study. Higher BMI, pre-operative sagittal imbalance such as PI-LL mismatch and SVA as well as lesser ratio of CSA of the paravertebral muscles to disc were the independent risk factors for PJK. Clinical outcomes including VAS for back pain and ODI was significantly improved in non-PJK group compared with PJK group at last follow-up. This study has strength due to its relative homogeneity (diagnosis and distal fusion level) of patients compared to that in other reports that included all ASD with a wide range of age.



## The prevalence and risk factors of back pain in patients with adolescent idiopathic scoliosis - a large-scale cross-sectional study

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**INTRODUCTION:** Adolescent idiopathic Scoliosis (AIS) is the commonest pediatric spinal deformity. The presence of structural deformity may adversely affect spinal biomechanics. However, little is known regarding the prevalence rates of spinal pain and their impacts on AIS patients. Additionally, since early onset of spinal pain may increase the risk of subsequent recurrent/chronic spinal pain, it is important to identify various risk factors for spinal pain in AIS patients so that proper management can be implemented. As such, the objective of the current study was to investigate the prevalence and impact of spinal pain on AIS patients and their associated risk factors.

**METHODS:** A consecutive sample of conservatively treated AIS patients (aged between 10 and 17 years) were recruited from a scoliosis referral center. Each participant completed a battery of questionnaires designed/chosen by a team of clinicians specialized in scoliosis management. Patients' characteristics, physical activity levels, lifetime and existing thoracic pain (TP) and low back pain (LBP), and scoliosis treatments were collected by a questionnaire. Additionally, the Insomnia Severity Index, Epworth Sleepiness Scale, and the anxiety and depression subscales of the Depression Anxiety Stress Scales were used to evaluate patients' sleep quality, anxiety, and depression, respectively. The subjective findings were matched with the corresponding X-ray findings (e.g., Coronal and sagittal Cobb angles, Nash and Moe grading of apical vertebral rotation, Lenke classification, etc.). From the reported lifetime prevalence of spinal pain, participants were stratified into "no pain", "TP", "LBP", and "TP+LBP" groups. Between-group differences in physical and psychological characteristics were compared. Risk factors for current spinal pain (TP+LBP) were analyzed using a multivariate logistic regression. Odds ratios (ORs) were calculated.

**RESULTS:** A total of 983 AIS patients (73.0% females; average age of 14.7+1.8 years) were recruited. The lifetime prevalence rates of TP, LBP and TP+LBP were 4.0%, 25.5%, and 4.1%, respectively. Additionally, the point-prevalence of TP+LBP was 13.3%. Compared to the no pain group, patients in the three lifetime painful groups reported significantly more severe insomnia and lower physical activity levels ( $p < 0.05$ ). Patients in the LBP and TP+LBP groups were also characterized by significantly older age, more severe daytime sleepiness, larger coronal Cobb angles in thoracic and lumbar regions, and greater apical vertebral rotation at the lumbar region. The multivariate analysis found that the Type 5 Lenke curve (OR=6.5), severe insomnia as measured by the Insomnia Severity Index (OR=3.2), older age (OR=1.25), and coronal Cobb angle in the lumbar region (OR=1.04 per degree) were significantly related to the presence of current spinal pain in AIS patients.

**DISCUSSION:** This is the first large-scale study to investigate the impacts of different spinal pain in affecting AIS patients' physical and psychological well-being. The close association between specific spinal phenotypes (i.e., the Lenke curve type and Cobb angles in the lumbar region) and spinal pain corroborate the hypothesis that spinal deformity can increase the risk of spinal pain. Future longitudinal studies should investigate the effectiveness of physiotherapy scoliosis-specific exercises and bracing in improving the spinal deformity and related spinal pain.

SP19

**Influence of skeletal muscle mass and spinal alignment on surgical outcomes for lumbar spinal stenosis**

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**Purpose**

We consider the relationship between spinal alignment and skeletal muscle mass with clinical outcomes following surgery for lumbar spinal stenosis.

**Methods**

Our target population included 34 women who underwent surgery for lumbar spinal stenosis (LSS) (mean age 74.5 years). Before surgery and 6 months following surgery, systemic bone mineral density and lean soft tissue mass were measured using DXA. Skeletal muscle mass index (SMI) was calculated as the sum of arm and leg lean mass in kilograms divided by height in meters squared. Spinal alignment was measured. Clinical outcomes included JOA score, leg pain and low back pain VAS, and Roland-Morris Disability Questionnaire (RDQ). Along with these clinical outcomes, we examined bone mineral density, skeletal muscle mass, and spinal alignment before and after surgery. We used the Spearman correlation coefficient to examine the associations between clinical outcomes and preoperative muscle mass and spinal alignment.

**Results**

Sarcopenia (SMI<5.46) was observed in 8 of 34 subjects (23.5%). Compared with normal subjects (SMI>6.12), RDQ tended to be higher in subjects with sarcopenia (p=0.08), but there were no significant differences. Regarding correlation between clinical outcomes and preoperative muscle mass, RDQ had a significant negative correlation with SMI (r=-0.38, p<0.05). Regarding correlation between clinical outcomes and spinal column alignment, there was a significant positive correlation between postoperative RDQ and PT (r=0.45, p<0.05). As for correlation between spinal column alignment and muscle mass, SMI and PT had a significant negative correlation (r=-0.36, r<0.05).

**Discussion**

Good postoperative outcomes were negatively correlated with low preoperative appendicular muscle mass. This suggests that postoperative outcomes were inferior in cases of decreased appendicular muscle mass (sarcopenia). Posterior pelvic tilt due to decreased limb muscle mass may contribute to postoperative back pain. This is the first report showing that preoperative reduced limb muscle mass and posterior pelvic tilt are predictive factors in the persistence of low back pain postoperatively.

## Epidural fat accumulation affects the surgical outcome in patients with lumbar spinal stenosis

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**Introduction:** Lumbar spinal epidural lipomatosis (SEL) is a relatively rare condition characterized by an abnormal accumulation of adipose tissue in the epidural space. We previously reported that SEL is causally related to obesity-associated chronic inflammation (1). In addition, lumbar spinal stenosis (LSS) patients with SEL showed more severe pain than those without SEL (2). However, there is a lack of evidence demonstrating the efficacy of surgery for LSS patients with SEL. The aim of this study was to examine the surgical outcomes after posterior decompression in LSS patients with SEL.

**Methods:** A total of 186 (132 male and 54 female) patients who underwent posterior decompression surgery for LSS between October 2008 and April 2015 were retrospectively reviewed. Based on axial views of preoperative lumbar MRIs, we calculated the epidural fat/spinal anteroposterior diameter (EF/SD) index at each level from L1/2 to L5/S1. We divided the patients into two groups according to the EF/SD scores: lipomatosis group (L group; maximum EF/SD,  $\geq 0.6$ ) and normal group (N group; maximum EF/SD,  $< 0.6$ ). The scores for the Roland-Morris Disability Questionnaire (RDQ) and Japanese Orthopedic Association Back Pain Evaluation Questionnaire (JOABPEQ) at pre-operation and 1 year and 2 years postoperatively were evaluated.

**Results:** In our series of 186 patients, the L group included 43 (33 males and 10 females; mean age, 74.4 years; mean BMI, 25.5 kg/m<sup>2</sup>) and N group included 143 (99 males and 44 females; mean age, 70.5 years; mean BMI, 23.9 kg/m<sup>2</sup>). There were significant differences in age and BMI between the two groups. In the L group, the spinal level with EF/SD index of  $\geq 0.6$  showed the following distribution: 6 cases (14.0%) with L2/3, 32 (74.4%) with L3/4, 4 (9.3%) with L4/5, and 1 (2.3%) with L5/S1. The RDQ score at all stages was significantly higher in the L group than in the N group ( $p < 0.005$ ). In the N group, the RDQ score significantly improved at 1 year postoperatively and was maintained at 2 years postoperatively, whereas in the L group, the RDQ score improved to the same extent as in the N group at 1 year postoperatively, but significantly worsened at 2 years postoperatively ( $p = 0.04$ ). Similar results were observed in terms of JOABPEQ scores. Although there were no significant differences in VAS scores of low back pain, leg pain, and leg numbness at 1 year postoperatively between the two groups, VAS score of low back pain at 2 years postoperatively was significantly higher in the L group than in the N group ( $p = 0.02$ ).

**Discussion:** The surgical outcomes of LSS patients with SEL were generally favorable at 1 year postoperatively, but worsened at 2 years. Although the influence of age and BMI on surgical outcome should be considered, the present study highlighted epidural fat accumulation as a critical underlying factor for the poor surgical outcome in patients with SEL.

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## **The feasibility and efficacy of an active prehabilitation program on the postoperative recovery of patients following surgery for spinal stenosis**

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### **Introduction**

Degenerative lumbar spinal stenosis is a prevalent condition in older adults that often leads to deconditioning. Although the benefits of surgery outweigh those of conservative approaches, physical rehabilitation may be used to improve function and to minimize the risk of persistent dysfunction, especially in the preoperative period, considered a salient period for health changes. This study aimed to assess the feasibility and efficacy of an active preoperative intervention program on the improvement of clinical parameters and functional physical capacity in patients awaiting surgery for lumbar spinal stenosis.

### **Methods**

Fifty-six patients were randomly allocated to either a 6-week supervised preoperative rehabilitation program (experimental group) or hospital standard preoperative care (control group). The intervention protocol consisted of three 30-minute sessions per week, aiming to improve trunk and lower limbs strength and muscular endurance, and spinal stabilization with intensity and complexity of exercises being increased gradually. Feasibility related outcomes such as enrolment, attrition and adverse events were considered. Efficacy outcomes included: pain intensity and low back disability, patient's global impression of change, lumbar extensor muscle endurance, of lumbar flexor and extensor muscles, maximum voluntary contraction of knee extensors, active lumbar ranges of motion, and walking capacities. All outcomes were measured at baseline, 6 weeks later and again 6 weeks after surgery. Clinical outcomes were collected at 3 and 6 months postoperatively via mail follow-ups.

### **Results**

Twenty-seven participants (93%) completed the full 6-week exercise program and 49 (88%) and 46 (82%) were evaluated at the preoperative and postoperative assessment respectively. Sixty-three percent of participants reported improved global status following the intervention compared to 13% in the control group. Significant improvements were found in favour of the experimental group at the preoperative assessment for leg pain intensity, lumbar extensor muscle endurance and walking capacities. Although not statistically significant, trends were observed in favour of the experimental group with regard to lumbar ranges of motion. No major adverse events were encountered.

### **Discussion**

Active prehabilitation is feasible and can be used to safely improve both clinical status and physical capacities even in deconditioned patients with lumbar stenosis. The significant improvements seen preoperatively did not however translate into short-term improved postoperative recovery. Additional outcome measures are required in order to better capture the changes in functional status occurring over a short period of time.



## Relationships between Vitamin D and paraspinal muscle: human data and experimental rat model analysis

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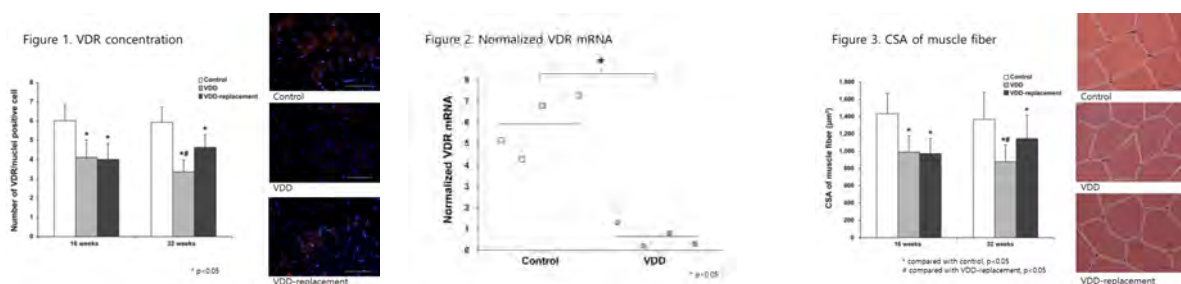
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**INTRODUCTION** Vitamin D deficiency (VDD) has been closely linked with skeletal muscle atrophy in many studies, but to date no study has focused on paraspinal muscle. In the present study, we conducted a prospective analysis of serum vitamin D concentration, muscularity and fatty infiltration in lumbar paraspinal muscles with magnetic resonance imaging (MRI) studies of asymptomatic or mild symptomatic volunteers. We also developed an experimental rat model of VDD and performed radiologic and histologic analysis of the paraspinal muscles in terms of muscle volume and intramyonuclear VDR concentration, and VDR gene expression level.

**METHODS** We measured serum vitamin D concentration in 91 elderly women and stratified them according to their vitamin D status in three groups: control, vitamin D insufficiency, and VDD, and obtained magnetic resonance imaging data of the lumbar spine and evaluated the quality and quantity of the paraspinal muscles. Additionally, we designed experimental rat models for VDD and VDD-replacement and analyzed the radiologic and histologic data of paraspinal muscles through comparison with control rats (n = 25, each group).

**RESULTS** In the human studies, a significant decrease was noted in the overall paraspinal muscularity and increase in fatty infiltration in the VDD group as compared to the other groups (p<0.05). In the rat experiment, a decrease was noted in paraspinal muscle fiber size and intramyonuclear vitamin D receptor (VDR) concentration and VDR gene expression level, and total muscle volume of the VDD rats as compared to the control rats (Figure 1, 2, p<0.05). Vitamin D replacement after VDD could partially restore the muscle volume, muscle fiber size and intramyonuclear VDR concentration levels (Figure 3, p<0.05) of the paraspinal muscles.

**DISCUSSION** Several studies have already shown that the loss of skeletal muscle is closely associated with the VDD status.<sup>1-4</sup> However, there have been no clinical studies before ours that sought to determine whether VDD changes the volume and extent of fatty infiltration of paraspinal muscles in humans. Many researchers have emphasized the role of paraspinal muscles in maintaining the sagittal balance and functional capacity of the lumbar spinal column.<sup>5-7</sup> Further, it has been proved that paraspinal muscles decrease in individuals with various spinal diseases.<sup>8-10</sup> Thus, the triggering of spinal disease due to the loss of paraspinal muscle is another major area of concern that needs to be addressed. In the present study, we found strong correlations between serum vitamin D concentration and paraspinal muscularity. Although rats and humans differ in many aspects, such as lifestyle, posture, and walking mechanisms, we found that in the rat model, VDD can induce paraspinal muscle atrophy and decrease the concentration of intramyonuclear VDR and VDR gene expression level, while vitamin D replacement promotes at least partial restoration of muscle volume and intramyonuclear VDR concentration in paraspinal muscles under VDD conditions. We believe that our findings will provide further insight into the role of vitamin D in paraspinal muscles.



## Heavy manual work is associated with an increased risk of severe lumbar spinal stenosis on MRI scans

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### INTRODUCTION

Heavy occupational physical activity is associated with osteoarthritis and radiographic lumbar spondylosis. To date however, there has been no research to investigate the contribution of occupations and physical workplace exposures to lumbar spinal stenosis (LSS) as investigated by magnetic resonance imaging (MRI) in a population-based cohort.

### METHODS

The Wakayama Spine Study recruited a population sample of adults from a range of different occupations. Information was collected about demographic factors, occupation, workplace exposures for the job held for the longest period of working life, leg pain, and back pain and all participants underwent total spinal MRI in a mobile MRI unit (Excelart 1.5T; Toshiba, Tokyo, Japan). The severity of LSS, including central stenosis was rated on a four-grade scale such as none, mild, moderate, and severe by a spine surgeon. Using the job exposure information, occupational groups were classified in 6 groups: Clerical/ Technical; Agricultural/ Fishermen; Factory/ Construction; Clinical/ Housekeeper/ Shop assistants/ Hairdressers/ Dressmakers; Teachers and Others/No answer.

### RESULTS

Complete data were available for 722 participants (245 males, 477 females; mean age, 70.9 years; range, 53-93 years). In total, 239 (33%) of subjects were defined with severe LSS and became the cases for these analyses and the remaining 483 patients were controls. Mean age was significantly different between these two groups (case: 74.1±9.2, control: 69.4±9.9, P<0.001 by Student t-test). We performed logistic regression analyses to estimate odds ratio (OR) and 95% confidence interval (CI) for associations between occupational group and severe LSS. Unadjusted analysis showed that Agricultural/Fishermen and Factory/Construction workers had a significantly higher risk of severe LSS when compared with Clerical/Technical experts (Agricultural/Fishermen: OR 1.99, 95%CI 1.22-3.26, Factory/Construction: OR 2.08, 95%CI 1.09-3.96). However, the significant associations were lost after adjustment for: age, sex, BMI, smoking, and usual walking speed. A significant interaction was observed between LSS and obesity which explained the attenuation of effects with adjustment. However, stratification of the analyses by age (<75 years and ≥75 years) showed that the associations with severe LSS remained for Factory/Construction workers aged < 75 years even after adjustment for all the same confounders (Factory/Construction: OR 3.97, 95%CI 1.46-10.85).

### DISCUSSION

Exposure to heavy manual work in the Factory/Construction industries was associated with severe LSS, particularly among people aged <75years at the time of the MRI scan. Our data add to those on osteoarthritis of the knee and hip, as well as lumbar spondylosis, suggesting a relationship between musculoskeletal degenerative disease and heavy manual work. More research is required but attention to ergonomic factors during working life may reduce the burden of long-term musculoskeletal symptom improving quality of life at older ages.

## Diabetes mellitus and lower ABI are associated with symptomatic lumbar spinal stenosis: The Wakayama Spine Study

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**Introduction:** Much of the pathology of Lumbar Spinal Stenosis (LSS) remains unknown. Even if patients have the same degree of spinal stenosis on the images, not everyone has symptoms. It has been reported that Diabetes Mellitus (DM) or Peripheral Artery Disease (PAD) are associated with symptomatic LSS (sLSS), but in the case control study, there are selection bias and confounding factors, so the association is still controversial. In this study, we examined related factors for sLSS by a cross sectional study in the general population.

**Methods:** We studied 968 participants (men: 319 and women: 649) in Wakayama Spine Study (base line survey) conducted between 2008 and 2010. In accordance with North American Spine Society guidelines, specialists in orthopedic surgery made diagnoses of presence or absence of sLSS from interview results, medical examination results and MRI findings. We graded radiographic LSS on 4 levels scale (none, mild, moderate, severe) according to Suri classification from cross-section MR images. In addition, we examined basic anthropometry, asked about smoking/drinking habit, and also measured Ankle Brachial Index (ABI) and HbA1c.

**Statistics:** We extracted moderate and severe radiographic LSS, then by groups, 1) compared measurement/evaluation items according to presence or absence of sLSS between the 2 groups, and 2) performed multiple logistic regression analysis these objective variable is presence or absence of sLSS and explanatory variable is items  $p < 0.2$  by comparing the two groups.

**Results:** 451 participants have moderate stenosis (with sLSS: 36) and 288 participants have severe stenosis (with sLSS: 52). In the moderate stenosis group, subjects with sLSS significantly have higher coexistence rate of DM and lower ABI than non-LSS participants. Although sLSS participants tend to be older ( $p = 0.19$ ), there is no significant difference in the percentage of men and women, BMI and drinkers/smokers. In the severe stenosis group, there is no difference in the all measurement items. As a result of the multiple logistic regression analysis, in the moderate stenosis group, the prevalence of DM (OR 3.92 [95% CI: 1.52-9.34]) and lower ABI (1 SD (=0.09) declined OR 1.36 [1.04-1.81]) are significant related factors for sLSS.

**Conclusions:** In the case of the moderate stenosis on MR images, DM and lower ABI are significant related factors for sLSS. On the other hand, in the case of severe stenosis, the both are not associated with sLSS. When anatomic stenosis becomes severe, the effect of intrinsic factors might be masked.

**Novel small molecule inhibitors of sclerostin with the potential to enhance spinal fusions**

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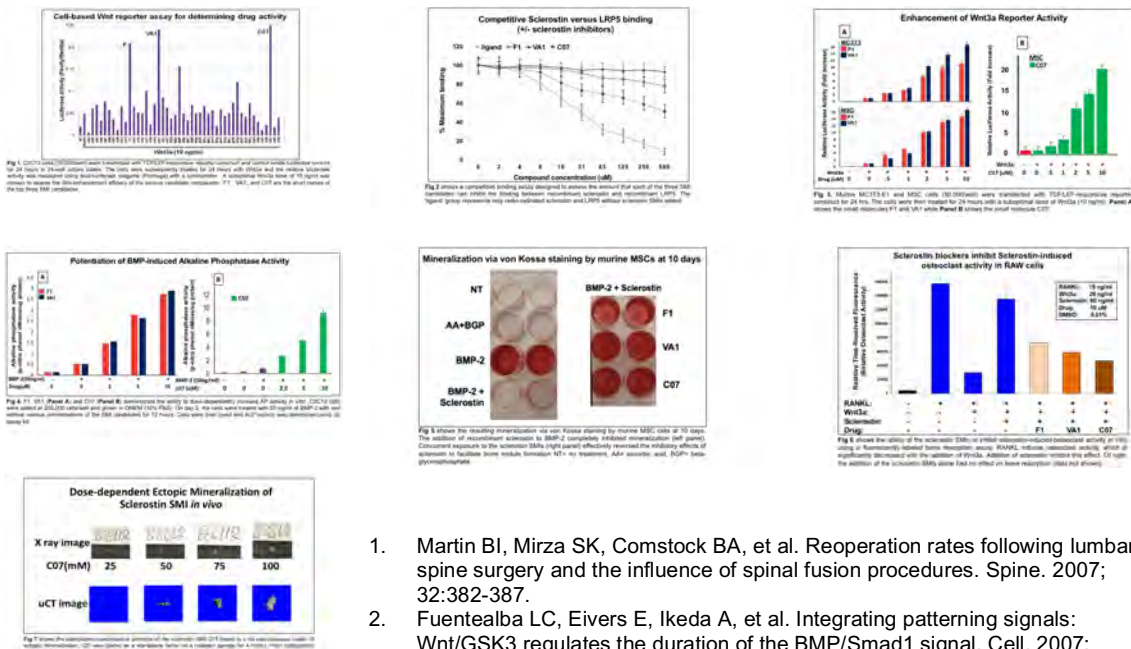
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**Introduction:** The environment within the posterolateral spine is one of the most clinically challenging bone healing environments in all of orthopaedics. Pseudarthrosis rates range from 10-40%.<sup>1</sup> BMP-2 is the only FDA approved biologic bone graft substitute but its routine use has been limited due to its high cost and promotion of local osteoclastogenesis resulting in osteolysis. To address this clinical problem, we propose to locally block the Wnt inhibitor sclerostin using novel small molecule inhibitors (SMIs), thereby promoting canonical Wnt signaling within the fusion bed to enhance bone formation. Sclerostin inhibition results in an anabolic bone forming effect that simultaneously decreases bone resorption, effectively uncoupling bone formation from resorption.<sup>2</sup> This is ideal in the posterolateral spine and intervertebral space where *de novo* bone is required.

**Methods:** We pursued a validated strategy to computationally identify SMIs with the ability to disrupt the interaction between sclerostin and its receptor LRP5/6. We then tested the three leading SMI candidates in a competitive binding assay to assess whether they could in fact prevent recombinant sclerostin from binding to recombinant LRP5, as predicted *in silico*. Next, the SMIs were tested in several validated *in vitro* biochemical assays using murine MC3T3 and MSCs, assessing their ability to (1) enhance canonical Wnt signaling, (2) potentiate BMP signaling, and (3) produce mineralization via von Kossa staining. The SMIs were then tested for their ability to inhibit osteoclast activity in a bone resorption assay using RAW(264.7) cells. Finally, the leading SMI candidate was placed on a collagen sponge as a standalone osteoinductive agent and implanted subcutaneously in rats. At 4 weeks, the explants were assessed for ectopic mineralization using radiographs/mCT.

**Results:** We identified three potential sclerostin SMI candidates based on *in silico* screening: F1, VA1, C07 (Fig1). All three SMIs were able to displace radio-iodinated recombinant sclerostin from LRP5, with C07 being the most effective (Fig2). All SMIs also enhanced both Wnt/b-Catenin and BMP signaling in a dose-dependent manner (Figs3,4). In the mineralization assay, the inhibitory effect of recombinant sclerostin (80 ng/ml) was completely reversed by the addition of all three sclerostin SMI candidates at 10 mM, facilitating bone nodule formation (Fig5). All three SMIs significantly inhibited sclerostin-induced osteoclast activity in the bone resorption assay (Fig6). When placed subcutaneously, C07 produced dose-dependent ectopic mineralization in a challenging *in vivo* subcutaneous environment (Fig7).

**Discussion:** Utilizing our previously validated *in silico* screening process, we identified multiple small molecules that are able to inhibit sclerostin's interaction with its receptor. Subsequent *in vitro* experiments confirmed that these SMIs result in the expected known effects of sclerostin blockade: (1) enhancement of canonical Wnt signaling, (2) potentiation of BMP signaling, (3) enhancement of osteogenic activity (mineralization) *in vitro* and *in vivo*, and (4) inhibition of bone resorption. Unlike with BMPs, these sclerostin SMIs resulted in bone formation being effectively uncoupled from resorption. Importantly, this was accomplished as standalone osteoinductive factors. We believe that these exciting results warrant further investigation of these SMIs as novel cost-effective biologic bone graft substitutes for achieving consistent spinal fusions.



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## Analysis of lumbar total disc replacement removals and revisions: a 17-year experience

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**INTRODUCTION:** One concern expressed about lumbar total disc replacement (TDR) has been safety. One measure of safety is the need for subsequent surgery to removal or revise an implant. This may be of particular importance considering TDR removal/revision generally requires re-operation through the anterior approach with the corresponding increased risk of vascular injury. The purpose of this study was to analyze the incidence of, and reasons for, removal or revision of lumbar TDR devices.

**METHODS:** A consecutive series of 1,707 lumbar TDR patients, beginning with the first case experience in 2000, was reviewed to identify those undergoing re-operation for TDR removal or revision. Only patients who were at least 6 months post-operative were included. Among the 1,707 patients, the mean follow-up was 42.7 months with a median of 30 months and a maximum of 195 months. Six different devices were used in the series. For each case of device removal/revision, the reason, duration from index surgery, and procedure performed were recorded.

**RESULTS:** In the series of 1,707 patients, there were 17 patients who underwent TDR removal (0.99%) and 3 additional patients underwent TDR revision (0.17%). The rates based on the total number of 2,023 TDR devices implanted in the 1,707 patients, were 0.89% removals and 0.15% revisions. The reasons and timing of removal/revisions were analyzed. Removals included: 8 for migration and/or loosening, 3 developed problems after a trauma, 1 had vertebral body fractures (osteoporosis), 1 TDR was too large and replaced with smaller device, 1 had ongoing pain, and 1 had an infection seeded from a chest infection at 146 month post-TDR. Revisions included 1 repositioning the core (technique error), 1 repositioned device after displacement, and 1 core replacement due to wear/failure.

With respect to timing, 40% of removals/revisions occurred within one month after the index surgery, and a total of 85% occurred within 2 years. Of note, 40% of the revisions/removals occurred in the first 25 TDR cases performed by individual surgeons. There were no vascular complications causing clinical sequelae during the removal/revision surgeries.

**DISCUSSION:** In this large patient series, 1% of lumbar TDRs were removed/revisioned. Only one revision was related to device failure or wear. Many of the subsequent procedures were performed within a month of implantation. Also of note, many occurred within the first 25 TDR cases for individual surgeons, suggesting a learning curve. In cases of TDR removal/revision, as with any repeat anterior spine surgery, one should be acutely aware and prepared for vascular injury should it occur. The low rate of removal/revision in this large institutional experience over a 17 year period provides support for the safety of these devices.

## Stiffness matters: PART II - the effects of plate stiffness on load-sharing and the progression of fusion *in vivo*

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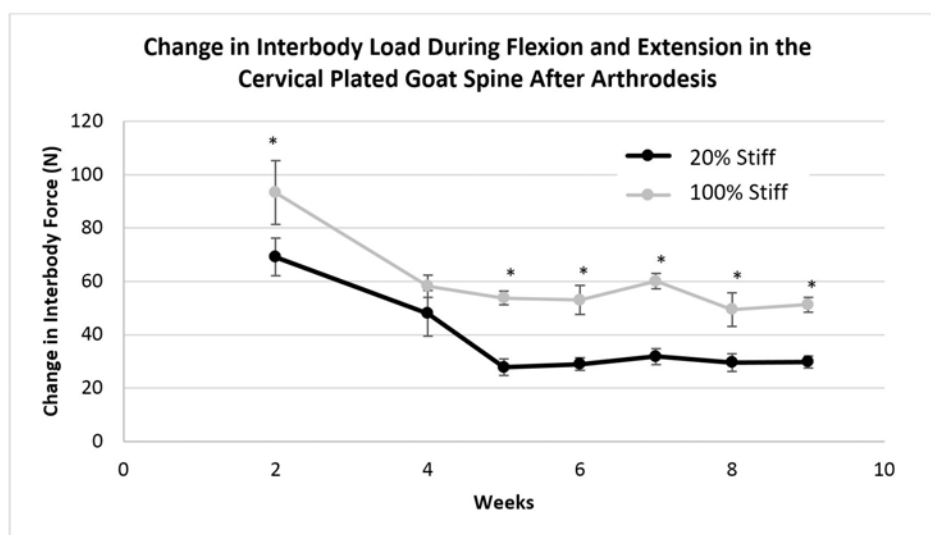
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**Introduction:** Following anterior cervical discectomy and fusion (ACDF), the biomechanics of the arthrodesis is primarily dictated by the plate. The properties of the plate prescribe the extent of load-sharing versus stress-shielding. Load-sharing promotes interbody bone formation while stress-shielding can inhibit maturation of bone. A plate which has high stiffness may stress-shield the interbody space and can also cause load-reversal which results in high loads in the interbody space during extension and can contribute to cage subsidence or graft failure. While these biomechanical principles are well accepted, they have never been validated *in vivo*. Measuring *in vivo* biomechanics of the cervical spine is critical to understanding the complex relationships between implant design, interbody loading, load-sharing, and the progression of fusion. The purpose of this study was to measure *in vivo* interbody forces in real time in the cervical spine following ACDF during the time course of fusion in a large animal model.

**Methods:** We designed, fabricated, and validated a force-sensing "smart" interbody implant to directly measure load-sharing in the spine *in vivo*. We also developed custom cervical plates of distinct bending stiffnesses. After IACUC approval, ten Alpine-Nubian cross-bred goats underwent ACDF and received either a high stiffness or low stiffness plate. Interbody implant-load cells were placed in the interbody space of all animals and data from the interbody implants were collected weekly out to 14 weeks as an indicator of forces transmitted through the interbody space. During each data collection session, real time interbody forces were measured as animals performed flexion and extension exercises. Forces were determined at maximum flexion and maximum extension for each animal and the difference between maximum flexion and maximum extension were compared across time points and between treatment groups. Plain radiographs and histology were used to assess fusion.

**Results:** Interbody forces during flexion/extension were highly dynamic and exceeded 300 N in some cases. In animals that received high stiffness plates, maximum forces were in extension whereas in animals that received lower stiffness plates, maximum forces were in flexion. Interbody forces were more consistent in the lower stiffness group across the entire range of motion. As fusion progressed, the average difference in load between flexion and extension for animals in both groups decreased over time as shown. Differences in interbody load between low and high stiffness groups were statistically significant. Analysis of radiographs and histology indicated that animals in the lower stiffness group had more extensive bone formation and superior rates of fusion compared to the animals in the higher stiffness group.

**Discussion:** The magnitude of interbody forces in the cervical spine is dynamic and correlates to activity and posture of the head and neck. The magnitude and consistency of forces in the interbody space correlates to plate stiffness with more compliant plates resulting in more consistent load-sharing. Stiffer plates cause load-reversal whereas less stiff plates do not. The magnitude of interbody forces decreases as fusion matures suggesting that smart interbody implants may be used as a diagnostic tool to indicate the progression of interbody fusion.



## Cost-effectiveness of psychologically informed physical therapy in patients after lumbar spine surgery

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**Introduction:** Psychosocial factors have been found to be important predictors of poor outcomes in patients undergoing lumbar surgery for degenerative conditions. Recent research has demonstrated the potential effectiveness of a psychologically informed treatment approach for patients at-risk for poor outcomes following spine surgery.<sup>1</sup> Economic evaluation of PIPT is critical in order to inform dissemination to clinical practice. The purpose of this study was to compare the cost-effectiveness of a 6-session telephone-based PIPT program with a 6-session telephone-based Education program using Markov decision-analysis. The PIPT treatment focused on cognitive and behavioral strategies of goal setting, graded activity, relaxation techniques, distraction, problem solving, and cognitive re-structuring (replacing negative thoughts with positive ones). **Methods:** Economic evaluation of a randomized controlled clinical trial conducted at an academic medical center (NCT01131611). Eighty-six patients, 21 to 81 years of age, undergoing surgical treatment of a lumbar degenerative condition using laminectomy with or without arthrodesis were randomized into either a PIPT intervention group (n=43) or an Education group about postoperative recovery (n=43). Postoperative quality-adjusted life-years (QALYs) were calculated from a validated questionnaire (EQ-5D) that was completed by patients at 3 month and 1 year follow-up. Direct health care costs from hospital discharge to 1 year postoperatively were derived from registry data and adjusted based on Medicare national-allowable payment amounts. Costs included outpatient visits to health care providers, diagnostic tests, devices, epidural steroid injections, emergency department visits, back-specific medications, and outpatient rehabilitation. A Markov state-transition model was constructed, based on data from a randomized clinical trial, and all parameters were varied individually in 1-way sensitivity analyses. Participants could be in one of three health states after spine surgery based on a change in the Oswestry Disability Index (ODI) score (*better*, *not better*, *better than get worse*). Initial placement and transitions between states were based on an improvement or worsening of the ODI score beyond the published minimal clinically important difference (MCID) of 12.8 points. **Results:** At 1 year after surgery, 89% were *better*, 2% were *not better*, and 8% were *better than get worse* in the PIPT group, while the Education group had 68% in the *better*, 8% in the *not better*, and 25% in the *better than get worse* health state. The total per person cost for the PIPT group was \$2,493 and for the Education group was \$2,595. The PIPT group cost \$102 less per person and gained 0.09 more QALYs compared with the Education group in base-case analysis, which indicated that PIPT was the dominant (less expensive, more effective) strategy. In sensitivity analyses, PIPT remained the favored strategy at a \$20,000/QALY threshold when all values were individually varied over plausible ranges. **Discussion:** Using Markov modeling, the PIPT program was less costly and more effective than an Education program when used after surgery for patients with degenerative lumbar spine conditions. Results support a biopsychosocial approach to postoperative spine management and the integration of cognitive-behavioral strategies into physical therapy care. Telephone-based PIPT appears to be an economically reasonable, and perhaps cost saving, intervention.

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## Incidence and characteristics of clinical L5/S1 adjacent segment disease following L5 floating lumbar fusion

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**INTRODUCTION:** Spinal fusion surgery is effective for patients with degenerative lumbar diseases with segmental instability. However, adjacent segment degeneration (ASD) occurs following lumbar spine fusion at a certain frequency because of increases in intervertebral stress and adjacent segment motions. The L5/S1 segment has distinctive biomechanical properties different from other lumbar segments. Therefore, during lumbar fusion surgeries, whether the L5/S1 segment without clinical symptoms should be included in the fusion segment remains controversial. Several studies on radiological L5/S1 ASD have been reported, however, little has been reported on L5/S1 ASD with clinical symptom (clinical L5/S1 ASD). The purpose of this retrospective study was to evaluate the incidence, characteristics and risk factors for clinical L5/S1 ASD following L5 floating lumbar fusion.

**METHODS:** Lumbar spinal fusions were performed for 497 patients between 2007 and 2017 in ours and two related institutions. Among these, 306 patients who received L5 floating lumbar fusion (61.6%) were included in this study. Clinical L5/S1 ASD was defined as newly developed back pain and/or radiculopathy relating to the L5/S1 segment. The following items were retrospectively evaluated: onset time of clinical symptom, medical treatment for clinical symptom, preoperative Japanese Orthopaedic Association (JOA) score, and preoperative L5/S1 disc degeneration (MRI grading or intradiscal vacuum phenomenon by CT evaluation). Patients without ASD after L5 floating lumbar fusion were selected as the control group. Each patient in the control group was matched to an ASD patient according to age, sex and fusion levels. To identify the risk factors for ASD, these two groups were compared for body mass index (BMI), systemic disorders and preoperative L5-S1 disc degeneration by logistic regression analysis.

**RESULTS:** L5/S1 ASD with neurological manifestation in lower extremities occurred in 18 patients (5.9%) after L5 floating lumbar fusions. The mean age at the time of surgery was  $64.7 \pm 13.6$  years. The preoperative mean JOA score was  $10.8 \pm 4.8$ . The mean onset time was  $17.4 \pm 21.1$  months after surgery. In 10 patients (56%), clinical L5/S1 ASD occurred within one year after surgery. MRI analysis showed an early stage of degeneration in the L5/S1 disc in 10 patients (56%), and advanced stage in 8 patients (44%). Conservative treatments were performed in 15 patients (83%) and reoperation was performed in 3 patients (17%). There was no significant association of preoperative candidate factors between the control and clinical L5-S1 ASD groups.

**DISCUSSION:** Clinical L5/S1 ASD was identified in 5.9% of patients following L5 floating lumbar fusion. Among these, 56% of patients showed early stage degeneration at the L5/S1 disc without preoperative clinical symptoms. Although this study could not identify significant risk factors for clinical L5/S1 ASD, a careful follow-up is necessary after L5 floating lumbar fusion surgery.



## The impact of postoperative physical therapy on patient-reported outcomes in patients undergoing spine surgery

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**Introduction:** The purpose of this study was to examine the association between attending outpatient physical therapy (PT) during the postoperative period and patient-reported outcomes at 1 year following lumbar spine surgery. Since randomized controlled trials outside the United States have found no significant difference between physical therapy and educational controls, the hypothesis was that the utilization of PT would not have a significant impact on 1-year postoperative outcomes. **Methods:** 782 participants undergoing a lumbar laminectomy with or without fusion were enrolled into a single center, prospective registry and completed a preoperative assessment. Follow-up assessments occurred at 3 months and 1 year after surgery. Patients were asked whether they had out-patient PT in the past three or nine months depending on the assessment time point. A PT variable was created for analysis (No PT, PT 0-3 months, PT 0-3 and 3-12 months, PT 3-12 months). Patients also completed validated questionnaires to assess disability (Oswestry Disability Index: ODI), quality of life (EQ-5D), and back pain (11-point Numeric Rating Scale) at all timepoints. Linear mixed-effects models were used to examine the effect of PT group on outcomes over time. All analyses controlled for baseline outcome scores, age, gender, smoking status, insurance type, body mass index, presence of neurogenic claudication, surgery type, number of levels, ASA grade, and preoperative depression and narcotic use. Significance was set at  $p < .05$ . **Results:** Over the 1-year period, 238 patients had no PT (31%), 285 had PT from 0-3 months only (36%), 197 had PT from 0-3 and 3-12 months (25%), and 62 had PT from 3-12 months only (8%). Patients attending PT were more likely to be older (mean age 62.5 vs. 59.9;  $p=.001$ ) and undergoing a fusion (64% vs. 57%;  $p=.04$ ) compared to patients not attending PT. The mixed-effects models found a significant relationship between PT and all patient-reported outcomes, with patients in the PT 0-3 months only group having ODI scores 3.5-points higher, EQ-5D scores .03-points lower, and back pain scores .35-points higher than the No PT group ( $p < .05$ ). The PT 0-3 and 3-12 months group had ODI scores 5.6-points higher, EQ-5D scores .05-points lower, and back pain scores .41-points higher than the No PT group ( $p < .05$ ). Finally, the PT 3-12 months only group had ODI scores 7-points higher, EQ-5D scores .06-points lower, and back pain scores .62-points higher than the No PT group ( $p < .01$ ). **Discussion:** This retrospective analysis of prospectively collected registry data found that patients utilizing physical therapy after lumbar spine surgery had worse postoperative outcomes at 1-year in terms of higher disability and pain and lower quality of life, after controlling for demographic and clinical characteristics. Traditional postoperative physical therapy may not be the most effective rehabilitation approach after spine surgery. Randomized controlled trials have demonstrated that psychologically informed rehabilitation may be more appropriate due to the high levels of depression, anxiety and fear of movement found in this patient population.

## Organization of the motor units in the longissimus

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### Introduction

Early motor control studies suggested that a distinction exists between deep and superficial back muscles regarding their contribution to spinal stability. Based on these studies, it was hypothesized that deep lumbar muscles (multifidus) contribute to intersegmental motion while superficial back muscles (erector spinae) control the orientation of the spine. Erector spinae are divided in three muscles: the iliocostalis, the longissimus and the spinalis. As opposed to most appendicular muscles, these three muscles possess multiple end plates due to their segmental innervation. Consequently, the detection of motor unit action potential propagation along their muscle fibres can be difficult. This raises the question of how motor unit territories are organized in the erector spinae and how contractile activity is distributed along the length of these muscles. Therefore, the aim of this study was to identify the size and localisation of motor unit territories in the longissimus muscle using fine intramuscular wires electrodes.

### Methods

Eight healthy participants were recruited for this study. First, they were asked to lay in prone position. Then, participants had fine intramuscular wires inserted into the longissimus muscles (lumbar part) under ultrasound guidance to record multi-unit electromyography (EMG) activity. Insertions was performed unilaterally in 7 recording sites per participant (L1, L1-L2, L2, L2-L3, L3, L3-L4 and L4). A tungsten needle was also used to record single motor unit activity. The tungsten electrode was inserted near one of the recording site. Then, participants were asked to perform a series of weak voluntary contractions: gradually increasing ramp and hold isometric back extension until a motor unit with regular discharge rate can be identified and recorded. Participants were asked to perform additional voluntary contractions with a higher intensity until new motor units are recruited. The tungsten electrode was then moved to the location of another fine-wire recording sites to record action potential from new motor units. The detection of motor unit action potentials recorded from the EMG signals was processed using Spike2 software.

### Results

A total of 71 motor units were identified along the longissimus muscle. Of 71 motor units, 34 spanned the upper recording sites (L1 to L3), 30 spanned the lower recording sites (L3 to L4), and 7 motor units spanned all recording sites (L1 to L4). The size of motor unit territories was 5.9 cm from L1 to L3 and 3.1 cm from L3 to L4.

### Discussion

Results from the current study showed a clear distinction in motor unit territories between the upper and lower lumbar region of the longissimus muscle. Findings of this study raise a critical question regarding the potential functional significance of the segmental innervation of the longissimus. The next step will be to explore how motor units in the superficial low back muscles are organized when the stability of the spine is challenged (examples: under the influence of muscle fatigue, experimental pain, or delayed onset muscle soreness).

## Regional patterns of lumbar paraspinal muscle degeneration in astronauts after long-duration spaceflight on the international space station

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### INTRODUCTION

National Aeronautics and Space Administration (NASA) crewmembers have a 4.3 times higher risk of a herniated intervertebral disc (IVD), compared to the general and military aviator populations<sup>1</sup>. The highest risk occurs during the first year after a mission. Microgravity exposure during long-duration spaceflights results in ~5cm lengthening of body height, spinal pain, and skeletal deconditioning<sup>1-2</sup>. Previously we reported on the lumbar paraspinal muscle (PSM) changes in aggregate, for six NASA crewmembers<sup>3</sup>. This update reports on individual muscle group changes with a larger cohort of astronauts. The immediate objective is to evaluate lumbar PSM functional cross-sectional area changes induced by a 6-month space mission on the International Space Station (ISS). The long-term objective of this project is to promote spine health and prevent spinal injury during long space missions as well as here on Earth.

Study Design Prospective case series

Level of Evidence 4

### METHODS

Institutional Research Board approval was obtained from NASA and the University of California, San Diego. Eight NASA crewmembers (2 female and 6 males, age 46-55 years) were imaged supine with a 3T MRI. Imaging was conducted pre-flight, immediately post-flight and then ~45 days after landing. Functional cross-sectional area (FCSA) measurements of the PSMs were performed at the L3-4 level. FCSA was measured by grayscale thresholding within the posterior lumbar extensors to isolate lean muscle on T2-weighted scans<sup>3-4</sup>. Repeated measures ANOVA was used to determine significance at  $p < 0.05$ , followed by post-hoc testing.

### RESULTS

Overall lean PSM mass, as indicated by the FCSA, decreased immediately after the mission, and recovered over the next 6 weeks,  $p = 0.03$ . Multifidus muscle FCSA went from 797 mm<sup>2</sup> to 728 to 860 at the time points,  $p = 0.01$ . Figure 1. Quadratus lumborum muscle FCSA went from 1108 mm<sup>2</sup> to 882 to 1007,  $p = 0.001$ . Figure 2. Erector spinae muscle FCSA went from 3579 mm<sup>2</sup> to 3163 to 3627,  $p = 0.16$ . Psoas muscle FCSA went from 2817 mm<sup>2</sup> to 2721 to 2783,  $p = 0.35$ .

### DISCUSSION

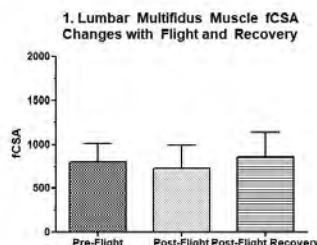
The data reveal lumbar spine PSM atrophy after long-duration spaceflight. Surprisingly the most significant atrophy was seen in the quadratus lumborum muscle. Significant changes were also seen in the multifidus muscles. Much attention has been focused on the role of the lumbar multifidi. These findings suggest the role of the quadratus lumborum muscles in lateral side bending, axial torsional activity, hip stabilization and breath support may also be very important. This study identifies specific muscle groups to possibly target to reduce spinal degradation from spaceflight. Whether new exercise countermeasures can prevent in-flight PSM atrophy, improve spinal pain and function, shorten recovery time, and how such exercise might be performed in a microgravity environment require further study.

### DISCLOSURES

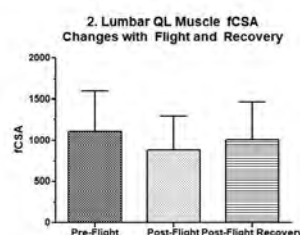
Funding was received from NASA grants NNX10AM18G and NNX13AM89G. No conflicts of interest are declared.

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Repeated Measures ANOVA	
P value	0.0144
P value summary	*
Are means signif. different? (P < 0.05)	Yes
Number of groups	3
F	5.831
R square	0.4544



Repeated Measures ANOVA	
P value	0.0011
P value summary	**
Are means signif. different? (P < 0.05)	Yes
Number of groups	3
F	11.44
R square	0.6204

## Incorporation of residual stresses from swelling and fiber tension in a disc finite element model

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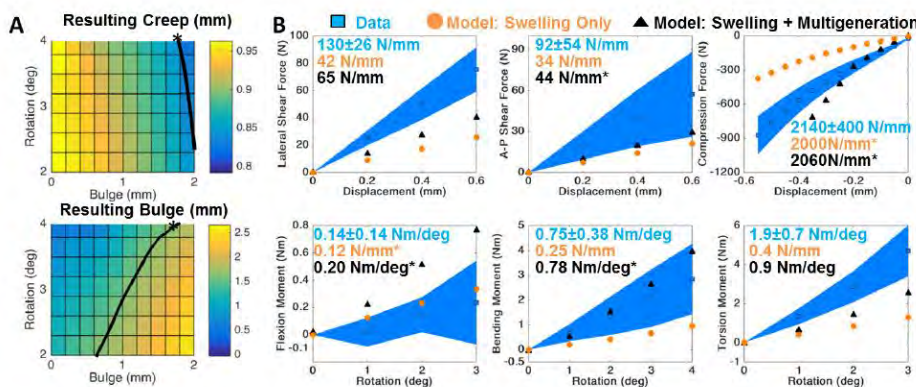
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**INTRODUCTION:** Residual stresses due to swelling and fiber tension exist in the disc, however they are not well described in finite element models (FEM). Since these residual stresses arise during development and growth, when the disc materials are formed, the objective of this study was to apply a multigenerational growth approach to incorporate residual stresses arising from both swelling and fiber tension in a disc FEM, and to validate the model using disc segment testing in all six degrees of freedom.

**METHODS:** FEBio was used to develop two FE models: one included residual stress due to swelling and the other included residual stress due to both swelling and growth. Swelling stresses were modeled using osmotic swelling pressure via fixed charge density. Residual stresses from growth were modeled using a multigeneration approach applied to the AF fibers. A parametric study on two parameters (initial disc rotation,  $\alpha$ , and initial disc bulge,  $b$ ) was performed using simulated swelling under 50 N axial compression and 0.2 MPa 12 hr compressive creep, and the parameter values that resulted in bulge and creep displacement closest to experimental data were selected. Simulations: Using the selected  $\alpha$  and  $b$ , both FE models were run to simulate disc loading and compared to experimental measures via the following protocol. Experimental protocol: Moderately degenerated (grade 2-3) cadaveric human lower lumbar discs ( $n=6$ ) that were preloaded to 0.2 MPa NP pressure and tested in 6 degrees of freedom: lateral shear, anterior-posterior (A-P) shear, torsion, lateral bending, flexion-extension and compression. For each motion, the two FEMs were compared to the discs' 95% CI stiffness at 70–90% of peak load.

**RESULTS:** From the parametric study a combination of  $b=1.8$  mm and  $\alpha=4^\circ$  rotation matched experimental disc bulge and creep displacement (Fig. 1A). The model that included both sources of residual stress matched the experimental nonlinear loading response curves and the stiffness better than osmotic swelling alone for all loading directions (Fig 1B). Indeed, when both osmotic and growth residual stresses were included, the FEM predicted 4 of 6 loading directions within the experimental 95% CI for stiffness. When only osmotic loading residual stresses were included, the model predicted stiffnesses within the 95% CI for only 2 of the 6 directions (Fig 1B).

**DISCUSSION:** This study demonstrated that including residual stresses from both swelling and fiber tension are needed to describe the multi-axial loading of the disc. Moreover, for the first time, a multigenerational approach produced these residual stresses based on experimental data to achieve the desired constitutive properties of the disc tissues. By including AF fibers at different initial stretches, the AF residual stresses are greater than from only swelling. This approach improves model predictions of disc mechanics. Inclusion of only swelling-induced residual stress is sufficient to predict the disc's response to compression, as is common in the literature, but these results show the disc's response to other motions requires inclusion of AF fiber residual stress.



**Figure 1:** (A) Results of parametric study on  $\alpha$  and  $b$ . Black lines show combinations of  $\alpha$  and  $b$  which match experimental data. (\*) denote where lines intersect. (B) Comparisons between 6DOF response for experimental data, swelling-only model, and swelling/growth model. (\*) denote within 95% CI.

## Ontario inter-professional spine assessment and education clinics (ISAEC): patient, provider and system impact of an integrated model of care for the management of low back pain (LBP)

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**Introduction:** ISAEC uses an interdisciplinary shared-care model to provide upstream secondary and tertiary standardized clinical evaluation, stratified education and self-management recommendations for low back pain patients. ISAEC was designed to integrate care between ongoing patient self-management, primary care and specialist care including standardized imaging and referral criteria. The objectives of this study are to determine the impact of an evidenced based shared-care model of care (ISAEC) on 1) Patient reported satisfaction and outcome; 2) Primary care provider (PCP) satisfaction and knowledge transfer; 3) Surgical referral appropriateness; and 4) Utilization of spinal imaging from the perspective of the health care system.

**Methods:** 1) Mixed methods study for patient and provider evaluation (patient reported outcomes measures (Oswestry Disability Index (ODI) / Start Back Chronicity Risk Assessment) as well as process and satisfaction surveys). 2) Institute for Clinical Evaluative Sciences (ICES) administrative data analysis comparing spine imaging test ordering by ISAEC and non-ISAEC physicians and determine the direct cost impact.

**Results:** From November 2012 to February 2016, 4532 patients have been assessed. The mean wait time for secondary assessment was 12 days. The majority of patients (68%) were diagnosed with back-dominant pain. The majority of presentations (68%) were considered complex (e.g. positive for psychosocial factors (52.2%)). Patient satisfaction (n=1922) was 99%, and 95% felt they understood their condition better. For 811 patients enrolled in a longitudinal study, 54% of patients reported a perceived improvement in their symptoms with a mean reduction in ODI score of 10 was observed at 6 months (Baseline=36% / 6 months=26%).

At 4 and 12 months into the program, enrolled PCPs (n=134 /220) on average showed a two-fold increase in their confidence managing LBP (assessment and management, referral for imaging and specialist consultation). 97% of PCPs reported overall satisfaction with the ISAEC model of care and felt that ISAEC services would be useful to all PCPs. Within the ISAEC network of providers, surgical referral appropriateness was 96% (compared to 20-30% prior to ISAEC) and <4% of overall ISAEC patients have gone on to surgical interventions. Average wait-time for surgical assessment was 5.4 weeks, 4.3 weeks, and 2.2 weeks at the metropolitan, urban, and rural centres respectively compared to 6-18 month prior to formation of the ISAEC network.

Compared to non-ISAEC PCPs, the overall annual utilization for all LBP-related diagnostic imaging ordered by ISAEC-PCPs fell 28% in year 1 and an additional 5% in year 2 compared to their non-ISAEC peers. This translated to an annual estimated per physician cost avoidance of \$3150 and \$4175 in year 1 and 2 respectively based only on imaging.

**Conclusion:** In single-payer public healthcare delivery system, a shared-care, stratified education and self-management model of care for LBP provides significant positive multidimensional impact on patients, providers and the health care system. Overall, the ISAEC model was able to improve on the quality and appropriateness of care, while reducing cost.

## **Preliminary findings from an active surveillance reporting system for spinal manipulative therapy regulated providers and low back pain patients**

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**Introduction:** Low back pain (LBP) is a prevalent condition commonly treated with conservative care, including spinal manipulative therapy (SMT). Adverse events (AEs) associated with SMT have been studied in different research designs, including clinical trials. However, clinical trials are not the optimal methodology to study rare AEs. Furthermore, most observational studies lack standardized instruments and operational definitions for AEs related to SMT. This study conducted an active surveillance reporting system, the appropriate methodology for studying AEs, with SMT practitioners using a standardized instrument in order to identify, and report AEs associated with SMT.

**Methods:** Data were recorded from 1422 patients seen by 18 healthcare professionals from two professions registered to provide SMT. Data were collected using a standardized, content validated paper-based instrument which included patient demographics, reasons for treatment, and symptoms before and immediately after SMT was provided. Symptoms before and immediately after SMT were assessed for their change status (improved, no change, worsened) and severity (mild, moderate, severe and serious). AEs were conservatively defined as "any unfavorable sign, symptom, or disease temporally associated with the treatment, whether or not caused by the treatment, specifically any worsening or new symptom with moderate severity or higher".

**Results:** Among the 1422 patients from whom data were collected, 591 (41.5%) sought care for LBP treatment. The average age of LBP patients was 50.3 years old and 58% were female. Before treatment, the 591 LBP patients reported a total of 1669 symptoms including discomfort/pain, stiffness, weakness, tiredness/fatigue, headache, dizziness, numbness/tingling, nausea/vomiting and difficulty walking. Immediately after treatment, 866 symptoms (51.8%) were reported. Most symptoms reported immediately after SMT were mild (73.3%) or moderate (24.3%), with the minority of symptoms being rated as severe (2.4%). While LBP patients also reported that the majority of symptoms improved immediately after SMT (70.6%), 26.5% of symptoms did not change and 2.3% of symptoms were reported to have worsened (AE) after SMT. Specifically within the reported AEs, 90% were rated as mild symptoms and 10% were rated as moderate. There were no new symptoms reported immediately after SMT and no worsened symptoms rated as severe or serious.

**Discussion:** This is the first study to conduct an active surveillance reporting system within healthcare professionals regulated to perform SMT. The LBP patients presented with several co-existing symptoms before and immediately after treatment, which may be related or unrelated to their LBP. There was a 48% reduction of symptoms observed immediately after SMT treatment. Although preliminary, these results show a smaller AE rate when compared to previous studies looking at AEs following SMT. By identifying the AEs observed following an intervention involving SMT in LBP patients, risk factors can potentially be identified and mitigation strategies developed.

**SP36**

**Which material properties and which morphology parameters are most important for numerical models of the lumbar spine?**

**Benedikt Schlager, Frank Niemeyer, Fabio Galbusera, David Volkheimer, René Jonas, Hans-Joachim Wilke**  
Publish consent withheld

## Risk factors for cage migration and cage retropulsion following transforaminal lumbar interbody fusion: does osteoporosis carry higher risk?

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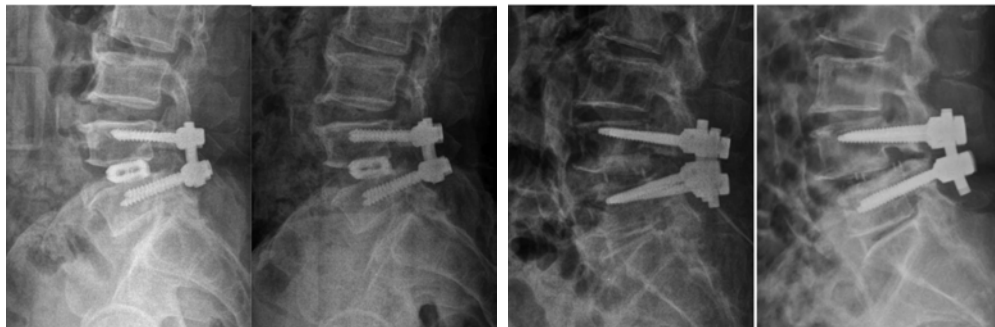
**INTRODUCTION** Transforaminal lumbar interbody fusion (TLIF) is a widely accepted surgical procedure, but complications of cage migration (Fig. 1, CM) or cage retropulsion (Fig. 2, CR) are associated with poor outcomes. This prospective observational longitudinal study seeks to identify risk factors associated with these serious events.

**METHODS** Over a 5-year period, 881 lumbar discs in 784 patients were treated using TLIF at 3 spinal surgery centers. Patient records, operative notes, and radiographs were analyzed for factors potentially related to CM or CR.

**RESULTS** Of 881 lumbar discs treated with TLIFs, CM was observed in 56, and CR was observed in 17. Our study found some risk factors for CM and CR in multivariate analysis. Osteoporosis was found to be a significant risk factor for CM ( $P < .001$ ) and CR ( $P < .001$ ). A pear-shaped disc was also found to be significantly related to CM ( $P = .002$ ) and CR ( $P = .001$ ). The unilateral single cage was a significant risk factor for CM ( $P = .02$ ) and CR ( $P = .03$ ). The endplate injury was significantly correlated with CM ( $P < .001$ ) and CR ( $P < .001$ ). The posterior position of cage was not a significant factor in CM, but a significant factor in CR ( $P = .04$ ). The initiation of CM was found in 35 patients (62.5%) within 0-1 months, 20 patients (35.7%) within 1-3 months and 1 patient (1.8%) within 3-6 months after surgery. The termination of CM was detected in 24 patients (42.8%) within 1-3 months, 30 patients (53.6%) within 3-6 months, and 2 patients (3.6%) within 6-9 months. A difference in overall fusion rates was identified, with a rate of 97.1% (801 of 825) for no CM, 46.4% (26 of 56) for a CM, and 17.6% (3 of 17) for a CR at 1.5 years postoperatively ( $p < .001$ ).

**DISCUSSION** In our study, levels with osteoporosis experienced CM and CR with significantly greater frequency than those with normal BMD. Some cadaveric studies have reported that BMD was a significant factor relating to cage stabilization.<sup>1-3</sup> Furthermore, the fixation strength of pedicle screws depends on the mechanical properties of the trabecular bone at the bone-screw interface.<sup>4</sup> Consequently, osteoporosis could lead to loosening of the pedicle screws, which are then unable to provide axial compressive strength sufficient. Before insertion of cage, endplate injury was found to be a significant risk factor for CM and CR in our study. The importance of preserving the bony endplate to prevent CM has been reported in other studies.<sup>5,6</sup> Endplate preparation is a vital step in creating a successful fusion. However, if the vertebral body has endplate injury, the interface between the cage and the vertebral body may not have sufficient strength to support cage's stabilization. Our study suggests that osteoporosis, a pear-shaped disc, the posterior position of cage, endplate injury and the unilateral single cage are risk factors for CM and/or CR. When considering TLIF, the surgeon should be aware of these risk factors.

Figure 1. Cage migration without retropulsion (CM)      Figure 2. Cage migration with retropulsion (CR)





## Older age is independently associated with increased hospital charges and resource utilization in degenerative lumbar surgery: an analysis of 2,010 cases at a single institution

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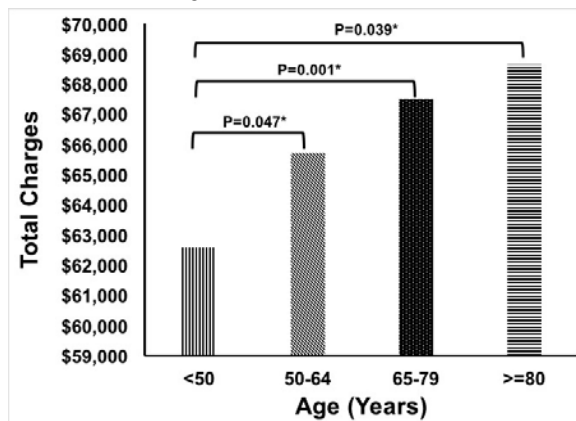
**Introduction:** Medicare Severity-Diagnosis Related Groups (MS-DRG) used by Center of Medicare Services for hospital reimbursement do not take patient age into account. The aim of our study was to determine if older age was independently associated with increased resource utilization and overall hospitalization charges in patients undergoing surgery of the lumbar spine for degenerative conditions.

**Methods:** A retrospective review of all lumbar surgeries for degenerative conditions was performed at a single orthopaedic hospital for a 4-year period from Sept 2011 through Aug 2015. Operations consisting of microdiscectomy, irrigation and debridement, staged operations, and those performed for diagnoses other than for lumbar degenerative conditions such as those for spinal deformity, tumors and infection were excluded. Hospital financial data was used to determine the overall charges. A total of 2,010 cases that met the inclusion criteria were identified (Table 1) and analyzed. Significance was set at P<0.05.

**Results:** Of the 2,010 cases, 37% were lumbar decompression-alone, and 63% were lumbar fusion surgeries. The median patient age was 64 years (IQR: 54 to 71 years). The median hospital charges were \$52,417 (IQR: \$29K to \$64K) for all patients, \$24,474 (IQR: \$20K to \$31K) for the decompression group, and \$60,454 (\$53K to \$73K) for the fusion group. Among the lumbar fusion group, the mean hospital charges were significantly higher in all older groups; compared to patients <50 years, the mean adjusted hospital charges were \$3,158 higher (P=0.047) in the 50-64 years group, \$4,945 higher (P=0.001) in the 65-79 years group, and \$6,092 higher (P=0.039) in the ≥80 years group (Figure 1). For the entire cohort, increased patient age was found to be independently associated with increased total hospital charges in both univariate (P<0.001) and multivariate (P=0.002) linear regression models (the latter adjusted for patient gender, ASA score, revision surgery status, levels fused, levels decompressed, and use of interbody device). Additional multivariate analysis revealed that increased age was associated with increased overall length of hospital stay (P<0.001), but not increased operative time (P=0.664).

**Conclusions:** Older age is independently associated with increased hospital charges and length of stay in patients undergoing lumbar spine surgery for degenerative pathology. Patient age ought to be an important metric for consideration for resource allocation and determining hospital reimbursement.

**Figure 1:** Distribution of Total Charges by Age Group for Patients Treated with Lumbar Fusion Surgery for Degenerative Conditions. The height of the bars are set at the mean total charges for each group after adjusting for number of levels fused.



**Table 1:** Characteristics of 2,010 Patients Undergoing Lumbar Surgery for Degenerative Conditions

	Age Group				P-Value
	<50 years	50-64 years	65-79 years	≥80 years	
N (%)	385 (19%)	643 (32%)	879 (44%)	103 (5%)	-
Age, years (mean ± s.d.)	39 ± 8	58 ± 4	71 ± 4	83 ± 3	<0.001 <sup>^</sup>
% Female	41%	48%	48%	41%	0.091 <sup>±</sup>
% Fusion Cases	53%	68%	66%	49%	<0.001 <sup>±</sup>
Levels Fused (mean ± s.d.)	0.8 ± 1.2	1.0 ± 1.1	1.1 ± 1.2	0.7 ± 0.8	<0.001 <sup>^</sup>
% Interbody Cases	31%	46%	43%	26%	<0.001 <sup>±</sup>
% Revision Cases	15%	18%	18%	14%	0.393 <sup>±</sup>
ASA Grade Distribution	ASA 1: 16% ASA 2: 65% ASA 3: 18% ASA 4: <1%	ASA 1: 3% ASA 2: 51% ASA 3: 44% ASA 4: 2%	ASA 1: 1% ASA 2: 35% ASA 3: 61% ASA 4: 3%	ASA 1: 0% ASA 2: 14% ASA 3: 83% ASA 4: 4%	<0.001 <sup>±</sup>
Length of Stay (mean ± s.d.)	2.3 ± 1.3	3.0 ± 1.6	3.5 ± 2.1	3.9 ± 2.5	<0.001 <sup>^</sup>

Statistical Tests <sup>^</sup>denotes ANOVA test; <sup>±</sup>denotes Chi-Squared test

## The evaluation of brain activity in patients with chronic low back pain using a non-contact brain activity detection sensor

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### Introduction

In patients with chronic pain, visual stimulation, such as viewing images associated with pain, causes changes in functional magnetic resonance imaging (fMRI) that detects brain activity. In this study, we extracted red, green, blue (RGB) data from facial images recorded with a video camera and used a non-contact brain activity detection sensor to evaluate brain activity to assess the potential of this method for evaluating brain activity in patients with chronic lower back pain.

### Methods

This study included 29 subjects: 19 patients with chronic lower back pain treated at our clinic between January and July 2017 (four males and 15 females; mean age 70.8 years) in the lower back pain group and ten healthy males (mean age 39.8 years) in the control group. Chronic lower back pain was defined as a pain that lasted for longer than three months with a score of 5 or higher on the Numerical Rating Scale (NRS).

The subjects listened to questions related to lower back pain, and their facial images were converted to RGB data. The changes in RGB data when subjects heard the question was quantified as an RGB correlation coefficient between 0 and 1, wherein higher values indicate more brain activity. We compared the RGB correlation coefficient between the control group and the lower back pain group.

In the lower back pain group, polarization of the RGB coefficient occurred at 0.7. Therefore, we divided the patients with RGB coefficient of < 0.7 in the low (L) group and those with RGB coefficient of  $\geq 0.7$  in the high (H) group. We then made intergroup comparisons using the Japanese Orthopedic Association Back Pain Evaluation Questionnaire (JOABPEQ), the Oswestry Disability Index (ODI), and the Pain Catastrophizing Scale (PCS).

### Results

The mean RGB correlation coefficient was  $0.59 \pm 0.08$  in the control group and  $0.66 \pm 0.03$  in the lower back pain group, representing slightly higher correlations in the lower back pain group ( $P=0.07$ ). A comparison between the groups L and H revealed that the psychological disorders indicated by the JOABPEQ were lower in the H group (groups L vs. H: 41.3 vs 25.9  $P=0.05$ ).

There were no significant differences in any other parameters on the JOABPEQ. In the PCS, group H scored significantly higher on the subscale of rumination (groups L vs. H: 15.0 vs 18.8  $P=0.04$ ). There were no significant intergroup differences in the ODI or NRS measurements.

### Discussion

The RGB correlation coefficients calculated using this sensor were unassociated with measurements of lower back pain or functional disability by the NRS or ODI but were associated with the JOABPEQ psychological disorders and the rumination scores of the PCS. These results suggest that this sensor can potentially be used to evaluate brain activity in patients with chronic lower back pain who have psychological disorders.

## Obesity is associated with increased OR time, hospital stay, and postoperative wound complications in lumbar fusion surgery: analysis of 1,196 cases at a single institution

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**Introduction:** The aim of our study was to determine the association of obesity with operating room time, length of stay, hospital charges, and postoperative irrigation and debridement surgeries (I&D) in patients treated with lumbar fusion surgery for degenerative pathologies.

**Methods:** A retrospective review of all lumbar surgeries for degenerative conditions was performed at a single orthopaedic hospital for a 4-year period from Sept 2011 through Aug 2015. Patients were stratified by their body mass index (BMI) into 4 categories: "Normal" (BMI 18.5-24.9), "Overweight" (BMI 25-29.9), "Obese" (BMI 30-34.9), and "Morbidly Obese" (BMI≥35). Six patients, with BMI<18.5, were excluded from the analysis. Multivariate linear regression analysis was performed and adjustments were made for patient age, comorbidities, levels fused, revision surgery status, and use of interbody device. Significance was set at P<0.05 for all analyses.

**Results:** Of the 1,196 patients who underwent lumbar fusion surgery, 21.8% were normal BMI (mean BMI: 22.7 ± 1.6), 39.4% were overweight (mean: 27.5 ± 1.5), 26.2% were obese (mean: 32.1 ± 1.4), and 12.6% were morbidly obese (mean: 38.0 ± 2.9). There was no significant association between BMI and patient age (P=0.533) or sex (P=0.287). Number of major medical comorbidities increased significantly with BMI category (P<0.001). A multivariate model revealed that compared to normal BMI patients, the adjusted mean operating room time was 25±6 mins longer in the overweight group, 40±7 mins longer in the obese group, and 50±8 mins longer in the morbidly obese group (P<0.001 each). Morbidly obese patients had significantly longer length of hospital stay compared to normal BMI patients (4.0 vs. 3.5 days, P=0.02). Multivariate analysis revealed that the mean adjusted hospital charges for the index surgery were significantly greater in each of the higher BMI categories; compared to the normal BMI group, the total charges in the obese group were higher by \$3,162±\$1,325 (P=0.01), and in the morbidly obese group were higher by \$4,738±\$1,639 (P<0.01). The incidence of postoperative surgical I&D increased significantly with BMI category (P=0.036); multivariate logistic regression analysis revealed that obese patients had 3.6-fold odds (P=0.040), and morbidly obese patients had 5.7-fold odds (P=0.012), of undergoing postoperative surgical I&D compared to normal BMI patients.

**Conclusions:** Higher BMI was associated with increased OR time, length of stay, total hospital charges, and incidence of postoperative surgical I&Ds in patients treated with spinal fusion surgery.

**Figure 1:** Association of BMI with Incidence of Postoperative Irrigation and Debridement After Lumbar Fusion Surgery for Degenerative Conditions

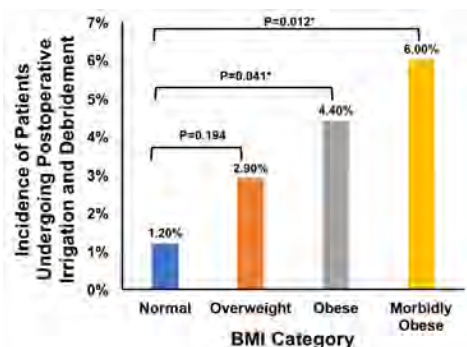


Table 1: Characteristics of 1,196 Patients Undergoing Lumbar Surgery for Degenerative Conditions Stratified by BMI Category

	BMI Group				P-Value
	Normal	Overweight	Obese	Morbidly Obese	
N (%)	261 (21.8%)	471 (39.4%)	313 (26.2%)	151 (12.6%)	-
BMI (mean ± s.d.)	22.7 ± 1.6	27.5 ± 1.5	32.1 ± 1.4	38.0 ± 2.9	<0.001 <sup>†</sup>
Age (mean ± s.d.)	59.9 ± 15.6	63.0 ± 11.8	62.2 ± 11.3	60.7 ± 11.7	0.533 <sup>†</sup>
Levels Fused (mean ± s.d.)	1.50 ± 0.80	1.46 ± 0.73	1.50 ± 0.86	1.48 ± 0.75	0.909 <sup>†</sup>
% Interbody Cases	78%	69%	68%	85%	<0.001 <sup>†</sup>
% Revision Cases	18%	21%	20%	18%	0.766 <sup>†</sup>
ASA Grade Distribution	ASA 1: 8% ASA 2: 58% ASA 3: 33% ASA 4: 1%	ASA 1: 3% ASA 2: 52% ASA 3: 44% ASA 4: 1%	ASA 1: 2% ASA 2: 42% ASA 3: 54% ASA 4: 2%	ASA 1: 0% ASA 2: 11% ASA 3: 86% ASA 4: 3%	<0.001 <sup>†</sup>
# of Major Medical Comorbidities	0: 72% 1: 20% 2: 7% ≥3: 1%	0: 55% 1: 32% 2: 12% ≥3: 1%	0: 41% 1: 43% 2: 14% ≥3: 2%	0: 33% 1: 43% 2: 20% ≥3: 5%	<0.001 <sup>†</sup>
Operating Room time (mean ± s.d.)	279 ± 93	303 ± 84	318 ± 87	329 ± 108	<0.001 <sup>†</sup>
Length of Stay (mean ± s.d.)	3.5 ± 1.7	3.7 ± 1.9	3.7 ± 1.4	4.0 ± 1.9	0.127 <sup>†</sup>
% Cases Requiring Surgical Irrigation & Debridement	1.2%	2.9%	4.4%	6.0%	0.036 <sup>†</sup>

Statistical Tests: <sup>†</sup> denotes ANOVA test; <sup>\*</sup> denotes Chi-Squared test

## Is diffuse idiopathic skeletal hyperostosis associated for lumbar spinal stenosis

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**Introduction:** Lumbar spinal stenosis (LSS) is the most common indication for spinal surgery in patients older than 65 years old. Factors related to the onset and progression of LSS have not yet been identified.

Diffuse idiopathic skeletal hyperostosis (DISH) have negative impact on poor outcomes in case of spinal fracture. The reason is thought that DISH increases mechanical loading on the non-fused segment or fracture site and leads spinal instability. The same mechanism might be adapted in case with LSS on disease onset or symptom severity. The concentration of stress in the lumbar region due to longer lever arm by the ossification of thoracolumbar DISH may leads acceleration of lumbar degenerative change. However, the associations between LSS and DISH have not been investigated in detail.

The purpose of this cross-sectional comparative study was to elucidate the association between LSS and DISH by adjusting for confounding factors.

**Methods:** This study included 2363 patients requiring surgery for LSS and 787 general inhabitants without symptoms of LSS. Patients requiring surgery were consecutive patients who underwent surgery for LSS without prior lumbar surgery. The general inhabitants were participants of part of the population-based cohort study and included participants without LSS symptom by direct assessment of a spine surgeon. Standing whole-spine radiographs were used to diagnose DISH based on the criteria proposed by Resnick et al. The prevalence and localization of DISH were investigated in LSS requiring surgery and non-LSS group. The association between DISH and LSS was analyzed using multiple logistic regression adjusted for age, sex, body mass index (BMI), DM, and LSS to obtain an adjusted odds ratio (aOR). The distribution of DISH and association between DISH and stenotic level were also analyzed.

**Results:** DISH were identified in 750 patients in LSS requiring surgery group and 128 inhabitants in non-LSS group. The prevalence of DISH was significantly higher in patients with LSS (31.7%) than those non-LSS (16.3%). The distribution of fused vertebrae by DISH was similar, platykurtic distribution, in both group, but observed more caudal shift for one level in LSS group than non-LSS group. The Multivariate analysis showed DISH (aOR 1.65  $p < 0.001$ ) as independent associated factor for symptomatic LSS, other than male, higher BMI, and DM. In the LSS requiring surgery group, L4-5 level were most affected levels in both patients with and without DISH, however, upper lumbar lesion were more performed decompression in patient with DISH than those without DISH ( $P < 0.001$ ). Moreover, the multilevel stenosis which required  $\geq 3$  levels decompression were more frequent in patients with DISH (169 pts, 39.2%) than those without DISH (581 pts, 30.0%,  $p < 0.001$ ).

**Discussion:** The result shows positive association between LSS requiring surgery and DISH. The presence of DISH may increase onset or severity of LSS. The magnified mechanical load might increase upper lumbar level or multilevel stenosis. An awareness of the high prevalence of LSS in patients with DISH can lead to early diagnosis and treatment.

In conclusion, patients with LSS requiring surgery were likely to have DISH, compare with non-LSS inhabitants.

## Risk factors for kyphotic recurrence after temporary short-segment fixation for thoracolumbar burst fractures

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### Introduction

Management for thoracolumbar burst fractures remains a matter of discussion. In annual meeting of ISSLS 2017, we presented a comparative study of temporary short-segment fixation with or without vertebroplasty. In that presentation, the fractured vertebral body itself was reduced and maintained after surgery and the correction loss (kyphotic recurrence) was observed at the disc level mainly after implant removal, both with and without vertebroplasty. Therefore, we investigated the risk factors for kyphotic recurrence after temporary short-segment fixation for thoracolumbar burst fracture.

### Methods

This prospective multicenter study included 71 patients with thoracolumbar burst fracture who underwent surgery by ligamentotaxis procedure using Schanz screws. There are 48 men and 23 women with an average of 40 years. They were followed at least one year after implant removal. Their implants were removed around 1 year after initial surgery after confirming union of the fracture. We measured two angles in lateral radiograph in standing position (except before surgery), the vertebral body angle (VBA) which was measured between the superior and inferior endplates of the injured vertebra, and the kyphotic angle (KA) which was measured between the superior endplate of the intact vertebra cephalad to the fracture and the inferior endplate of the intact vertebra caudad to the fracture before and just after operation, approximately 1 year after initial operation and the final follow-up examination. We also measured canal compromise ratio by CT scan. A multiple logistic regression analysis was performed to identify the risk factors for postoperative correction loss. We defined 10° or more correction loss in KA as kyphotic recurrence. The factors that we evaluated were age, gender, affected level, combination of vertebroplasty, load-sharing score, AO classification (type A or B), preoperative VBA, KA,  $\Delta$ VBA,  $\Delta$ KA and canal compromise ratio.

### Results

VBA was corrected to 12.3° after surgery and the total loss of correction was 0.7°. KA was corrected to 11.8° after surgery and the total loss of correction was 9.1°. CT scans revealed a mean spinal canal narrowing of 46.9% before surgery, 25.9% after surgery, and 14.7% by the 2-year follow-up examination, showing further improvement. The multiple logistic regression analysis revealed preoperative KA ( $P=0.028$ ) and preoperative canal compromise ratio ( $P=0.007$ ) were risk factors for kyphotic recurrence. These results may suggest that the extent of disc destruction at the time of injury is closely related to the likelihood of kyphosis recurrence.

### Conclusion

This study investigated the risk factors for kyphotic recurrence after temporary short-segment fixation for thoracolumbar burst fractures. Severe preoperative kyphotic angle and high preoperative canal compromise ratio by CT were the risk factors for postoperative kyphotic recurrence.

## The utility of gait analysis in patients with symptomatic adult degenerative scoliosis

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**Introduction:** Patients with adult degenerative scoliosis (ADS) demonstrate an altered gait pattern. Such differences include decreased step length and reduced range of motion in the upper and lower extremities, asymmetry of trunk rotation and altered ground reaction forces. Spinal alignment surgery has been shown to improve function and quality of life as assessed by patient reported disease specific and generic health clinical outcome questionnaires. These measures are considered objective, however can be misleading, inaccurate and lack sensitivity and specificity, due to multiple biases and data collection methods. The purpose of this study is to evaluate the utility of gait analysis as an objective outcome measure in patients with adult degenerative scoliosis before and after surgical intervention.

**Method:** Sixteen patients with symptomatic ADS who have been deemed appropriate surgical candidates underwent clinical gait analysis the week before surgery (Pre) and three months (Post) after surgery. Fifty reflective markers were incorporated to collect full body three-dimensional kinematics using 10 cameras. The patients walked at his/her self-selected speed along a 10 m walkway. Spatiotemporal parameters (i.e.: gait speed, cadence, step time, and step length and width) were calculated and analyzed with one way ANOVA to determine differences between times.

**Results:** Spinal alignment surgery improved the gait pattern in these ADS patients. A significantly faster walking speed (Pre:  $0.80 \pm 0.1$  vs Post:  $0.91 \pm 0.2$  m/s  $p=0.012$ ) and cadence (Pre:  $92.17 \pm 9.5$  vs Post:  $103.36 \pm 10.2$  steps/min  $p=0.001$ ) was measured at the three month post-surgery test in these patients in comparison to their pre-surgery. Step time (Left: Pre:  $0.69 \pm 0.1$  vs Post:  $0.60 \pm 0.1$  s  $p=0.004$ ; Right: Pre:  $0.64 \pm 0.1$  vs Post:  $0.58 \pm 0.1$  s  $p=0.005$ ), single support time (Left: Pre:  $0.50 \pm 0.0$  vs Post:  $0.43 \pm 0.1$  s  $p=0.006$ ; Right: Pre:  $0.49 \pm 0.1$  vs Post:  $0.43 \pm 0.0$  s  $p=0.005$ ) and double support time (Pre:  $0.37 \pm 0.1$  vs Post:  $0.31 \pm 0.1$  s  $p=0.003$ ) dramatically decreased at three months after surgery. Step length and width did not significantly change after surgery.

**Conclusions:** Clinical gait analysis verified significant differences before and after spine surgery in those treated for adult degenerative scoliosis. Based on our preliminary results, surgical correction of spinal alignment in these patients' improved their spatiotemporal parameters. These patients walked faster in a more symmetrical and efficient fashion after spinal re-alignment surgery. These results support the utility of gait analysis as an objective outcome measure when evaluating and treating adult degenerative scoliosis patients. The use of gait analysis may be more sensitive and specific than the current patient reported outcome measures when evaluating patients with spinal deformities.

## Associations between sarcopenia and degenerative lumbar scoliosis in Japanese older women

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**INTRODUCTION** Age-related sarcopenia can cause various forms of physical disabilities. We investigated how sarcopenia affects degenerative lumbar scoliosis (DLS) and lumbar spinal canal stenosis (LSCS).

**METHODS** Subjects comprised 40 elderly women (mean age: 74 years) with spinal disease whose chief complaints were low back pain and lower limb pain. They included 15 cases of DLS (mean 74.8 years), and 25 cases of LSCS (mean age: 72.9 years). We performed whole-body dual-energy X-ray absorptiometry (DXA) to analyze body composition, including appendicular and trunk skeletal muscle mass index (SMI; lean mass (kg) /height (m)<sup>2</sup>) and bone mineral density (BMD). Diagnostic criteria for sarcopenia was an appendicular SMI < 5.46. To check spinal alignment, Lumbar Scoliosis (LS), Sagittal vertical axis (SVA), Thoracic kyphosis (TK), Lumbar lordosis (LL), Pelvic tilt (PT), Pelvic incidence (PI), Sacral slope (SS), and Vertebral rotational angle (VRA) were measured. Clinical symptoms were determined from JOA scores, low back pain VAS, and Roland-Morris Disability Questionnaire (RDQ). Criteria for DLS were lumbar scoliosis > 10°, and a sagittal vertical axis (SVA) >50 mm. Sarcopenia prevalence, and correlations between spinal alignment, BMD, and clinical symptoms with appendicular and trunk SMIs, and correlation between spinal alignment and clinical symptoms were investigated.

**RESULTS** DLS cases had significantly lower body weight, BMI, lean mass arm, and total lean mass than LSCS cases. Sarcopenia prevalence rates were 4/25 cases (16%) in LSCS and 7/15 cases (46.6%) in DLS, revealing a high prevalence in DLS. Appendicular SMIs were DLS: 5.61, LSCS: 6.13 (p<0.05), and trunk SMIs were DLS: 6.91, LSCS: 7.61 (p<0.01) showing DLS to have significantly lower values than LSCS. Spinal alignment correlations revealed appendicular SMI was negatively correlated to PT (p<0.05), and trunk SMI was found to have a significant negative correlation with SVA, PT, LS, and VRA (p<0.05). Trunk SMI was found to have a significant positive correlation with BMD (p<0.05). As for clinical symptoms, RDQ was negatively correlated to appendicular SMI, and positively correlated to PT (P<0.05).

**CONCLUSION** Sarcopenia complications were noted in 16% of LSCS patients and a much higher percentage, or 46.6%, of DLS patients. Appendicular SMI and trunk SMI were both lower in DLS, suggesting sarcopenia may be involved in scoliosis. Appendicular skeletal muscle was related to posterior pelvic tilt, while trunk muscle affected stooped posture, posterior pelvic tilt, lumbar scoliosis, and vertebral rotation. Decreases in trunk muscle mass were also associated with osteoporosis. Moreover, RDQ had a negative correlation with appendicular skeletal muscle mass and a positive correlation with PT, suggesting that sarcopenia may be associated with low back pain as a result of posterior pelvic tilt. Our research reveals for the first time how sarcopenia is involved in spinal deformations, suggesting decreases in pelvic/lumbar support structures such as trunk and appendicular muscle mass may be involved in the progression of spinal deformities and increased low back pain.

## Early healthcare utilization after primary lumbar decompression/discectomy predicts revision surgery at two years

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### INTRODUCTION

Lumbar decompression for spinal stenosis, and discectomy for herniated disc are effective procedures in appropriately selected patients.<sup>1-4</sup> However, there is risk of re-operation in up to 13% patients due to inadequate decompression, persistent pain, intra- or post-operative complications, and/or progressive degenerative changes.<sup>5-9</sup> Various patient and clinical risk factors for re-operation in patients undergoing decompression and discectomy have been reported from numerous studies.<sup>6,7,10-12</sup> Additionally, patients requiring readmission early after surgery result in additional resource use and costs<sup>8,9,13-16</sup>, however the impact of early healthcare utilization on the long-term risk of re-operation has not been investigated.

### METHODS

Insurance claims data (2007 – Q3 2015) was used to study patients who underwent primary lumbar discectomy for herniated disc, or decompression for spinal stenosis. Patients who had early revision surgery (<3 months), or who did not have continuous insurance enrollment for six-months pre-operatively and twenty-four months post-operatively were excluded. The first occurrence of delayed reoperation (between 6 and 24 months) was queried from the database and served as the primary endpoint. We defined high healthcare users as patients who had advanced imaging (MRI, CT scan) or electrodiagnostic studies, epidural injections, two or more emergency department (ED) visits or office visits longer than 30 minutes in the first three-months after index surgery. Additionally, we studied failure to initiate physical therapy, and failure of wean off narcotics as possible risk factors. Log rank survival curves were generated to depict the survival (freedom from reoperation) at two-years. To analyze significance of risk factors for delayed reoperation, a Cox proportional hazards model was used to study above mentioned variables after adjusting for other confounders. Adjustment for age, gender, ethnicity, comorbidity burden, type of procedure, and number of levels was done.

### RESULTS

We included a total of 10,384 patients with a mean age of 65.6± 10.7 years. The cumulative delayed reoperation rate at two-years in our cohort was 5.6% (581/10,384). Demographic and clinical profile of subgroups (delayed reoperation vs. no reoperation) has been given in Fig 1. Pattern of healthcare utilization within first three-months of surgery is given in Fig 2. Survival curve for patients with and without high healthcare utilization is given in Fig 3. Results of the cox model are given in Fig 4.

### DISCUSSION

The aim of our study was to see if patients with high healthcare utilization (indicating suboptimal outcome) early after index surgery are predictive of delayed re-operation at two-years. We excluded patients who had early re-operation within 3-months as a higher risk of re-operation is expected in patients with sub-optimal outcomes early on. Our adjusted analysis found that patients who required imaging such as MRI or CT scan, epidural injections, electrodiagnostic studies, prolonged office visits or ≥2 ED visits, and were unable to wean off narcotics within the first three months remained at risk for re-operation at two-years. Additionally, initiation of guided physical therapy was not associated with lower risk of re-operation. There is residual risk of re-operation at two-years in patients with higher healthcare utilization early after primary lumbar decompression/discectomy.

Fig 1. Demographic and clinical profile of patient subgroups

		Delayed Reoperation N (%)	No Reoperation N (%)
No. of patients	Total	581	9,803
	Mean (SD)	65.6 (10.7)	65.6 (10.7)
Age	60-64	102 (17.6)	1,712 (17.6)
	65-69	138 (23.8)	2,212 (22.6)
Region	Midwest	102 (17.6)	1,712 (17.6)
	South	138 (23.8)	2,212 (22.6)
Gender	Male	302 (52.0)	5,112 (52.1)
	Female	279 (47.9)	4,691 (47.9)
Education	High School	102 (17.6)	1,712 (17.6)
	College	138 (23.8)	2,212 (22.6)
Comorbidity	Diabetes	102 (17.6)	1,712 (17.6)
	Hypertension	138 (23.8)	2,212 (22.6)
Procedure	Discectomy	102 (17.6)	1,712 (17.6)
	Decompression	138 (23.8)	2,212 (22.6)
Level	L4-L5	102 (17.6)	1,712 (17.6)
	L5-S1	138 (23.8)	2,212 (22.6)
Completion	Open	102 (17.6)	1,712 (17.6)
	Micro	138 (23.8)	2,212 (22.6)
Technology	Open	102 (17.6)	1,712 (17.6)
	Micro	138 (23.8)	2,212 (22.6)
Reoperation	Early	102 (17.6)	1,712 (17.6)
	Late	138 (23.8)	2,212 (22.6)

Fig 2. Early (<3 months) healthcare utilization in patient subgroups

	Delayed Reoperation N (%)	No Reoperation N (%)
High healthcare utilization	241 (41.5)	1,751 (17.9)
Failure to wean off narcotics	396 (68.2)	5,288 (53.9)
Initiation of physical therapy program	228 (39.2)	3,854 (39.3)

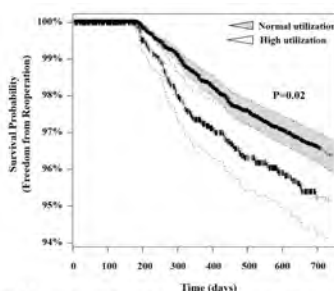


Fig 3. Log-rank survival curve for patients with and without high healthcare utilization in the early (<3 month) post-operative period

Fig 4. Adjusted estimates and hazard ratio of early (<3 months) healthcare utilization variables for delayed reoperation

	Estimate	Standard Error	Chi-square	Hazard Ratio	95 % Confidence Interval	P value
High healthcare users	0.28	0.13	2.09	1.32	1.02 – 1.71	0.03
Initiation of physical therapy program	-0.09	0.12	-0.81	0.91	0.72 – 1.14	0.42
Failure to wean off narcotics	0.63	0.13	4.89	1.87	1.46 – 2.41	<0.001



## Features and problems of corrective long spinal fusion for adult spinal deformity with multiple vertebral fractures due to severe osteoporosis

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**INTRODUCTION:** Recently, the number of adult spinal deformity patients combined with multiple vertebral body fractures due to severe osteoporosis has markedly increased. These patients often have not only severe osteoporosis, but also have other medical problems. In addition, surgery is urgent if the patient has a paralysis associated with a burst fracture. Therefore, adult spinal deformity with osteoporotic multiple vertebral fracture is different in many aspects from ordinary adult spinal deformity. The purpose of this study is to clarify its features and problems of corrective long spinal fusion for adult spinal deformity by comparing accompanied with or without severe osteoporosis.

**METHODS:** Sixty seven adult spinal deformity patients including multiple vertebral fractures due to very severe osteoporosis, who underwent corrective long spinal fusion with S2AIS as a distal anchor, and minimum follow-up period over 3 months were enrolled. Comparative study was conducted between severe osteoporosis combined group (OP group) and non-combined group (NOP group) within 3 months after surgery. We evaluated the presence or absence of underlying diseases, pelvic sagittal parameters (SS, PI, PT) and sagittal vertical axis (SVA), perioperative complications including proximal junctional kyphosis (PJK).

**RESULTS:** There were 36 patients (average age  $73 \pm 7.2$  years) in the NOP group and 31 cases ( $77 \pm 5.8$  years) in the OP group. Eighteen cases (50%) in the NOP group and 29 cases (90.1%) in the OP group were found to be associated with the underlying diseases, 9 of them (29.3%) had multiple underlying diseases. There was no significant difference in mean operation time, proximal screw fixation level, and postoperative sagittal parameters between the two groups. The progression of kyphosis of more than 10 degrees was defined as PJK, which occurred in 4 patients (12.5%) in the NOP group and 15 cases (48.4%) in the OP group within 3 months after surgery ( $p=0.0007$ ), of which 7 cases (46.7%) required additional surgery. There was no significant difference in other perioperative complications. On the other hand, regardless of the presence or absence of severe osteoporosis, there were no cases that S2AI screws became a problem clinically.

**DISCUSSION:** In severe osteoporosis cases, significantly more underlying diseases were combined, requiring careful treatment from various aspects as a systemic disease. Although there was no significant difference in many perioperative complications between two groups, clearly a large number of PJKs occurred in the NOP group, which seemed to be an urgent issue. S2AI screw was a reliable distal anchor even for patients with severe osteoporosis.

## Modic changes and disc degeneration 27 to 45 years after spinal fusion for adolescent idiopathic scoliosis

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### INTRODUCTION

Although Modic changes (MC) have been associated with low back pain in published papers, no studies have looked at the association between MC in non-fused segments and low back pain in patients who underwent adolescent idiopathic scoliosis (AIS) surgery many years ago. The purpose of this study was to investigate the long-term prevalence of the MC and lumbar disc degeneration (DD) in the non-fused segments of the surgically treated AIS patients and compare with age- and sex-matched healthy controls.

### METHODS

Study subjects consisted of 194 patients with AIS who underwent spinal fusion with Harrington instrumentation between 1968 and 1987. We tried to contact all patients by mail. Twenty-six patients (AIS group) underwent lumbar MRI, whole spine X-ray, and patient-reported outcomes (SRS-22 and ODI). Mean age at the time of follow-up was 50.8 years (range: 40 to 64), and an average of 36.1 years (range: 27 to 45) had elapsed since surgery. T1-, T2-weighted MR images were taken of the lumbar spine in the sagittal plane and T2-weighted images taken in the coronal plane. DD in non-fused segments was rated using Pfirrmann classification. Vertebral endplate changes were assessed as MC. Three independent examiners who were not informed about the clinical data of the patients performed MRI evaluations. The 29 healthy individuals who matched the patients in age, gender, and body mass index demographics were enrolled as CTR group.

### RESULTS

Based on MRI, there was a significantly higher frequency of cases with MC in the AIS group (AIS: 57.7%, CTR: 13.8%,  $p < 0.01$ ) (Figure 1). Subjects with MC in the AIS group had greater lumbar curves ( $32.7^\circ$  and  $19.7^\circ$  in subjects with and without MC, respectively;  $p = 0.002$ ). MC of 61.9% (13 out of 21 segments) was present in the concave side of the curve (Figure 2). The magnitude of lumbar coronal curve was found to be a significant risk factor of Modic changes (Odds ratio: 1.141,  $p = 0.025$ ). There were no significant differences in the frequency of subjects with DD classified as Pfirrmann grade 4 or 5 (AIS: 61.5%, CTR: 65.5%,  $p = 0.76$ ). X-rays showed no significant differences between the two groups in terms of TK, LL, PI or PT. The SRS-22 scores for function (AIS: 4.3, CTR: 4.9,  $p < 0.01$ ) and self-image (AIS: 3.0, CTR: 4.0,  $p < 0.01$ ) were significantly lower in the AIS group. The ODI scores were significantly worse in the AIS group (AIS: 8.3, CTR: 4.3,  $p = 0.04$ ). There were no significant differences observed between the two groups in the other scores.

### DISCUSSION

Although the prevalence of degenerative disc disease was basically the same as that in healthy individuals, there was a high prevalence of MC while function scores on the SRS-22 and ODI scores were poor in the AIS patient group. The magnitude of lumbar coronal curve was found to be a significant risk factor of MC. It is recommended that lumbar coronal curves be minimized after AIS surgery to decrease low back pain over the long-term.

Figure 1:  
The prevalence of lumbar spine degeneration.  
Comparison between AIS group and CTR group.

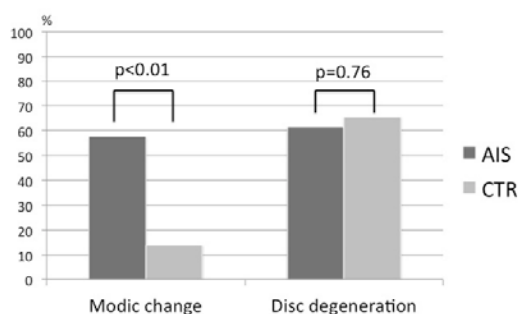
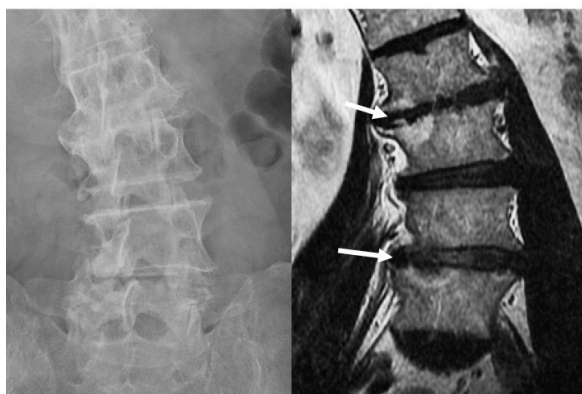


Figure 2



## The correlation of biomechanical parameters measured by balance analysis with the functional parameters measured by self-reported questionnaires in patients with adult degenerative scoliosis

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**INTRODUCTION:** Patients with adult degenerative scoliosis (ADS) demonstrate an altered balance. Balance is defined as the ability of the human body to maintain its center of mass (COM) within the base of support with minimal postural sway. Sway is the movement of the COM in the horizontal plane when a person is standing in a static position. Self-reported measures are routinely used in the clinical setting to capture data related to back and leg pain symptoms, function and perceived disability, in the setting of adult degenerative scoliosis. However, few studies have examined the correlation between patients' self-reported clinical outcome and objective biomechanical balance analysis. The purpose of this study was to determine the correlation between self-reported assessments of function with objective biomechanical measures of function.

**METHODS:** Data were prospectively collected from patients (N=30) with symptomatic ADS who were deemed appropriate surgical candidates. Functional balance analysis was performed the week before surgery. The functional balance test was similar to a Romberg's test in which the patients were required to stand erect with their feet together and eyes open in their self-perceived balanced and natural position for a full minute. COM and head displacements in the sagittal and coronal planes during the functional balance test were calculated using a custom algorithm. We further measured and calculated total sway amount by the overall length of the COM displacement line in the horizontal plane in all directions. Furthermore, back pain and leg pain Visual Analogue Scale (VAS), and Oswestry Disability Index (ODI) scores were obtained on the same day of testing. Correlations were determined between the self-report clinical outcome questionnaire measures and objective balance analysis biomechanical data using Pearson's Product Correlation in SPSS.

**RESULTS:** The ODI was correlated with horizontal COM sway in the sagittal ( $r=0.53$ ,  $p=0.003$ ) and coronal ( $r=0.42$ ,  $p=0.023$ ) planes, and COM total sway ( $r=0.52$ ,  $p=0.004$ ). Furthermore, ODI was correlated with horizontal head sway in the sagittal ( $r=0.43$ ,  $p=0.021$ ) and coronal ( $r=0.36$ ,  $p=0.050$ ) planes, and head total sway ( $r=0.37$ ,  $p=0.049$ ). The ODI standing question was correlated with COM total sway ( $r=0.44$ ,  $p=0.017$ ), horizontal head sway in the sagittal ( $r=0.39$ ,  $p=0.036$ ) and coronal ( $r=0.36$ ,  $p=0.050$ ) planes, and head total sway ( $r=0.41$ ,  $p=0.028$ ). The leg VAS was correlated with COM total sway ( $r=-0.33$ ,  $p=0.050$ ). The back VAS was not correlated with any functional balance parameters.

**DISCUSSION:** This study demonstrated a strong correlation between biomechanical parameters as measured with objective balance analysis and functional disability as measured with patient reported outcome measures including the VAS and ODI. Functional balance analysis can be a useful tool to evaluate patients with spine deformity and to assess the outcomes of treatment in this group of patients. Objective motor performance measures will improve the evaluation and understanding of the biomechanical effects of spinal disorders on locomotion. Functional balance and disability are strongly correlated in surgical ADS patients.

## **Percutaneous kyphoplasty for osteoporotic vertebral compression fractures via unilateral versus bilateral approach: a meta-analysis**

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**Introduction:** Percutaneous Kyphoplasty (PKP) has been recognized as an efficient way to relieve pain for patients with osteoporotic vertebral compression fractures (OVCFs), and PKP for OVCFs could be divided into unilateral and bilateral approaches. Until now, there is still no consensus about the optimal approach. The objective of the research was to compare the efficacy of lateral and bilateral PKP approaches for OVCFs.

**Methods:** A comprehensive literature search was performed from the PubMed, Cochrane Library and Embase between January 2008 and May 2017. The clinical efficacy of the two approaches was evaluated by comparing perioperative outcomes (operation time, the volume of injected cement, X-ray exposure times and mean radiation dose), clinical outcomes (kyphotic angle reduction, restoration rate, visual analogue scale [VAS], Oswestry Disability Index [ODI] and SF-36), and operation-related complications (cement leakage and adjacent vertebral fracture). Data was analyzed using Review Manager 5.3.

**Results:** A total of 791 patients from 10 studies were included in our meta-analysis. The pooled results showed significant differences in surgery time (weighted mean difference [WMD] -19.67, 95% confidence interval [CI] [-25.20 to -14.14];  $P < .001$ ); volume of injected cement (WMD -2.03, 95%CI [-2.63 to -1.42];  $P < .001$ ); mean radiation dose in patients (WMD -1.06 95CI [-1.23 to -0.90];  $P < .001$ ); and cement leakage (WMD 0.58 95CI [0.38 to 0.90];  $P = 0.01$ ) between these two approaches. However, the pooled results showed no significant differences in X-ray exposure times, kyphotic angle reduction, restoration rate, VAS, ODI, SF-36 and adjacent vertebral fracture.

**Discussions:** Theoretically, pain relief in the bilateral group should be more effective due to larger volume of injected cement and higher stability. However, our study showed that patients with OVCFs could obtain similar satisfactory clinical results via both unilateral and bilateral PKP approaches. Considering less operation time, radiation dose in patients and cement leakage, we suggest that a unilateral approach in PKP is advantageous.

## Low virulence bacteria in degenerative intervertebral discs: A cross-sectional study with comparisons between cervical and lumbar spine

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**Introduction** Low virulence bacterial infections could be a possible cause of intervertebral disc degeneration and/or back pain. Controversies are continuing over whether these bacteria, predominantly *Propionibacterium acnes* (*P. acnes*), represent infection or contamination. However, current studies mainly focus on the lumbar spine, with very limited data on the cervical spine, and there is no comparison between the cervical spine and the lumbar spine. Our study is to investigate the prevalence of intra-discal bacteria and its associations with characteristics of patients or discs in degenerative cervical and lumbar spine.

**Methods** 43 patients (25 men and 18 women) who underwent anterior cervical fusion and 46 patients (25 men and 21 women) who underwent posterior or anterior lumbar interbody fusion, or endoscopic discectomy were enrolled. Radiological assessments included X-ray, CT and MRI of the cervical or lumbar spine. Endplate Modic changes, the presence of disc herniation, spondylolisthesis and spinal canal stenosis were recorded. Disc and muscle tissues were collected under restrict sterile conditions. Samples were enriched in tryptone soy broth and subcultured under anaerobic conditions, followed by identification of the resulting colonies by PCR method.

**Results** We excised 144 intervertebral discs, 81 cervical and 63 lumbar, from 89 patients and positive disc cultures, mainly of which were *P. acnes* and coagulase-negative *Staphylococci* (CNS), were noted in nine cervical discs (*P. acnes* vs CNS: 3 vs 6) and in ten lumbar discs (*P. acnes* vs CNS: 4 vs 6). Positive disc cultures were noted in nine patients (20.9%) in cervical spine and in nine patients (19.6%) in lumbar spine and their muscle contamination incidence was 6/43 (14.0%) in the cervical spine and 0/46 (0.0%) in the lumbar spine. CNS was more common than *P. acnes* in cervical discs, but almost the same in lumbar discs. Meanwhile, the CNS contamination was more common in surgeries. A younger patient age, and the extrusion or sequestration type of disc herniation, was associated with positive disc culture in the cervical spine. None of the patient or discs characteristics was related to disc cultures in the lumbar spine.

**Discussion** Our data shows that CNS is more prevalent than *P. acnes* in cervical disc, but almost the same in lumbar discs. We could not draw definite conclusion that these bacteria are results of infection in cervical spine because the rate of muscle contamination during cervical surgery is also high. The bacteria are correlated with extruded or sequestered discs in cervical spine, which indicate they may infect, if this is the case, the cervical discs predominantly through a full-thickness annulus fissure.

## Does *propionibacterium acnes* presence in intervertebral disc which is acquired in percutaneous endoscopic lumbar discectomy?

Jinsuk Seo, Junseok Bae, Sangho Lee, Sangha Shin, Sangsoo Eun, Hanjoong Keum

### Introduction

Recent studies suggest low-virulent anaerobic bacteria as a pathogen of low back pain with disc herniation or spinal infection. Nevertheless, there has been controversy against the relationship between anaerobic bacteria causing low grade infection in herniated disc and possibility of intraoperative skin contamination. To avoid intraoperative skin contamination, we performed percutaneous endoscopic lumbar discectomy (PELD) which is a minimal invasive technique with lesser skin incision and no muscle exposure than open lumbar surgery. The aim of this study is investigate the presence of *Propionibacterium acnes* in intervertebral disc which is acquired in percutaneous endoscopic lumbar discectomy. Additionally, we investigated whether modic change, degree of disc degeneration, and disc herniation were associated with *P. acne*.

### Methods

In this prospective study, we enrolled 100 consecutive patients with low back pain. PELD was performed and herniated disc fragment and partial intervertebral disc were obtained. Grade of disc degeneration, type of Modic changes, were evaluated. Preoperative and postoperative outcome was assessed by using Visual analogue (VAS, 0-10 points) and Oswestry disability index 0-100 (ODI).

### Results

We found no positive culture of *P. acne* from the acquired disc. The mean age of 100 patients was 48.4 years (range, 20 -84 years) and there were 62 male patients and 38 female patients. 76 patients had history of epidural steroid injection and acupuncture treatment and 23 patients had undergone lumbar surgery. Of 23 patients, 12 (52.2%) had underwent surgery at the same level. The mean VAS score ( $7.6 \pm 0.88 \rightarrow 2.3 \pm 0.94$ ) and ODI score ( $54.1 \pm 10.9 \rightarrow 16.7 \pm 7.4$ ) decreased significantly after surgery ( $P < 0.05$ ). The study population comprised 11 patients of bulging disc, 29 patients of protrusion, 34 patients of subligamentous extrusion, and 26 patients of transligamentous sequestration. In addition, 20 of 100 patients showed Modic changes in MRI image. Patients with modic change type 1 were 9 (18%), modic change type 2 were 7 (14%), and modic change type 3 were 4 (8%). The degree of disc degeneration was classified into grade 1, 2, 3, 4, or 5. Of the 100 patients, none was found to belong to grade 1, 11 patients were grade 2, 36 patients were grade 3, 39 patients were grade 4, and 14 patients were grade 5.

### Discussion

In this prospective study, no patients had *P. acnes* present at the site of the disc herniation. Difference from other all studies, we acquired disc material from PELD. All the Previous studies, excised disc materials were acquired by open surgery; laminectomy and discectomy or deformity surgery. The cannula is directly inserted into the intervertebral disc space, which no skin or muscle is contacted when the disc sample is acquired. PELD does not include such a process, therefore the possibility of contamination is very low. Rigal et al. performed 385 disc biopsy with anterior video-assisted approach allowing no skin contact and only 6 samples were positive. According to our study, degree of disc herniation, the presence of modic change and type were not associated with *P. acne*. But continuous irrigation during the PELD may wash away the microorganism and not be detected.

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## Low levels of physical activity among patients with degenerative disc disease who are to undergo spinal fusion surgery

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**Background:** The number of patients undergoing lumbar fusion surgery for degenerative disc disease (DDD) has increased worldwide. Patients undergoing spinal surgery are assumed to be less physically active than individuals without pain. Physical activity (PA) is of essence, to avoid negative health consequences such as cardiovascular disease, obesity, cancer and diabetes. The variables in the fear-avoidance model have been suggested to be barriers to physical activity in patients with low back pain. Little is known about physical activity in patients with DDD and how physical activity is associated with the fear-avoidance variables.

**Objective:** To investigate objectively measured (accelerometry) steps per day and minutes at moderate- to vigorous-intensity physical activity (MVPA) per week, and the association between steps per day and the fear-avoidance variables in patients with DDD.

**Design:** A cross-sectional study design.

**Method:** One-hundred and eighteen patients (63 women and 55 men, mean age 46), with DDD were recruited from 3 orthopaedic clinics in Sweden. Physical activity was analysed with ActiGraph GT3X+ accelerometers and analysed as number of steps per day and MVPA per week. The accelerometers were worn for 7 days, 8 to 12 weeks before surgery. The data were analysed with the software ActiLife v6.12.0. Data were compared to the WHO's recommendations on PA for health ( $\geq 150$  minutes MVPA per week). This recommendation is comparable to 7 500 steps per day. A purposeful multiple linear regression analysis was performed with steps per day as the dependent variable and the fear-avoidance variables (fear of movement, pain catastrophizing, self-efficacy, disability and depression) as the independent variables.

**Results:** On average the patients walked 7 493 (95% CI: 7007-7980) steps per day and 63 patients (54%) did not reach the recommendations of steps per day. On average the patients spent 198 minutes per week (95% CI: 172-224) in total accumulated MVPA and 82 minutes per week (95% CI: 60-103) in MVPA accumulated in at least 10-minute duration. Ninety-six patients (84%) did not reach the WHO recommendations of physical activity. Moreover, 32 patients (28%) did not spend any time on the intensity level required for the health benefits. In the multiple linear regression analysis two variables were statistically significant, disability (standardized  $\beta = -.295$ ,  $p < 0.006$ ) and fear of movement (standardized  $\beta = -.197$ ,  $p < 0.034$ ).

**Conclusion:** The results suggest that a majority of patients who are planned to undergo surgery for DDD do not reach the WHO health recommendations of physical activity. These low physical activity levels might increase the risk of developing negative health conditions such as cardiovascular disease, obesity, cancer and diabetes. Moreover, a high level of fear of movement and disability is associated with fewer steps walked per day. These aspects must be considered when preparing these patients for surgery, in order to improve the outcome of surgery.

## The influence of an interspinous distraction device on the foraminal size in the follow-up after surgery

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### Introduction

Interspinous distraction (IPD) devices such as the COFLEX device are used in some patients with lumbar spinal stenosis to treat symptoms related to spinal root compression. Indeed, the COFLEX device aims to increase the size of the neuroforamen, thereby potentially relieving neuroforaminal stenosis and spinal root compression. However, limited to no data is available on the effect of interspinous distraction devices on the neuroanatomy of the lumbar spine. This study aimed to investigate the effect of an IPD on the neuroforaminal size, compared to the preoperative situation and compared to standard lumbar decompression.

### Methods

60 patients who were participants of the earlier randomized controlled "FELIX"-trial were included in this study. The patients had already been randomized in the earlier trial to receive treatment with either standard decompression surgery or a COFLEX device on one or two levels. CT-scans of the lumbar spine were acquired preoperatively and at 1 year postoperatively. Qualitative assessment of the CT-scans was performed independently by two neurosurgeons who were blinded for patient information. Parameters assessed included positioning of the IPD, lysis around the device and bone growth. Quantitative assessment was performed by a researcher blinded for patient information and qualitative assessment. Measurements were made on the CT-scans at baseline and 1 year postoperatively to determine the dimensions of the neuroforamen for each patient and on each lumbar level. The neuroforaminal parameters investigated were foraminal height (FH, mm), foraminal cross sectional area (FCSA, mm<sup>2</sup>), and foraminal antero-posterior diameter (FAPD, mm).

### Results

Statistical analysis was conducted using t-tests and linear mixed model analysis. Qualitative assessment showed that the IPD appeared adequately positioned in the majority of cases and that there was no failure of the device in the form of lysis in any of the patients. Analysis of the measurements at baseline showed that the foraminal dimensions did not increase in the lower lumbar levels. In fact, no significant differences in neuroforaminal dimensions between lumbar levels could be evidenced at all at baseline. Furthermore, we established that there was no significant difference of effect on the size of any of the neuroforaminal parameters (FH, FCSA or FAPD) between COFLEX and standard decompression (P-value between 0,576 and 0,646). The neuroforaminal dimensions did not change significantly between baseline and 1 year postoperatively (P-values 0,113-0,755) for either standard decompression or IPD implantation. However, the mean postoperative foraminal height was greater in the standard decompression group compared to the IPD group, although this difference was not significant (P-value 0,579).

### Discussion

The implantation of an IPD device in lumbar spinal stenosis does not seem to provide advantage on the preservation of neuroforaminal size compared to standard decompression one year after surgery. Moreover, as the earlier FELIX-trial pointed out, the implantation of an IPD does not significantly improve clinical outcome compared to standard decompression, and is associated with a higher reoperation rate<sup>1</sup>. Therefore the clinical usefulness of IPD devices should be questioned.

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## Differences in clinical and radiological outcomes depending on timing of balloon kyphoplasty for osteoporotic vertebral fracture

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### INTRODUCTION

The pain of osteoporotic vertebral fracture (OVF) usually lasts 4-6 weeks and the majority of OVFs heal within a few months. However, in some patients, OVFs cause functional deterioration, severe pain, and limited mobility because of deformity and intractable back pain. Balloon kyphoplasty is widely performed as a surgical intervention for OVF and the effects have been investigated in many previous studies. The characteristics of OVFs differ markedly depending on the time after onset, because the vertebral compression progresses for several weeks, which may be linked to vertebral cleft. However, the influence of procedure timing on patient outcomes has not been studied formally. The purpose of this study was thus to investigate differences in clinical and radiological outcomes according to the surgical timing of balloon kyphoplasty for OVF.

### METHODS

Participants in this study comprised 72 consecutive patients from 9 hospitals who underwent balloon kyphoplasty between 2012 and 2016. All patients > 65 years old who were referred because of back pain were asked to complete a short questionnaire about the presence, severity, and duration of pain. Inclusion criteria were: vertebral fracture with a recognizable intravertebral cleft on lateral radiograph in a supine position; site of fracture at Th5 or lower; intractable back pain after > 3 weeks of conservative treatment; worsened pain during sitting or standing positions; and visual analogue scale (VAS) score for back pain > 40. In addition, hyperintensity on T2-weighted imaging or diffuse hypointensity on magnetic resonance imaging (MRI) at 1 month after onset was an inclusion criterion in patients who underwent kyphoplasty within 2 months, as our previous study showed that these findings were associated with delayed union and intractable back pain at 6 months after kyphoplasty.

### RESULTS

A total of 72 patients were effectively analyzed. Of these, 27 patients (38%) underwent vertebroplasty within 2 months after onset. Mean age was 79.9 years in the Early group and 77.9 years in the Late group ( $p=0.155$ ). The proportions of sex, site of injury, and follow-up period were also comparable in both groups. However, the Late group showed a greater number of fracture lines ( $p = 0.008$ ) and greater angular motion of the fractured vertebrae ( $p=0.005$ ). The Late group also showed greater kyphotic angle ( $p=0.005$ ) and compression of anterior vertebral height ( $p=0.001$ ). Final outcomes adjusted for age and preoperative outcome, analyzed by analysis of covariance, showed lower VAS scores for low back pain in the Early group. Final kyphotic angle was greater for the Late group than for the Early group. In addition, final percentage of anterior vertebral height remained higher in the Early group. Regarding postoperative complications, cement leakage, cement dislodgement, ASD, new fracture, and reoperation displayed similar results between Early and Late groups.

### CONCLUSION

Vertebral height and kyphotic angle before and after balloon kyphoplasty were improved in cases who underwent the procedure within 2 months after symptom onset. VAS scores for back pain were lower in the Early group. Our results suggest that early surgery is warranted to prevent progression of vertebral collapse.

## The association of radiculopathy with lateral lumbar listhesis?

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### Introduction

Lateral lumbar listhesis may alter canal or foraminal dimensions, leading to stenosis<sup>1-6</sup>. It has been associated with back pain and increased surgical intervention in adult lumbar spinal deformity, however its association with lumbar radiculopathy remains uncertain<sup>7-8</sup>. Therefore, we sought to 1) determine the association of radiculopathy with lateral lumbar listhesis, 2) describe a classification of radiographic lateral listhesis, and 3) validate this classification for radiculopathy.

### Methods

Adults with lumbar spinal deformity between 2011 and 2015 were enrolled. Patients with prior thoracolumbar surgery, lumbar spondylolisthesis  $\geq$  grade 2, acute fracture, tumor or those with incomplete data were excluded. Nash and Moe vertebral rotation<sup>9</sup>, L4 lateral listhesis relative to L5, the number of vertebrae with lateral listheses, and whether a contralateral listhesis exists at the thoracolumbar junction or accompanies a caudal lateral listhesis were evaluated by radiograph. The presence of lumbar radiculopathy was recorded. Associations between the above radiographic factors and radiculopathy were evaluated by logistic regression. The most significant factors were used to develop a classification system. This system was validated with a new cohort, prospectively enrolled and evaluated from 2016-2017.

### Results

A total of 189 patients met the criteria for inclusion (mean age  $56.9 \pm 17.0$ , 82.8% female). The prevalence of lumbar radiculopathy was higher in patients with lateral lumbar listhesis than in those without (29.3% vs. 0%,  $p < 0.001$ ). Among patients with lateral listhesis, rotation at the caudal level of at least grade 2 (OR=9.45, 95% CI: 4.07-25.14), L4 involvement (OR=4.56, 95% CI: 1.85-12.35), and the number of consecutive listheses (OR=2.27 per level, 95% CI: 1.17-4.71) were associated with radiculopathy. A second, contralateral lateral listhesis at the thoracolumbar junction was not associated with radiculopathy in the general cohort, however was associated with a caudal listhesis at L3 or above (OR=7.12, 95% CI: 1.25-134.7).

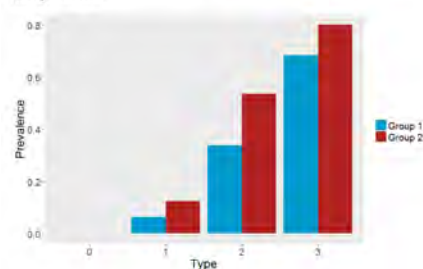
A classification system was developed based on (a) L4 involvement and (b) rotation of at least grade 2 at the caudal level. It includes three types: Type 1 (neither factor present), Type 2 (one of two factors present), and Type 3 (both factors present). Type 0 describes patients without lateral listhesis.

The prevalence of radiculopathy varied among types (6.4%, 33.8%, and 68.4% in Type 1, 2, and 3, respectively;  $p < 0.001$ ). When evaluated in a new cohort of 83 patients, a similar pattern of radiculopathy was found (12.5%, 53.7%, and 80.0%, in Type 1, 2, and 3, respectively;  $p = 0.002$ ) that was similar to the original cohort ( $p = 0.985$ , Figure 1).

### Discussion

Lumbar radiculopathy is associated with lateral lumbar listhesis in adult spinal deformity. Among 189 patients, higher-grade rotation, involvement of the L4 vertebrae, the number of consecutive listheses, and lateral listheses at the thoracolumbar junction when accompanied by a L3 listhesis and above were associated with radiculopathy. A radiographic classification system based on grade 2 or higher rotation and L4 involvement was validated in a second cohort of 89 patients. Type 2 or 3 lateral listhesis or multiple levels of lateral listhesis suggest radiculopathy and may alert surgeons of possible involvement in patients with spinal deformity.

Figure 1. Prevalence of radiculopathy by classification type in the original (Group 1) and new (Group 2) cohorts.



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## Relationship between short-term and long-term outcomes following spine surgery for lumbar spinal stenosis

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### INTRODUCTION

It is not known whether patients with good early outcomes after surgical management of LSS show consistent clinical results after long-term follow-up. Likewise, it is unclear whether patients with poor postoperative short-term clinical outcomes will gradually improve or continue with poor results during long-term follow-up. Therefore, this study aimed to clarify whether short-term clinical outcomes after LSS surgery could predict long-term outcomes. We hypothesized that short-term outcomes after surgical treatment of LSS would be significantly related to long-term outcomes.

### METHODS

A total of 295 patients who underwent spine surgery due to LSS from March 2012 to December 2015 were included in this study. At the early follow-up period (postoperative 6 months), patients were dichotomized into 2 groups on the basis of 2 different methods: the 'ODI criteria' and 'minimum clinically important difference (MCID)' methods. In the ODI criteria method, the patients were dichotomized into favorable (ODI ≤ 22) and unfavorable (ODI > 22) outcome groups at the early follow-up period. In the MCID criteria, the patients were dichotomized by the MCID value for the ODI scores. A decrease of 12.8 points from the preoperative value was set as the criterion for categorizing the "more-improved" and "less-improved" outcome group. The primary outcome was the number of patients in each group in the late follow-up period compared to those in each group in the early follow-up period. The secondary outcome was the changes of pain and disability through the entire periods in each group.

### RESULTS

According to the ODI criteria, 56 (66.7%) of 84 patients showed consistently favorable outcomes through the entire follow-up, and 35 (23.8%) of 147 patients were converted from unfavorable to favorable outcome during the late follow-up (Figure 1). Based on the MCID criteria, 94 (73.4%) consistently belonged to the more-improved group and 20 (19.4%) were converted from less-improved to the more-improved outcome group during the late follow-up (Figure 2). Based on the ODI criteria, the mean preoperative VAS for back pain and leg pain, and ODI scores were better in the favorable outcome group. However, based on the MCID criteria, the more-improved group showed a lower VAS for back pain, VAS for leg pain, and ODI scores in both early and late follow-up periods.

### DISCUSSION

Clinical status at the time of short-term follow-up after surgery was significantly related to the clinical course or prognosis at the long-term period, and 62 to 76% of patients maintained their early postoperative surgical outcomes to the late follow-up periods. Among the patients who showed good surgical outcome at the early follow-up period, about 66 to 73% of the patients consistently showed good outcome, and about 23 to 30% of the patients changed to the poor outcome at the late follow-up period. In the patients showing poor surgical outcome at the early follow-up, about 53 to 56% remained in the poor surgical outcome group, and about 19 to 23% changed to the good surgical outcome at the late follow-up period.

Figure 1.

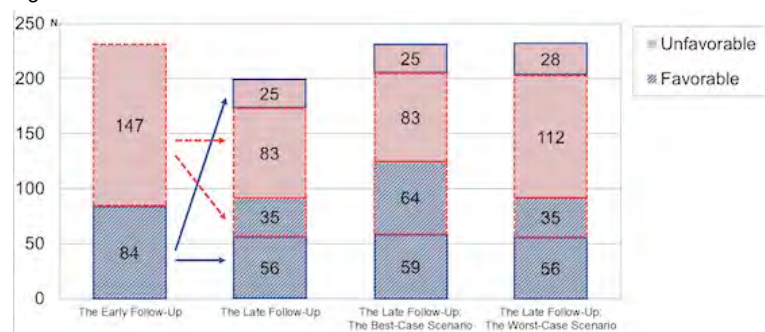
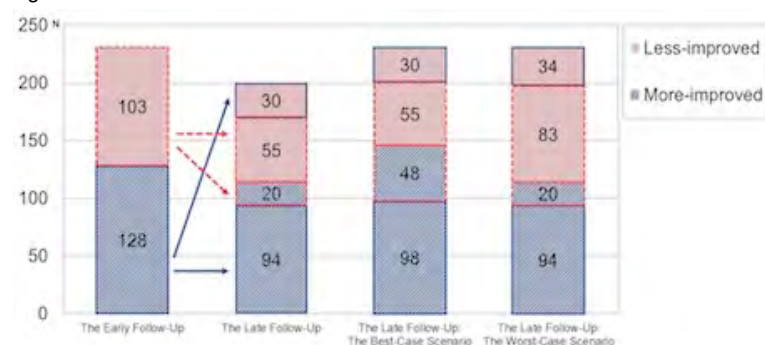


Figure 2.



**SP57**

**Population level analysis of health-related quality of life in patients with spinal disorders**

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**Introduction**

Clinicians are interested in the outcomes of treatment for individual patients. Payers and policymakers, however, are focused on the outcomes for populations. While the logistics are daunting, as the movement towards value-based care accelerates it will be necessary for clinicians to provide population-level data on their patient outcomes. The goal of this paper is to describe at the population-level the outcomes for patients with spinal disorders at an academic spine practice.

**Methods**

This is a retrospective analysis of registry data collected at an academic practice devoted to care of spinal disorders in the United States. The practice consists of five spine surgeons and two physiatrists. EQ-5D questionnaires are provided to patients at the time of their original consult and at each subsequent encounter. Results are entered into a database by a dedicated full-time research coordinator. The inclusion criteria were patients who had a baseline EQ-5 and a followup EQ-5D collected at least 90 days later. Data from 2013 to 2017 were analyzed. Patients were placed into four groups corresponding to the severity of disability on the baseline EQ-5D (<0, 0-.32, .32-.65, .66-1.0, with 1.0 representing perfect health). 0.3 was defined as the minimally clinically important difference on the EQ-5D.

**Results**

2580 patients met the inclusion criteria. Baseline and followup EQ-5D scores for each group and for each year analyzed are presented in Figure 1. Over the five year period only the most severely disabled group (those with baseline EQ-5D<0) had a clinically important improvement.

Spine Patients who filled at an EQ5D for the first time in the fiscal year and atleast 90 days later							
Group		FY2013	FY2014	FY2015	FY2016	FY2017	Grand Total
<0	N	12	8	1	4	1	26
	Avg Intial Score	(0.05)	(0.04)	(0.04)	(0.04)	(0.04)	(0.05)
	Avg Last Score	0.26	0.42	0.80	0.54	0.17	0.37
	Avg Score Delta	0.31	0.46	0.84	0.58	0.21	0.41
	Avg Episode Days	490	631	213	336	189	488
0-.32	N	118	132	105	100	33	488
	Avg Intial Score	0.25	0.25	0.26	0.26	0.25	0.25
	Avg Last Score	0.48	0.48	0.52	0.48	0.56	0.49
	Avg Score Delta	0.23	0.23	0.27	0.22	0.31	0.24
	Avg Episode Days	628	494	410	314	174	450
.32-.65	N	276	232	217	155	66	946
	Avg Intial Score	0.44	0.45	0.44	0.44	0.44	0.44
	Avg Last Score	0.62	0.63	0.65	0.63	0.65	0.63
	Avg Score Delta	0.18	0.18	0.21	0.19	0.21	0.19
	Avg Episode Days	613	559	425	300	177	475
>.65	N	295	292	283	188	62	1120
	Avg Intial Score	0.77	0.78	0.77	0.78	0.77	0.77
	Avg Last Score	0.73	0.75	0.74	0.75	0.75	0.74
	Avg Score Delta	(0.04)	(0.03)	(0.03)	(0.02)	(0.02)	(0.03)
	Avg Episode Days	603	541	400	291	171	459
<b>N Total</b>		<b>701</b>	<b>664</b>	<b>606</b>	<b>447</b>	<b>162</b>	<b>2580</b>

**Discussion**

Our results show minimal improvement in HRQOL in the overall population of patients treated in our spine practice. Present value-based payment systems focus on process measures and costs. As these systems evolve payment is likely to be increasingly linked to patient outcomes. In a fully mature value-based payment environment it will be crucial for spine practices to demonstrate, at a population level, that they make meaningful improvements in HRQOL.

## Does lumbar spinal surgery extend healthy life expectancy in the elderly?

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### INTRODUCTION:

With rapid aging of population, an increasing number of elderly people want to remain active and pain-free whenever possible, and to take the risk of surgery to improve their quality of life. However, it remains unclear whether lumbar spinal surgery affects life expectancy as well as walking ability in the rest of life. We examined the impact of lumbar spine surgery on healthy life expectancy (HLE) and life expectancy (LE) in the elderly population.

### METHODS:

We retrospectively reviewed 174 patients (70 men and 104 women) who had undergone a lumbar spinal surgery at the age of 80 years or older (80 to 94 years). Surgical procedures were decompression alone in 76 patients and instrumentation surgery in 98 patients. There was one perioperative death due to cerebral infarction. Postoperative complications were surgical site infection in six, instrumentation failure in two, and hematoma in one. Healthy life expectancy (HLE) was defined as the age when a patient becomes unable to walk independently even with cane/walker/arm rail. Life expectancy (LE) at the age of surgery was calculated using the national population statistics. Age of death, if any, was also recorded. Mean follow-up period was 5.0 years.

### RESULTS:

Life expectancy predicted at surgery (LE @surgery) was 91.7 years (90.6 years in male and 92.5 years in female), and the mean age at the final follow-up was 87.7 years (88.5 years in male and 87.2 years in female). At the final follow-up, 142 patients (82%) were alive, and 112 patients (64%) could walk independently. Healthy life expectancy (HLE) exceeded 87.2 years (88.2+ years in male and 86.6+ years in female).

Thirty-two patients (18%) died at the mean age of 87.6 years, whereas their LE @surgery was 92.0 years: lumbar spinal surgery did not extend LE itself. HLE in this group reached 87.0 years, and period between HLE and age of death was 0.6 years (0-3 years). The elderly retained walking ability 0.6 years before the age of death.

### DISCUSSION:

According to national population statistics of our country, life expectancy is 80.2 years in men and 86.6 years in women; healthy life expectancy is 71.2 and 74.2 years, respectively. Discrepancies between these indices reach 9.0 years in men and 12.4 years in women. This means that the elderly cannot live independently and require physical/social supports for 9.0-12.4 years in the rest of life. Smith et al (Spine 36: 817-824, 2011) demonstrated the potential benefits of surgical treatment for adult spinal deformity and suggested that the elderly, despite facing the greatest risk of complications, might stand to gain a greater improvement in disability and pain with surgery. The current study supported this conclusion, and showed that lumbar spinal surgery did not change life expectancy itself but could extend healthy life expectancy.

## Impacts of postoperative symptom improvement and disabilities on health related quality of life (HRQOL) and treatment satisfaction in the adult spinal deformity patients treated by corrective long fusion

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**INTRODUCTION:** Long spinal fusion is often performed to correct coronal and sagittal deformities for adult spinal deformity patients. However, the long spinal fusion sometimes cause disability in daily activities, especially in case with pelvic fusion. Purpose of this study was to investigate the impact of postoperative symptom improvements and disabilities on HRQOLs and treatment satisfaction in the adult spinal deformity patients treated by corrective long fusion from thoracic to pelvis.

**METHODS:** A consecutive 139 adult deformity patients who underwent corrective long fusion from thoracic to pelvis were included in this study. There were 22 males and 117 females with average age of 68. Four main symptoms including a) socio-mental, b) visceral (respiratory, digestive), c) leg symptoms, and d) back pain were evaluated by Numerical Rating Scale (NRS, 0-10), preoperatively and 2 years after the surgery. Difficulties of daily activities including e) gait, f) nail cut, g) lying in supine, h) wipe bottoms, i) wear pants, j) pick up objects from floor, and k) get down on all fours, were also evaluated by NRS at the same time periods. HRQOL was investigated by Oswestry Disability Index (ODI), and treatment satisfaction score (0-100) was evaluated by patients themselves at 2 years after the surgery. Relationship between change of each symptom (improvement: +, deterioration: -) and ODI/treatment satisfaction score were investigated.

**RESULTS:** Average scores of NRS in main symptoms, difficulties of daily activities, ODI, and satisfaction scores were summarized in **Table 1**. Average improvement of NRS (main symptoms) were a) 2.3, b) 0.7, c) 0.03, and d) 2.6, suggesting that greater improvements were observed in socio-mental and back pain. Average improvement/deterioration in daily activities were e) +2.1, f) -3.2, g) +0.9, h) -1.1, i) -1.6, j) -2.3, and k) 2.0. Average ODI was improved from 46.1% to 31.1%. Significant correlations ( $p < 0.01$ ) were observed between the  $\Delta$ ODI and d)  $r = 0.43$ , e)  $r = 0.55$ , g)  $r = 0.31$ , h)  $r = 0.26$ , i)  $r = 0.30$ , and j)  $r = 0.34$ . Average treatment satisfaction score was 76.0, and significant correlations ( $p < 0.01$ ) was observed between the satisfaction score and a)  $r = 0.35$ , c)  $r = 0.36$ , d)  $r = 0.31$ , and e)  $r = 0.30$ . These results suggested that improvements of main symptoms were directly associated with treatment satisfaction.

**DISCUSSION:** Although postoperative disabilities have affected HRQOLs 2 years after corrective long fusion for adult spinal deformity patients, these daily disabilities did not have greater impacts on the satisfaction for their surgical treatment.

**Table 1.** Average Scores of Numerical Rating Scales in Main Symptoms, Difficulties of Daily Activities, ODI, and Satisfaction Scores

	Main Symptoms				Difficulties of Daily Activities							ODI	Satisfaction
	a	b	c	d	e	f	g	h	i	j	k		
	Socio-Mental	Visceral	Leg Symptom	Back pain	Gait	Neil Cut	Lying in supine	Wipe bottoms	Wear Pants	Pick up	Get down		
Pre-op	7.1	3.5	4.8	7.0	7.4	4.9	5.2	3.9	4.6	4.9	6.1	46.1	76.1
P.O. 2Y	4.8	2.8	4.7	4.3	5.2	8.0	4.2	4.9	6.0	7.0	8.0	31.1	
Ave. $\Delta$	+2.3	+0.7	+0.03	+2.6	+2.1	-3.2	+0.9	-1.1	-1.6	-2.3	-2.0	+15.0	

## Clinical outcomes research in lumbar spine surgery: Are 2 year follow-ups necessary?

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**Introduction.** There has been generic dictum in spine and musculoskeletal clinical research that 2 year follow-up is necessary for patient reported outcomes, but the rationale for 2 year follow-up is not evidence based; thus, the purpose of this study was to determine patient reported outcomes follow-up times necessary to ensure effectiveness of a lumbar surgical intervention is appropriately evaluated.

**Methods.** Using patient reported outcomes from the Canadian Spine Outcomes and Research Network (CSORN) prospective database, the time-course to plateaued recovery after lumbar spine surgery was assessed for lumbar disc herniation, degenerative spondylolithesis, and spinal stenosis. One-way ANOVAs with post-hoc testing were used to analyse patient reported outcomes at baseline, three, twelve, and twenty-four months post-operatively on the following standardized patient reported outcomes: EQ5D, disability score, VAS leg and back, and SF-12 mental and physical scales.

**Results.** There were significant differences determined by one-way ANOVAs for all spine pathologies and specific patient reported outcomes ( $p < 0.0001$ ). Time to plateaued recovery after surgery for lumbar disc herniation, lumbar spondylolithesis or lumbar stenosis followed the same time-courses for the following patient reported outcomes: VAS back and leg 3 months, disability score 12 months, SF-12 physical 12 months, and SF-12 mental 3 months.

**Discussion.** Individual patient reported outcomes after surgery for lumbar spine pathologies follow specific time-courses to plateaued recovery; this indicates that a two-year follow-up is not required for all outcomes to be accurately assessed. Ultimately, the clinical research question should dictate the follow-up time and the outcome measures utilized; however, there is now further evidence to guide the specific duration of follow-up for each patient reported outcome.

## Long-term evaluation of a Canadian back pain mass media campaign

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**Introduction** According to the recent Global Burden of Disease Study, low back pain (LBP) remains one of the most prevalent disorders and the leading cause of disability worldwide. Clinical practice guidelines indicate that management of LBP should focus mainly on reassurance of the patient, advice to stay active, and addressing misconceptions about LBP. However, general public beliefs about back pain appear pessimistic and widespread misconceptions are held, which has led to population-based interventions aimed at improving beliefs. One of these campaigns was a mass media campaign that was undertaken in Alberta, Canada. The campaign aimed to improve LBP beliefs in the general public by focusing on messages related to the importance of staying active during an episode of LBP. Initial evaluation indicated modestly improved public LBP beliefs and annual bursts of campaign activity have been administered to the population ever since. We evaluated the long-term impact of this campaign on general public beliefs about LBP up to 7 years after the end of the initial evaluation.

**Methods** This study was designed as repeated cross-sectional population surveys without a control group. Ongoing changes in beliefs about staying active during an episode of back pain were studied using telephone and web-based surveys conducted from 2010 through 2015. Between 2010 and 2015, 11,637 randomly selected Alberta residents aged 18-65 years were surveyed using Computer-Assisted Telephone Interviews and web-based surveys. The surveys asked the respondents' level of agreement with the statement "If you have back pain you should stay active". The surveys also inquired about respondents' memory of exposure to campaign messaging. Pearson Chi-Square tests were performed to examine differences on these items across years. To account for covariates, logistics regression analysis was performed.

**Results** Annual increases (from 58.9% in 2010 to 72% in 2014) were observed in the percentage of survey respondents agreeing that they should stay active when experiencing back pain. This increase was statistically significant from 2010 through 2014 in crude models, and was attenuated after adjusting for reported exposure to campaign messaging. Respondents who reported exposure to campaign messaging were statistically significantly more likely to agree with staying active than respondents who did not report exposure to campaign messaging (adjusted odds ratio, 95% confidence interval = 1.96, 1.73 - 2.21). The percentage agreeing with the 'stay active' item was higher in those reporting exposure to campaign advertising (79.8 versus 66.8%,  $p < 0.001$ ).

**Discussion** Seven years after initial evaluation of the LBP mass media campaign, the campaign appears to have had an ongoing positive impact on public back pain beliefs specific to the statement "If you have back pain you should try to stay active". At the end of the initial campaign in 2008, 63.4% of respondents agreed with the statement. The current paper shows that the agreement increased over the years to a plateau of around 72%. A higher proportion of respondents who reported remembering the campaign agreed with the statement, suggesting that the changes in the back beliefs are due, at least in part, to exposure to the campaign.

1. Suman A, Bostick GP, Schopflocher D, Russell AS, Ferrari R, Battie MC, Hu R, Buchbinder R, Gross DP. Long-Term Evaluation of a Canadian Back Pain Mass Media Campaign. *European Spine Journal*, 2017; 26: 2467-2474.



## Risk of aspirin continuation in spinal surgery: a systematic review and meta-analysis

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### Introduction:

Aspirin is typically discontinued in spinal surgery because of increased risk of haemorrhagic complications. The risk of peri-operative continuation of aspirin in neurosurgery needed to be evaluated. The purpose of this review is to evaluate all available evidence about continuation of aspirin and to compare peri- and post-operative blood loss and complication rates between patients that continued aspirin and those who discontinued aspirin peri-operatively in spinal surgery.

### Study Setting:

Systematic review and meta-analysis.

### Methods:

A meta-analysis was conducted according to the PRISMA guidelines. Studies comparing aspirin continuation with discontinuation were included. Studies using a combination of anticlotting agents or non-spinal procedures were excluded. Operative outcomes (blood loss and operative length) and different complications (surgical site infection (SSI), stroke, myocardial infarction within 30 days post-operatively) were extracted. Overall prevalence and means were calculated for the reported outcomes in fixed-effects models with heterogeneity ( $I^2$ ) and effect modification (P-interaction) assessment.

### Results:

Out of 1339 studies, 3 case series were included in the meta-analysis. No significant differences in mean operating time were seen between the aspirin-continuing group (mean=201.8 minutes, 95%CI=193.3; 210.3;  $I^2=95.4%$ ; 170 patients) and the aspirin-discontinuing group (mean=178.4 minutes, 95%CI=119.1; 237.6;  $I^2=93.5%$ ; 200 patients); (P-interaction=0.78). No significant differences in mean peri-operative blood loss were seen between the aspirin-continuing group (mean=553.9 millilitres, 95%CI=468.0; 639.9;  $I^2=83.4%$ ; 170 patients) and the aspirin-discontinuing group (mean=538.7 millilitres, 95%CI=427.6; 649.8;  $I^2=985.5%$ ; 200 patients); (P-interaction=0.96). Similar non-significant differences between the 2 groups were found for cardiac events, stroke, and surgical site infections.

### Discussion:

This meta-analysis showed an absence of significant differences in peri-operative complications between aspirin continuation and discontinuation. Due to the paucity of included studies, further well-designed prospective trials are imperative to demonstrate potential benefit and safety.

## Bioactivity of a titanium-coated peek cage in posterior lumbar interbody fusion assessed by CT Hounsfield unit

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### INTRODUCTION

Titanium(Ti)-coated polyetheretherketone (PEEK) cages have been developed to enhance bioactivity of PEEK cages. However, it is still unknown whether bioactivity and osseointegration at the surface of a Ti-coated PEEK cage differ between a Ti-coated frame part and an open part filled with bone graft. This study was aimed to clarify the effect of Ti-coating on bioactivity of a PEEK cage by *in vivo* computed tomography (CT) analysis.

### METHODS

Twenty-two patients (10 males and 12 females; mean age, 67.1 years [20-82]) who underwent single- or two-level posterior lumbar interbody fusion (PLIF) since 2015 were included. Sixteen patients underwent single-level PLIF; 6 patients, two-level PLIF. The PLIFs were performed by inserting two Ti-coated PEEK cages in each intervertebral space concomitant with pedicle screw fixation. Local autologous bone was used for bone graft within the cages in all case. From the CT scans taken within one week (immediately after surgery), six months, and one year postoperatively (slice thickness, 0.5-0.625 mm; tube voltage, 120 kVp; tube current, 120-220 mA [automatic adjustment]), we created a sagittal plane along the long axis of each cage. Then, we set region of interests (ROIs) on the upper and lower cage surfaces of Ti-coated frame parts and open parts filled with bone graft on the sagittal planes (four ROIs for the frame and two ROIs for the open parts per one cage) (Figure 1). The Hounsfield Unit (HU) values of each ROI were measured automatically. We evaluated the postoperative changes in the HU values in each ROI and the difference of the changes over time between the frame and open parts. For the statistical analysis, Wilcoxon signed rank test and Repeated Measures ANOVA were used, and Bonferroni correction was performed for multiple comparison. A  $p < 0.05$  was considered statistically different.

### RESULTS

The median HU values (25%ile-75%ile) on the surfaces of the Ti-coated frame parts (224 surfaces) were 512.1HU (424.0-605.8) immediately after surgery, 472.6HU (377.5-611.0) six months postoperatively, and 475.7HU (385.3-583.8) one year postoperatively. Those of the open parts (112 surfaces) were 512.3HU (422.6-612.4) immediately after surgery, 459.5HU (348.0-541.8) six months postoperatively, and 475.7HU (348.0-585.4) one year postoperatively. The HU values decreased significantly in both the frame and open parts from immediately after surgery to six months postoperatively (frame part,  $p = 0.008$ ; open part,  $p = 0.002$ ); however, the postoperative changes in the HU values over time were not different between the frame and open parts ( $p = 0.34$ ) (Figure 2).

### DISCUSSION

The chemical inertness of PEEK can reportedly cause inflammatory reaction on the interfaces between the surfaces of pure-PEEK cages and adjacent vertebral endplates. This study showed that the postoperative changes in the HU values over time on the surfaces of the Ti-coated PEEK cages were not different between the frame parts with biologically active Ti-coating and open parts filled with local autologous bone. This suggested that Ti-coating on the frame of the PEEK cage could provide the PEEK frame with almost the same bioactivity as local autologous bone.

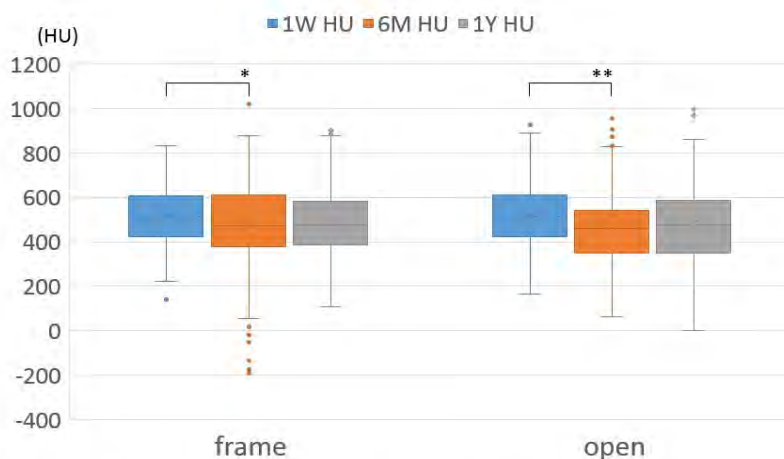


Figure 2. The postoperative changes median HU values in the frame and open parts. \* $p=0.008$ , \*\* $p=0.002$

## Clinical outcomes of thoracic and lumbar fractures in patients with diffuse idiopathic skeletal hyperostosis

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### INTRODUCTION

Spinal fractures in the ankylosed spine are often unstable due to the ossification of supportive and elastic soft tissues and may cause neurological deficit as a result of dislocation. The aim of this study is to investigate clinical outcomes and problems of thoracic and lumbar fractures in patients with diffuse idiopathic skeletal hyperostosis (DISH).

### METHODS

Between the year 2007 and 2017, 22 consecutive patients with DISH who had thoracic and lumbar fractures through an area of ankylosed spine were retrospectively reviewed. They were 13 males and 9 females with a mean age of 81.2 years. We evaluated injury morphology, fracture level, neurological status, treatment modality, complications and ADL. Mean follow-up period was 13 months.

### RESULTS

The majority of injury morphology was anterior tension band injury (AO- type B3), this type occurred in 20 patients (90.9%). Most fractures (20/22) were localized in the thoracolumbar junction (90.9%). At the time of injury 2 patients had a neurological deficit. Secondary deterioration of neurological status was observed in 8 of 20 patients (40.0%). The cause of delayed neurological deficit was mainly delayed diagnosis. Surgical treatment was performed in 15 of 22 patients (68.1%) and consisted of multilevel posterior fixation. Fourteen patients (93.3%) who received surgery improved ADL early, but postoperative complications occurred in 4 of 15 patients (26.6%). One patient eventually died of sepsis in the hospital. Seven patients (4 males, 3 females, mean age of 85.2 years) unavoidably received conservative treatment due to unacceptably high surgical risk and patient refusal of surgical treatment. Nonsurgical treatment was thorough rest of sitting position with hard bracing, and dorsal position was prohibited apprehensive of progressive fracture displacement and neurological deficit in all cases. 4 of 7 patients developed ADL deterioration due to disuse but there was no delayed neurological deficit.

### DISCUSSION

Surgical treatment is recommended for spinal fractures in the ankylosed spine, but most patients are old and often have severe co-morbidities. For patients at high risk for perioperative complications, we must be careful about perioperative management. Moreover in some cases we must refrain from surgery due to high surgical risk. The current study showed that our severe nonsurgical treatment was effective to prevent delayed neurological deficit, but more likely to develop ADL deterioration in spite of non-neurological deficit. To improve ADL early, we advocate surgical treatment with careful perioperative management in the treatment of spinal fractures in DISH.

## The inflammatory cytokine TNF- $\alpha$ regulates the biological behavior of nucleus pulposus mesenchymal stem cells through the NF- $\kappa$ B signaling pathway in a rat model in vitro

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**Introduction:** Nucleus pulposus mesenchymal stem cells (NPMSCs) are now considered as ideal cell source for intervertebral disc (IVD) regeneration; however, little is known about their response to tumor necrosis factor-alpha (TNF- $\alpha$ ), a critical inflammation factor contributing to accelerating IVD degeneration. Accordingly, the aim of this study was to investigate the regulatory effects of TNF- $\alpha$  at high and low concentrations on the biological behavior of healthy rat NPMSCs, including proliferation, migration, and nucleus pulposus differentiation.

**Methods:** In this study, NPMSCs were treated with different concentration of TNF- $\alpha$ (0, 0.1,1,10,50,100,200 ng/mL). Then we used Annexin V/PI flow cytometry analysis to detect the apoptosis of NPMSCs. CCK-8, EdU assay and cell cycle test were used to examine the proliferation capacity of NPMSCs. Migration ability of NPMSCs was detected by wound healing assay and transwell migration assay. Pellets method was used to induce nucleus pulposus differentiation of NPMSCs, and immunohistochemical staining, RT-PCR and western-blotting were used to examine the NPC phenotypic genes and proteins. The cells were further treated with the inhibitor Bay 11-7082 to determine the role of the nuclear factor-kappa B (NF- $\kappa$ B) pathway in the mechanism underlying the differentiation process.

**Results:** Treatment with a high concentration of TNF- $\alpha$  (50–200 ng/mL) induced the apoptosis of NPMSCs, the cell apoptosis index was elevated with the increasing dose of TNF- $\alpha$ , while low concentration of TNF- $\alpha$ (0.1-10 ng/mL) have no apoptosis inducing effect compared with control group ( $P>0.05$ ).CCK-8 and EdU assay showed higher proliferate capacity in low concentration (0.1–10 ng/mL) groups, and had a dose dependent effect. Besides, the percentage of cells in "S" phase is also increased after treated with low concentration of TNF- $\alpha$ . Wound healing assay and transwell assay demonstrated low concentration of TNF- $\alpha$  promoted the migration of NPMSCs. Besides, low concentration of TNF- $\alpha$  could inhibited their differentiation toward nucleus pulposus cells, which shown as decreased expression of NPC phenotypic genes and proteins(Sox-9, Collagen II and Aggercan). Moreover, we identified that the NF- $\kappa$ B signaling pathway is activated during the TNF- $\alpha$ -regulated differentiation of NPMSCs, and the NF- $\kappa$ B signal inhibitor Bay 11-7082 could reverse the adverse effect of TNF- $\alpha$  on the differentiation of NPMSCs.

**Discussion:** To our knowledge ,TNF- $\alpha$  usually induce the cell apoptosis and function as negative effect on regeneration, but according to our results, we found that low concentration of TNF- $\alpha$  mainly function as activator of NPMSCs, to promote their proliferation and migration to the lesion site. While with the processing of IVD degeneration, high concentration of TNF- $\alpha$  in the IVD exert negative effect by induce the apoptosis of NPMSCs, thus hindered the regenerate potency of degenerated IVD. Our findings firstly disclosed the dynamic biological reactivity of NPMSCs during IVD degeneration process, thus shed light on the mechanism of IVD regeneration and degeneration.

## Five-year postoperative good clinical outcomes after facet fusion using a percutaneous pedicle screw system for degenerative lumbar spondylolisthesis

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**INTRODUCTION:** We observed good clinical outcomes after posterolateral fusion (PLF) in terms of *in situ* fusion, a low incidence of adjacent segment disease (ASD), and the lack of need for slippage reduction in a long-term clinical and radiological follow-up study of PLF for degenerative lumbar spondylolisthesis (DLS). Furthermore, we previously found that facet fusion (FF) using a percutaneous pedicle screw (PPS) system as a minimally invasive evolution of PLF also resulted in good clinical outcomes. Here, we assessed clinical outcomes 5 years after FF.

**METHODS:** The indications for lumbar fusion were: 1) sagittal translation  $\geq 8\%$  on a flexion-extension lateral radiograph or 2) anterior wedging  $\geq 5$  degrees on a flexion radiograph and a disc range of motion (ROM)  $\geq 10$  degrees. Sixty-five of 82 consecutive patients (40 women, 25 men; mean age, 68.1 years; follow-up rate, 79.3%) who underwent FF for single-level DLS were retrospectively reviewed after a minimum follow-up of 5 years. The surgical method involved making a 5-cm skin incision, bilateral laminar fenestration, and FF with autologous bone harvested from the spinous process. PPS insertion was performed through the fascia. We evaluated the therapeutic effectiveness of FF using the Japanese Orthopaedic Association Back Pain Evaluation Questionnaire (JOABPEQ), Roland-Morris Disability Questionnaire (RMDQ), and visual analogue scale (VAS) preoperatively and at 1 and 5 years postoperatively. The revision surgery rate was also evaluated.

**RESULTS:** The therapeutic effectiveness rate, determined using the JOABPEQ, increased in all categories from 1 to 5 years postoperatively, including in the Low Back Pain score, which increased in 72.4% to 78.8% of the patients; however, the Walking Ability score showed a decrease from 94.3% to 81.6% of the patients. The mean RMDQ value and VAS score were significantly decreased at 1 year postoperatively and maintained at 5 years postoperatively. There was no statistically significant difference between the VAS scores for low back pain, buttock and lower limb pain, and numbness in the buttocks and lower limbs at 1 and 5 years postoperatively. There were two patients requiring revision surgery for ASD 2 and 3 years after the first surgery (revision surgery rate, 3.1%). Revision surgery for complications or poor clinical outcomes immediately after surgery was not required in any of the patients.

**DISCUSSION:** FF maintained good clinical outcomes 5 years postoperatively. The revision surgery rate of 3.1% at 5 years after FF was extremely low compared to previously reported rates of 12.1% (Park et al.) and 12.9% (Greiner-Perth et al.) at 5 years after interbody fusion. Considering that good RMDQ and VAS values were maintained, the decreased 5-year postoperative therapeutic effectiveness in Walking Ability, determined via the JOABPEQ, might have been caused by aging. Low back pain did not worsen 5 years after *in situ* fusion. Thus, FF is useful in the long-term management of DLS.

## Good clinical outcomes and fusion rate after facet fusion with cortical bone trajectory screws for degenerative lumbar spondylolisthesis

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**INTRODUCTION:** In a long-term clinical and radiological follow-up study of posterolateral fusion (PLF) for degenerative lumbar spondylolisthesis (DLS), we observed good clinical outcomes after PLF in terms of *in situ* fusion, low incidence of adjacent segment disease, and the lack of need for slippage reduction. Furthermore, we previously found that facet fusion (FF) using a percutaneous pedicle screw (PPS) system (PPS-FF) as a minimally invasive evolution of PLF also resulted in good clinical outcomes. We started performing the much less invasive FF technique using cortical bone trajectory (CBT) screws (CBT-FF) in 2013. Here, we assessed the fusion rate and clinical outcomes of this procedure.

**METHODS:** The indications for lumbar fusion were: 1) sagittal translation  $\geq 8\%$  on a flexion-extension lateral radiograph or 2) anterior wedging  $\geq 5$  degrees on a flexion radiograph and a disc range of motion (ROM)  $\geq 10$  degrees. Thirty-five patients (22 women, 13 men; mean age, 71.1 years) who underwent CBT-FF for single-level DLS were retrospectively reviewed after a minimum follow-up of 1 year. The surgical method involved making a 4-cm skin incision, bilateral laminar fenestration, and FF with autologous bone harvested from the spinous process. CBT screws were then inserted. We evaluated the FF rate using computed tomography (CT) and range of motion (ROM) at the fused level on a flexion-extension lateral X-ray film preoperatively and at the final follow-up and analysed the therapeutic effectiveness of FF using the Japanese Orthopaedic Association Back Pain Evaluation Questionnaire (JOABPEQ), Roland-Morris Disability Questionnaire (RMDQ), and visual analogue scale (VAS).

**RESULTS:** The FF rate was 82.9% (29/35 cases). At the final follow-up, all patients with an adequate FF on CT had no recognizable motion at the fused level. In six nonunion cases, the mean ROM significantly decreased from 12.7 degrees preoperatively to 2.4 degrees postoperatively. The therapeutic effectiveness on the JOABPEQ was demonstrated in the Walking Ability score in 80.0% of the patients and in the Low Back Pain score in 71.4%. The postoperative mean RMDQ value and VAS scores were significantly decreased.

**DISCUSSION:** CBT screw insertion is less invasive than PPS insertion because the former is performed directly through the exposed laminae, thus avoiding subcutaneous tissue exposure and paraspinal muscle damage by PPS insertion through the fascia. Although the CBT-FF fusion rate was lower than the previously reported PPS-FF fusion rate of 88.6%, good clinical outcomes were noted even in nonunion cases, likely because the ROM significantly decreased postoperatively, indicating stabilization of previously unstable spondylolisthesis. Moreover, preserving the intervertebral disc is very important and surgery with intervertebral disc preservation is the least invasive. There are potential revision surgery options, such as PLF and lumbar interbody fusion, in cases of FF failure. Thus, CBT-FF has several advantages for spinal fusion and is minimally invasive and useful in the management of DLS.

## Outpatient spine clinic utilization reduces emergency department visits following spine surgery

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**Introduction:** Visits to the Emergency Department (ED) following surgical intervention are a significant logistical and economic burden to patients and represent an additional stress to the healthcare system. While factors associated with readmission following spine surgery have been studied to some extent, drivers of post-surgical ED visits, including appropriate and inappropriate use, remain under-investigated.

**Methods:** TRICARE claims (2006-2014) were queried to identify patients who had undergone one of three common spine surgery procedures (lumbar arthrodesis, discectomy, decompression). ED utilization at 30- and 90-days were assessed as the primary outcome. Outpatient spine surgical clinic utilization was considered the primary predictor variable. Multivariable logistic regression tests were used to adjust for socio-demographic and clinical confounders.

**Results:** Between 2006-2014, 48,868 patients met inclusion criteria. Fifteen percent (n=7,183) presented to the ED within 30 days post-discharge. By 90 days, 29% of patients (n=14,388) presented to an ED. The 30- and 90-day complication rates were 6% (n=2,802) and 8% (n=4,034), respectively, and readmission rates were 5% (n=2,344) and 8% (n=3,842), respectively. Use of outpatient spine clinic services significantly reduced the likelihood of ED utilization at 30- (OR 0.48; 95% CI 0.46, 0.53) and 90-days (OR 0.55; 95% CI 0.52, 0.57).

**Discussion:** Within 90-days following spine surgery 29% of patients sought care in the ED. However, only one-third of these patients had a complication recorded, and even fewer were readmitted. This suggests a high rate of unnecessary ED utilization. Outpatient utilization of spine clinics was the only factor independently associated with a reduced likelihood of ED utilization and represents a viable target for improvement in longitudinal healthcare delivery.

## Changes in the use of preference sensitive surgery within accountable care organizations: the case of lumbar fusion procedures

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### Introduction

Accountable Care Organizations (ACOs) were devised as a means of improving coordination in healthcare delivery while reducing the overall costs of care. Early evidence has pointed to modest reductions in Medicare spending within ACOs. Within surgical care afforded by ACOs, savings are thought to be realized by improved care coordination as well as reductions in the use of expensive, preference sensitive procedures. Lumbar spine fusion is an example of a preference sensitive intervention that has been found to influence Medicare spending. In this context, we sought to investigate the impact of ACO formation on the use of preference sensitive procedures, using lumbar fusion as a case example.

### Methods

We queried Center for Medicare and Medicaid Services (CMS) fee-for-service claims for patients enrolled in Medicare Part A and B during the period 2009–2014, identifying patients who received lumbar spine fusion, discectomy or decompression procedures using a previously published International Classification of Disease–9<sup>th</sup> revision (ICD-9) coding algorithm.

Within the Medicare Shared Savings Program (MSSP) and Pioneer ACOs contracting with Medicare in 2012-2013, we matched providers identified by the organizations or CMS to claims associated with the surgical procedure and/or index surgical diagnosis. Patients were designated as part of the ACO cohort if the provider who made the surgical diagnosis or performed the procedure was a member of an ACO in the period 2012-2014. In this study, the period 2009-2011 was considered the pre-ACO period and that of 2012-2014 the post-ACO period.

We performed a difference-in-differences analysis comparing the use of lumbar fusion in ACOs and non-ACOs in the period before (2009-2011) and after (2012-2014) ACO formation. Propensity score adjustment was used to address differences in case-mix between the ACO and non-ACO cohorts. Multivariable logistic regression was used to adjust for socio-demographic and clinical confounders and compare the likelihood of receiving a lumbar spine fusion in ACOs and non-ACOs.

### Results

We identified 406,548 patients who met inclusion criteria, with 8,580 (2%) treated in ACOs. Within organizations that would form ACOs, the adjusted rate of spinal fusion increased from 51% to 55% between 2009-2011 and 2012-2014. Among non-ACOs, the use of spinal fusion increased from 52% to 59% over the same period ( $p=0.13$ ).

In the period 2009-2011, there was no significant difference ( $p=0.71$ ) in the likelihood of receiving a fusion between non-ACOs and organizations that would go on to form ACOs (Table 2). In 2012-2014, the odds of receiving a fusion in non-ACOs was 38% greater (95% CI 1.06, 1.78,  $p=0.02$ ).

### Discussion

In this study, we sought to determine the effect of ACO formation on the use of preference sensitive lumbar spine fusion. The use of spinal fusion increased between 2009-2011 and 2012-2014 within both ACOs and non-ACOs. Although the rate of growth was higher in non-ACOs, this finding did not reach statistical significance. The likelihood of receiving a lumbar spine fusion was significantly greater, however, among non-ACOs in the period 2012-2014. Our findings indicate that ACOs can more effectively control the use of preference sensitive procedures.



## The reverse knot X-shape suture for annular repair during microscopic lumbar discectomy; technical note and clinical outcomes

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### Introduction

Although repairing of the annulus fibrosus defect after lumbar discectomy may decrease the incidence of acute recurrent herniation, manual repairing technique has not been well studied due to narrow operative field during microscopic lumbar discectomy. Until now, many annular repair devices and techniques were designed but most of them were cost-inefficient. The aim to this study was to evaluate new technique for annular repair during microscopic lumbar discectomy.

### Methods

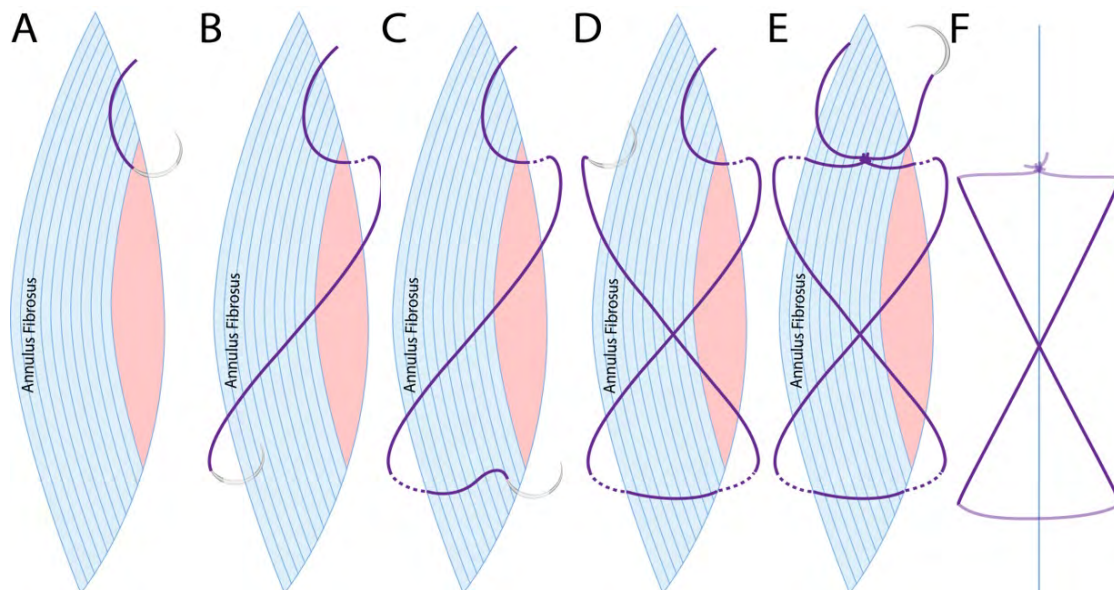
A total 26 herniated disc patients who underwent microscopic lumbar discectomy since 2015 were repaired annular defect using reverse knot X-shape suture technique (figure 1). We presented this technique by illustration and video clip. We also measured operation time, postoperative visual analog scale (VAS) for back and leg pain, Oswestry disability index (ODI) and radiologic parameters (global lordosis, segmental lordosis, intervertebral disc (IVD) height till postoperative 6 months and analysed by the student t test and fisher's exact test ( SPSS 20.0) to get statistical significance compared to non-repaired group (n=35).

### Results

All of patients were successfully repaired annular defect by reverse knot X-shape suture technique in the lumbar region. The segmental lordosis and involved IVD height of repaired group were significantly larger than those of non-repaired group. Although there was no significant difference in operative time, ODI, global lordosis, and clinical outcome with radiological findings in both group, postoperative 3 month VAS for leg was significantly improved in repaired group. One case of non-repaired group was performed revisional operation for reherniation.

### Discussion

The manual reverse knot X-shape suture technique in annular repair can be performed safely and effective under conventional microscopic discectomy without postoperative complication or short term recurrence of disc. Furthermore, this easy-to-use new technique applied in patients was cost effective compared to the other annular repair device. Although there is no innovative improvement of clinical and radiological outcome in repaired group compared to non-repaired group, repairing of annular defect can significantly improve the short term leg discomfort in patients. Therefore, we consider that this technique could give the additional benefit of conventional microscopic discectomy.



## **Which clinical and radiological variables could predict clinical outcomes of percutaneous endoscopic lumbar discectomy for treatment of patients with lumbosacral disc herniation?**

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**Introduction** : Percutaneous endoscopic lumbar discectomy (PELD) is one of minimal invasive techniques to treat the patients with low back and radiating pain resulted from lumbosacral disc herniation(LDH). We established this study to evaluate the clinical efficacy of PELD to treat the patients with low back and radiating pain due to LDH and to investigate which clinical and radiological variables could predict clinical outcome of PELD in terms of whole patients group and the subgroups of dominant back pain and dominant leg pain .

**Methods** : Seventy-five patients who had undergone PELD for treatment of low back and radiating leg pain resulted from LDH and could be followed up at least 12 months. Clinical outcomes were assessed using numeric rating scale for back and radiating leg pain(NRS back and leg), Oswestry disability index(ODI), and modified MacNab's criteria at 1 month(short term follow up) and at least 12months(long term follow up) after PELD. We divided into successful and unsuccessful outcome group according to improvement of NRS back, NRS leg, and ODI(%) at long term follow up period. We compared the various clinical and radiological variables between two groups in order to identify which variables could be the prognostic factors of clinical outcomes of PELD. This analysis was performed in terms of whole population, the subgroup of dominant back pain, and the subgroup of dominant leg pain respectively.

**Results** : Significant improvements were observed in NRS back, NRS leg, ODI(%), and modified MacNab's criteria at short term and long term follow up after PELD. Positive straight leg raising(SLR) was significantly related to successful outcome as to NRS leg and ODI(%) and longer pain duration also showed significant relationship with unsuccessful outcomes as to NRS leg in whole population. The subgroup of dominant back pain showed that longer duration of pain was significantly related to unsuccessful NRS leg. The subgroup of dominant leg pain showed that positive SLR had significant relationship with successful NRS leg as well as successful ODI(%).

**Discussion** : PELD was effective in terms of back and leg pain reduction as well as functional improvement in patients with LDH. Not only the patients with dominant leg pain but the patients with dominant back pain successfully obtain the clinical benefits by PELD. Positive SLR had the predictive ability to successful leg pain reduction and successful functional improvement. Longer pain duration was also related to unsuccessful reduction of radiating leg pain.

## The two important UPR pathway in Intervertebral Disk Degeneration: PERK and IRE1- $\alpha$

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### Introduction:

The microenvironment of degenerated intervertebral disc is characteristic of an inflammatory environment. The association between inflammation and endoplasmic reticulum (ER) stress has been described in many diseases, and the unfolded protein response (UPR) is activated following an ER-stress. Whether ER-stress plays an important role in intervertebral disc degeneration (IDD) remains elusive. The aim of this study was to investigate the expression of ER-stress in IDD, and to explore the underlying mechanism of IDD, ER-stress and inflammation.

### Methods:

The non-degenerated nucleus pulposus tissues (Pfirrmann<grade II) was harvested by surgical procedure from operating room and the nucleus pulposus cells were isolated and cultured, which we defined as normal nucleus pulposus cells (N-NPCs). The cells from degenerated nucleus pulposus tissues (Pfirrmann>grade III) were defined as degenerated NPCs (D-NPCs). Both groups were observed by transmission electron microscopy (TEM) analysis, real-time RT-PCR, western blot and immunohistochemistry (IHC). We also assessed the expression of UPR genes and synthesis function of NPCs with the ER stress activator tunicamycin (Tm) and pro-inflammatory cytokines IL-1 $\beta$  (10ng/ml) and TNF- $\alpha$  (5ng/ml). Gene silencing by specific siRNAs for UPR pathway (PERK, IRE1- $\alpha$  and ATF6) were used to pretreat NPCs following by TNF- $\alpha$  and IL-1 $\beta$  stimulation synergistically. Then UPR genes and synthesis capability related items were assessed.

### Results:

The expression of ER-stress was activated in D-NPCs compared to N-NPCs at both of mRNA and protein levels ( $p < 0.05$ ), and meanwhile the ER-stress response triggered by Tm treatment, IL-1 $\beta$  and TNF- $\alpha$  synergistically treatment was also activated in N-NPCs, but the activation level of ER-stress in IL-1 $\beta$  and TNF- $\alpha$  group is lower. Both proliferate capacity and expression of NPCs synthesis related protein were down regulated ( $p < 0.05$ ), when ER-stress activated. Interestingly, pro-inflammatory cytokines significantly upregulated the expression of IRE1- $\alpha$  and PERK, but not that of ATF6. Silencing experiments done also revealed that decreasing PERK and IRE1- $\alpha$  expression in N-NPCs can partially prohibit the reducing of collagen II, sox-9 and aggrecan when IL-1 $\beta$  and TNF- $\alpha$  treated.

### Discussion:

In this study, the results demonstrate that ER-stress acts as a key point to inflammatory response of NPCs and is closely linked with NP degeneration. Our findings revealed for the first time that UPR genes play a role in the proliferation and synthetic capacity of NPCs. These findings identify that the pathways of PERK and IRE1- $\alpha$  are as possible targets for regeneration of IDD and may help illustrate the underlying mechanism of ER-stress and UPR in occurrence and development of IDD.

**GP013**

**Tranexamic Acid in thoracic and lumbar fusions and perioperative blood loss**

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**Introduction:** Few studies have looked specifically at the effect of TXA on postoperative drain output. We sought to determine if TXA reduced postoperative, as well as intraoperative blood loss in thoracic and lumbar fusions using a retrospective cohort design.

**Methods:** We analyzed blood loss patterns in 617 consecutive adult patients undergoing lumbar and/or thoracic fusions requiring sub fascial drain placement at a single institution from January 2009 to 2016. These patients were divided into TXA and non-TXA cohorts, as well as high and low-dose TXA, and analysis was conducted using a propensity score to account for differences between cohorts.

**Results:** The TXA and non-TXA groups were demographically similar. The mean number of levels fused was higher in the TXA group (4.8 levels vs 3.1,  $p < 0.01$ ). There was a significant reduction in both intraoperative blood loss (77.7 mL per level, 95% confidence interval [CI]: 143.2 to 12.2 mL,  $p = 0.020$ ) and postoperative drain output (83.3 mL per level, 95% CI: 137.2 to 29.5 mL,  $p = 0.002$ ) in the TXA group when examined on a per-level fused basis, but no significant difference without controlling for number of levels. Postoperative blood loss was higher in the TXA group in surgeries involving >5 levels fused. There was a significant difference in both intraoperative blood loss (296.4 mL per level fused, 95% confidence interval [CI]: 423.4 to 169.5 mL,  $p < 0.001$ ) and postoperative drain output (113.4 mL per level fused, 95% confidence interval [CI]: 211.8 to 55.1 mL,  $p < 0.001$ ) when comparing the low dose to the high dose TXA groups, with the high dose group experiencing lower blood loss.

**Discussion:** Tranexamic Acid significantly reduced both intraoperative and postoperative drain blood loss in lumbar and thoracic fusions when examined on a per-level basis. However, with surgeries involving fusions greater than 5 levels, TXA may increase postoperative drain output, with those losses offset by reduced intraoperative blood loss. High dose TXA appears to further reduce both intraoperative and postoperative blood loss as compared to low dose TXA.

**TXA vs. no TXA, Adjusted for propensity score and Length of Surgery**

	Propensity as Covariate		
Outcome	Estimate†	95% CI	p-value
Intra-Op BL per Level	-77.7	(-143.2, -12.2)	0.020
Drain BL per level	-83.3	(-137.2, -29.5)	0.002
Total BL per level	-160.9	(-259.8, -62.0)	0.001
	Odds Ratio‡	95% CI	p-value
Received RBCs	0.82	(0.51, 1.32)	0.42
Admitted to ICU	0.51	(0.31, 0.84)	0.007
Reoperation	1.34	(0.74, 2.43)	0.34

†TXA – No TXA

‡TXA vs No TXA

## The effect of osteoporosis on clinical and radiological outcomes following one-level posterior lumbar fusion

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**Introduction:** It has been reported that loosening or subsidence was frequently found in osteoporotic patients following lumbar fusion surgery. However, few studies have compared clinical and radiological outcomes by bone mineral density following lumbar fusion surgery. The purpose of this study was to reveal the impact of osteoporosis on clinical and radiological outcomes in patients who underwent one-level posterior lumbar fusion surgery including posterior lumbar interbody fusion (PLIF) and posterolateral fusion (PLF).

**Methods:** This study included 43 osteoporotic patients (T-score  $\leq$  -2.5, group A) and 74 normal (T-score  $\geq$  -1.0, group B) and who underwent one-level posterior lumbar fusion (PLIF and PLF). BMD was assessed in lumbar spine (L1-L4) by dual energy X-ray absorptiometry (DEXA) preoperatively. Clinical parameters including visual analogue scale (VAS) for back pain, and leg pain, ODI, and EQ-5D were obtained pre- and postoperatively. Operation (PLIF or PLF) was undertaken in routine manner. Patients were followed up in postoperative 1-month, 3-months, 6-months, 1-year, and yearly thereafter. All patients were followed up at least 2 years. Fusion was determined by both dynamic (flexion and extension) lateral radiographs and reconstructive images of CT scans. Loosening and subsidence were assessed by plain radiographs and CT scans. Each clinical and radiological parameter was compared by osteoporosis and operative methods (PLIF or PLF).

**Results:** Clinical parameters showed no difference among groups by osteoporosis and operative methods preoperatively. Although back pain VAS at 6 months postoperatively was higher in the osteoporosis group (3.46 vs. 2.09,  $P=0.006$ ), this difference disappeared at 1 year postoperatively (3.05 vs. 2.68,  $P=0.606$ ). ODI or EQ-5D did not reveal any difference throughout follow-up periods. Subsidence rate was higher in group A (65.4% vs 17.6%,  $P<0.001$ ). Lower fusion rate was observed in PLF group compared to PLIF group (61.9% vs 92.1%,  $P=0.001$ ) although the fusion rate did not differ by osteoporosis (85.0% in group A vs 83.1% in group B,  $P=0.794$ ). Loosening rate did not show any between among groups although there was a trend of higher loosening rate in PLF group compared in PLIF group ( $P=0.065$ ). Although clinical outcomes did not differ by cage subsidence or loosening, lower fusion rate was observed in cases showing screws loosening (63.6% vs 91.9%,  $P=0.002$ )

**Discussion:** Although back pain was more severe for osteoporotic patients in early postoperative period after posterior lumbar fusion, clinical outcomes showed no difference according to osteoporosis in postoperative 1-year as acceptable fusion was achieved. Higher subsidence rate in osteoporotic patients was not associated with clinical outcomes and fusion rate. However, lower fusion rate was associated with loosening of screws, which occurred more frequently who underwent PLF. Thus, PLIF might be a good option to reduce the loosening rate and achieve acceptable fusion with good clinical outcomes regardless of high subsidence rate even in osteoporotic patients.

## Positive effect on bone regeneration by platelet-rich plasma combined with gelatin beta-tricalcium phosphate sponges: a study using a bone defect model of vertebral body in ovariectomized rats

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**INTRODUCTION:** We previously reported that platelet-rich plasma (PRP) promotes bone union in posterolateral lumbar vertebrae fusion model rats. No study has reported using PRP-impregnated gelatin $\beta$ -TCP for Osteoporotic vertebral fractures (OVF) treatment. The purpose of this study was to investigate whether PRP gelatin  $\beta$ -TCP sponges are effective for facilitating the development of vertebroplasties for OVF.

**METHODS:** All animal experiments were performed under the review and approval of the Animal Experimentation Ethics Committee of Kyoto Prefectural University of Medicine. We performed surgery to create a bone defect in the lumbar vertebral body and implanted materials into the defect 8 weeks after ovariectomy. We divided 96 rats into three groups according to the following implanted materials: (1) no material (control group) (2) gelatin  $\beta$ -TCP sponge with PRP (PRP sponge group); and (3) gelatin  $\beta$ -TCP sponge with PBS (PBS sponge group). For assessment of bone regeneration,  $\mu$ CT and histological evaluation were examined immediately after surgery and at 4, 8, and 12 weeks (n=8 at each time point).

**RESULTS:** The representative  $\mu$ CT images of the vertebral specimens are provided in Fig. 1. In the PRP sponge group, Bone tissue within the sponge was confirmed at postoperative week 4, and increased between weeks 8 and 12. In contrast, in the PBS sponge group, although bone tissue was confirmed within the sponge at week 4, no further growth of this tissue was observed during weeks 8 and 12. In implanted sponge area, Bone volume (BV) was significantly higher in the PRP sponge group at weeks 8 and 12. Histological findings of HE staining are displayed in Fig. 2. In the PRP sponge group, By week 8, dense distribution of fibroblasts and osteocytes was observed. By week 12, osteocyte cells were confirmed and new bone tissue was formed. In the PBS sponge group, fibroblasts and osteocytes could be confirmed, but cellular density was extremely low. Only sparse osteoblasts were observed in the anterior surface of the vertebral body.

**DISCUSSION:** In this study, we demonstrated that bone regeneration occurs in PRP-impregnated gelatin  $\beta$ -TCP sponges implanted into osteoporotic vertebral body defects. In the PRP sponge group, imaging and histological examination showed that visible osteogenesis was first induced and additional growth of bone tissue was observed in the transplanted sponge. The advantage of using PRP for tissue regeneration therapies is its highly safe nature, which arises from the fact that PRP is isolated from autologous blood. The other advantage is synergistic effects of the various growth factors contained in PRP and originally from bone tissue. We selected gelatin  $\beta$ -TCP sponges as a scaffold. Gelatin  $\beta$ -TCP sponges exhibit the capacity for sustained release of growth factors. The sponges also have a sponge-like porous structure well-suited for cellular migration, proliferation, and differentiation. These advantage could lead good effect for bone regeneration even in adverse condition like osteoporosis. In conclusion, the results of this study demonstrate that combined use of PRP and gelatin  $\beta$ -TCP sponges is effective for facilitating bone regeneration and could be useful for developing a new approach to vertebroplasty.

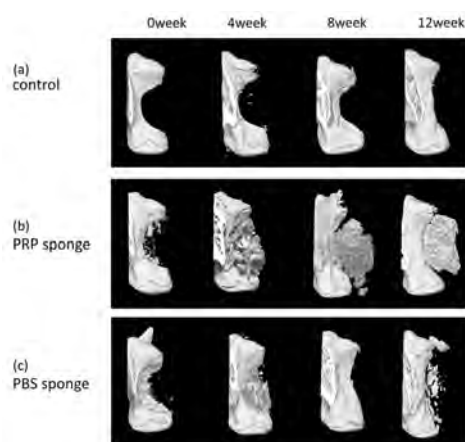


figure 1

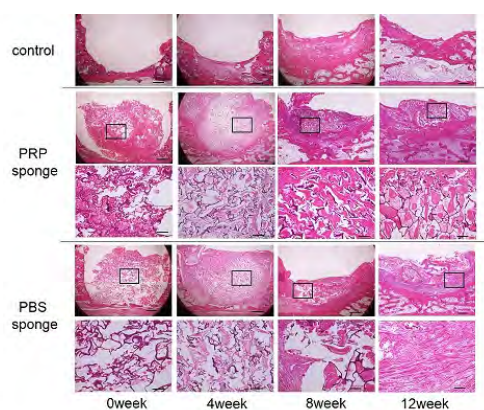


figure 2

## Diffuse idiopathic skeletal hyperostosis extended to the lumbar segment is a risk factor of reoperation in patients treated surgically for lumbar stenosis

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### Introduction

In patients with diffuse idiopathic skeletal hyperostosis (DISH), the segments without ossification are exposed to higher mechanical stress, which has been thought to cause poor clinical results in cases of acute spinal trauma. DISH might similarly affect clinical outcomes in patients with lumbar spinal stenosis (LSS), because of magnification of mechanical stress on lower non-fused segments. However, no studies have investigated in detail DISH as a potential risk factor of poor surgical results for LSS. The purpose of this study was to investigate the association between DISH and reoperation in patients treated surgically for LSS in long-term results.

### Methods

This study included 1063 responders to a postoperative postal survey out of 2363 consecutive patients who underwent surgery for LSS between 2002 and 2010. The survey included questions about reoperations performed at another hospital and the patient-reported outcomes. DISH was evaluated by preoperative standing whole-spine radiographs. Cox proportional hazards regression were performed to investigate DISH as a predictor of reoperation, with adjusting for demographics, concomitant pathologies (degenerative spondylolisthesis or degenerative lumbar scoliosis), and surgical procedures. Kaplan–Meier survival plot were also examined. Furthermore, characteristics of poor outcomes in patients with DISH were investigated. We also assessed selection bias by examining the differences between responders and non-responders to a postal survey.

### Results

Reoperations were performed in a total of 115 patients (10.8%) within an average of 8.6 years after the initial surgeries. Patients who only had DISH were not associated with reoperation, however, reoperations were performed significantly more often in patients with DISH extended to the lumbar segment (L-DISH) than in patients without (22% and 7.3%, respectively;  $p < 0.001$ ). Cox analysis showed that L-DISH was one of the significant independent predictors for reoperation (hazard ratio 2.05,  $p = 0.009$ ). More reoperations  $\geq 1$  year after the initial surgery were performed in patients with L-DISH than in those without L-DISH ( $p = 0.005$ ). The cause of reoperation did not differ between the patients with and without L-DISH. The patients with stenosis adjacent to the caudal end of DISH had a high reoperation rate (3 of 7 patients, 42.9%), although there were no significant ( $p = 0.443$ ). Several factors, but not L-DISH, were significantly associated with responders to the survey.

### Discussion

The present study indicated L-DISH was independently associated with reoperation for LSS. Surgery-free survival was significantly shorter in patients with L-DISH than in those without L-DISH. The decreased number of lumbar mobile segments due to L-DISH might lead to unfavorable outcomes. The result suggests a negative effect of increased mechanical load not only on the caudal end of DISH but also on the separated caudal remaining segment, except extremely far from DISH end. Although low follow-up rate was the biggest limitation of the study, the main regarding L-DISH is valid for discussion because the presence of L-DISH was not associated with either the responders or non-responders. Careful follow-up of patients is needed after surgery for LSS with L-DISH.

## Building unbiased population-averaged MRI atlases for image processing and assessment of lumbar paraspinal muscle morphometry

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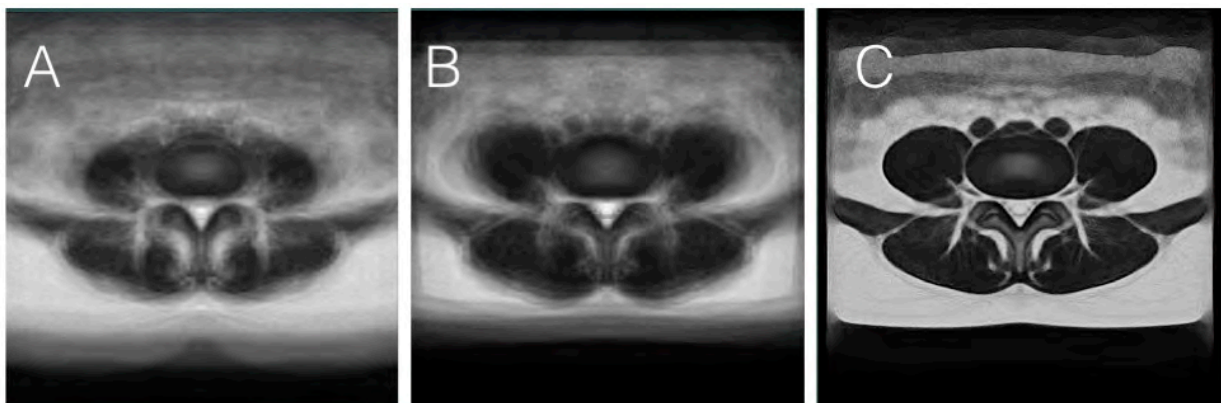
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**Introduction:** There is a growing body of evidence suggesting an association between lumbar paraspinal muscle degenerative changes (e.g atrophy, fatty infiltration, asymmetry) and low back pain (LBP). Quantitative paraspinal muscle morphometric measurements of cross-sectional area (CSA) or volume are commonly acquired from magnetic resonance imaging (MRI) in order to examine their relation with different LBP conditions. However, studies have used time-consuming and expertise-intensive manual segmentation techniques to obtain such measurements. Fully automatic segmentation methods with machine learning algorithms can effectively improve the efficiency of paraspinal muscle morphometry measurements, significantly reduce the assessment time and potentially yield more insightful results. However, automated segmentation methods require the individual MR images to be first aligned to a standard "reference" template. Although such templates/atlas are well established for cardiac and brain MR imaging, there has not been any for the lumbar paraspinal muscle. In this study, we developed a set of unbiased population-averaged MRI atlases for image processing and assessment of lumbar paraspinal muscle morphometry.

**Methods:** The lumbosacral MR images of a sample of 20 patients (female=10, male=10, age=30-39yo) attending spine clinics for commonly diagnosed lumbar pathologies were selected. Axial T2-weighted images of the L4-L5 level at mid-disc were used. The MR images were preprocessed to remove image intensity inhomogeneity and imaging protocol-dependent intensity variations. All images were linearly co-registered (e.g. data was transformed into one coordinate system so that corresponding anatomical features were matched/aligned to each other) using a special algorithm that improves the structural coherence of the aligned samples, and then population-wise nonlinear registration (e.g. alignment of non-uniform data) was performed to make the final atlas. To improve the image quality, left-right-mirrored images were used for registration, resulting in symmetric images. Three atlases were made: linear male, linear female, and nonlinear.

**Results:** The resulting atlases are shown in Fig. 1. The atlases describe the averaged morphology and image intensity features of the samples. From the atlases built with linear registration (Fig. 1A & 1B), the overall smaller size and increased fatty infiltration of the muscles can be easily observed for the female population. For the atlas made with nonlinear registration (Fig. 1C) using the MR images of the entire cohort, the anatomical features are much clearer, as if they are from an individual subject.

**Conclusion:** The proposed population-averaged atlases provide the standard imaging space data necessary for the development of an automated segmentation algorithm, which would greatly simplify the tedious aspect of MR imaging assessment of paraspinal muscle morphometry and provide a standardized procedure to facilitate comparison among studies. Our preliminary results of the L4-L5 level with the image processing techniques showed good results. We are now expanding this work to other lumbar spinal levels using larger samples to develop a fully automated atlas-based segmentation algorithm.





## Functional outcome of non-surgical and surgical management for de novo degenerative lumbar scoliosis: a mean follow-up of 10 years.

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**Introduction.** No studies have evaluated the long-term results of non-surgical and surgical management in de novo degenerative lumbar scoliosis (DNDLS). This study reports on the long-term functional outcome of patients being treated for DNDLS by non-surgical and surgical management.

**Methods.** This is a retrospective review of a single center database of DNDLS patients that underwent surgical or usual non-surgical management between 1996 and 2007. In a total of 88 patients, 50 (57%) underwent non-surgical and 38 (43%) surgical management. Baseline demographic, radiological, clinical and surgical-related variables were collected. An Oswestry Disability Index (ODI) 2.0 questionnaire was sent to all patients after written informed consent.

**Results.** Twenty-nine of 88 patients participated in the study, 15 (52%) had undergone surgical and 14 (48%) non-surgical management with a mean follow-up of 10.9 years (range 8-15 years). There were no significant differences ( $p>0.05$ ) between non-surgical and surgical patients at baseline for age, body mass-index, coronal Cobb angle and clinical data. None of the non-surgical patients had undergone surgery during follow-up. In the surgical group, 40% had revision surgery. There was no significant difference in ODI total scores between groups at final follow-up ( $p=0.649$ ). A larger proportion of patients in the non-surgical group reported an ODI total score of  $\leq 22$ , reflecting minimal disability (43% vs. 20%;  $p=0.245$ ).

**Discussion.** This is the first study that describes the long-term 10-year functional outcome of non-surgical and surgical management in a cohort of patients with DNDLS. No significant difference in functional outcome was found between groups after a mean follow-up of 10 years. Despite the significant potential for selection bias, these results indicate that non-surgical management of patients with DNDLS may lead to adequate functional outcome after long periods of time, with no cross-over to surgery. Further study is warranted to define which patients may benefit most from which management regimen.

## A novel method for the prediction of the pedicle screw stability: regional bone mineral density around the screw

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Yusuke Nakao<sup>2</sup>, Shiego Sano<sup>2</sup>, Takashi Nagai<sup>1</sup>, Koji Kanzaki<sup>5</sup>, Katsunori Inagaki<sup>1</sup>

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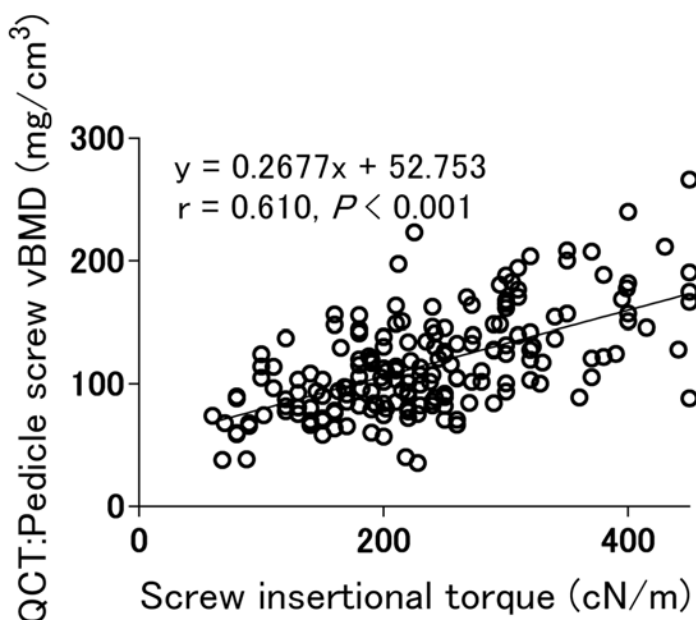
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**INTRODUCTION:** Pedicle screw fixation system is the gold standard technique for spinal fusion in treating various spinal disorders. Despite the advantage of biomechanical stability, screw loosening is a common complication. In previous studies, pullout strength and screw insertional torque were correlated, and, most importantly, affected by bone mineral density (BMD). Although the density and structure of the vertebral body are not homogeneous, no study has yet evaluated the relationship between screw insertional torque and regional BMD around the pedicle screw *in vivo*. The objective of this study was to investigate the ability of regional BMD around the pedicle screw to predict the screw fixation.

**METHODS:** Consecutive 50 patients (16 men and 34 women), scheduled for transpedicular fixation, were evaluated preoperatively for BMD measured by dual-energy absorptiometry (DXA) and quantitative computed tomography (QCT). Regional volumetric BMD around the pedicle screw (PS-vBMD) using the novel QCT technique was also evaluated. Among all patients, 190 screws (diameter: 7.5-8.5 mm, length: 40-45 mm, inserted from L1 to L5) were eligible for this study and were analyzed to identify factors contributing to insertional torque. The following factors were investigated: age, body mass index, laboratory data, bone turnover markers (TRACP-5b, total-P1NP), pedicle diameter, screw diameter, screw length, and 5 types of bone mineral density measures [DXA: spine-areal BMD (aBMD), total hip-aBMD, femoral neck-aBMD, QCT: central-vBMD, PS-vBMD].

**RESULTS:** Insertional torque was significantly correlated with each BMD measurement, and strongest with PS-vBMD [DXA: spine-aBMD; ( $r=0.48$ ,  $P<0.01$ ), total hip-aBMD; ( $r=0.32$ ,  $P<0.01$ ), femoral neck-aBMD; ( $r=0.38$ ,  $P<0.01$ ), QCT: central-vBMD; ( $r=0.58$ ,  $P<0.01$ ), PS-vBMD; ( $r=0.61$ ,  $P<0.001$ )]. Multiple regression analysis showed PS-vBMD was most strongly correlated with screw insertional torque ( $\text{std}\beta=0.494$ ,  $P<0.001$ ). A model containing the following five predictors was significantly associated with screw insertional torque: age, pedicle diameter, screw diameter, screw length, and PS-vBMD.

**CONCLUSIONS:** The preoperative measurement of PS-vBMD was technically feasible and reliably predictive of screw insertional torque during transpedicular fixation in a clinical setting. Larger studies with long-term, clinical results are needed to validate the findings of our study.



## Early reduction of ligamentum flavum 2 weeks after *in situ* posterior fusion without neural decompression for unstable degenerative lumbar spondylolisthesis

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**Introduction:** Unstable degenerative lumbar spondylolisthesis (DLS) with lumbar spinal stenosis (LSS) causes radicular symptoms (i.e., leg pain, claudication). Hypertrophy of the ligamentum flavum (LF) has been considered a major cause of LSS and nerve root compression, contributing to the symptoms. Reduction of LF and satisfactory clinical outcomes at long-term follow-up after anterior lumbar interbody fusion have been reported. However, the timing of the reduction of LF after lumbar fusion surgery remains unclear. In this study, we present longitudinal measures of early radiographic changes in the spinal canal and clinical outcomes after *in situ* posterior fusion without decompression.

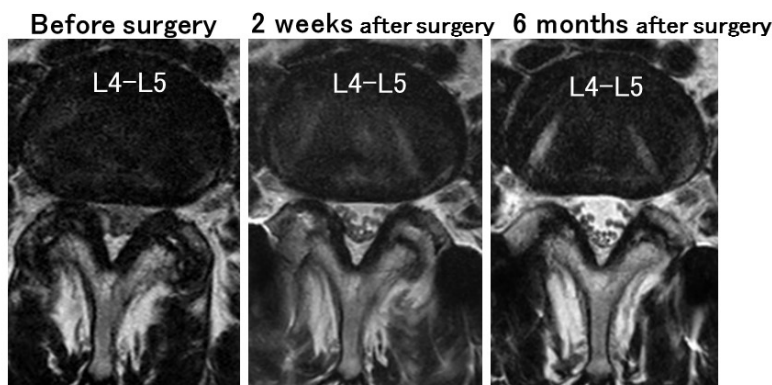
**Methods:** Twenty-three consecutive patients with persistent radicular symptoms caused by single-level unstable DLS and LSS without complete compromise were examined. All patients underwent instrumented facet fusion in the alignment achieved by posture reduction using autologous iliac bone without posterior laminectomy. Disc height (DH), disc angle (DA), and disc range of motion (ROM) were measured on plain lateral radiographs. Cross-sectional area of the LF (LFA), thickness of the LF at the lateral recesses (LFT), and cross-sectional area of the thecal sac (TSA) were measured on MR images. Patient-reported scores, including visual analogue scale (VAS) for leg pain and low back pain, and the Japanese Orthopaedic Association Back Pain Evaluation Questionnaire (JOABPEQ), were assessed. All measures were obtained preoperatively and at 2 weeks and 6 months postoperatively.

**Results:** Spinal fusion was achieved in 22 patients (96%). In the patient with inadequate fusion, ROM decreased from 16 degrees to 4 degrees postoperatively. DH and DA did not show significant changes 6 months after surgery. Significant decreases ( $p < 0.001$ ) in LFA and LFT (28% and 36%) were observed 2 weeks after surgery, and had continued to decrease by the 6-month follow-up by 57% and 67%, respectively. TSA increased by 33% at 2 weeks and by 84% at 6 months postoperatively ( $p < 0.001$ ). VAS scores for leg pain and low back pain were significantly reduced ( $p < 0.01$ ) to 15% and 30% of preoperative values at 2 weeks, and 10% and 27% at 6-month follow-up. JOABPEQ category scores for walking ability, low back pain, and social life function improved at 2 weeks and were maintained at 6 months. No patient required additional posterior decompression surgery.

**Discussion:** This is the first report to demonstrate early reduction of LF within 2 weeks after *in situ* posterior fusion without decompression, and sustained enlargement of the spinal canal at 6-month follow-up, despite a lack of change in DH and DA. Stabilization of the unstable segment may have induced an anti-inflammatory effect on the nerve roots that may provide immediate relief of pain and restoration of function after surgery. Furthermore, reduction of the mechanical stress on the structures in the spinal canal may have resulted in the reduction of LF, and canal enlargement, leading to lasting improvements in clinical outcomes. Thus, *in situ* posterior fusion without decompression may be sufficient and appropriate for managing unstable DLS.

### Case example

Instrumented facet fusion without decompression for L4 DLS in a 55-year-old woman



	Before surgery	2 weeks after surgery	6 months after surgery
LFA (mm <sup>2</sup> )	213	145	92
LFT (mm)	10.5	4.9	4.2
TSA (mm <sup>2</sup> )	78	119	195

## Morphological analysis of the intervertebral foramen and the lumbar facet joint

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### Introduction

We anatomically analyzed the morphology of the intervertebral foramen to conduct the transforaminal percutaneous endoscopic lumbar discectomy (TF-PELD) safely. Furthermore, to effectively perform the TF-PEVF (percutaneous endoscopic ventral facetectomy), we investigated the vertebral foramen and the ratio of the superior articular process (SAP) on the facet joint contact.

### Methods

Three hundred patients who were hospitalized in Tokushima Municipal Hospital and Tokushima University Hospital (150 female and 150 male, average age was 54 yrs.) were included in this study. We measured several parameters from L1 to S1 on the reconstruction CT sagittal scans. Parameters that we evaluated were disc height, SAP facet contact (ratio of the contact distance between SAP and the total facet contact distance), SAP position (distance from the SAP top to the underline of the upper vertebral body), foraminal distance (distance from the posterior border to the SAP's base), and foraminal area.

### Results and discussion

Foraminal area at lower level became smaller, significantly ( $p < 0.05$ ). There was a negative correlation between foraminal area and disc heights. Especially, at the lower levels, the relationship were significantly ( $p < 0.05$ ) higher. Tip of SAP position displaced to the superior side when the disc height became smaller, and the displacement would be leading the foraminal stenosis. These data indicated that foraminal stenosis is likely to develop at the lower lumbar levels. Foraminal distance was smallest at L4/5, suggesting that TF approach would be hard at the L4/5 level.

SAP facet contact in the lower levels would be smaller than the upper levels, and the difference was significant ( $p < 0.05$ ). We found the positive correlation between the disc height and SAP facet contact. SAP facet contact became smaller as the disc space would be narrow. The tendency was dominant in the lower intervertebral levels. During the PEVF surgery, SAP would be sometimes removed entirely. Even in such situation, nearly half of facet contact could be maintained in the lower vertebral body. Furthermore in the degenerated spine with the disc collapse, the preservation of facet contact after the PEVF would be promising.

There was significant difference between female and male in the disc height and foraminal distance. Disc height was larger with male and foraminal distance was wider with female.

### Conclusion

Foraminal area was smaller in the lower intervertebral levels. When disc was collapsed, the foraminal stenosis would easily appear. SAP could be resected during the PEVF; however, nearly half of the facet contact can be maintained even if SAP was resected completely, especially at the lower lumbar level. There were significant difference between male and female with disc height and foraminal distance. Disc height was larger in male and foraminal distance was wider in female.

The authors declare that there is no conflict of interests.

## Posterior bone graft in lumbar fusion surgery reduces the stress in the screw-rod system ~ a finite element study

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**INTRODUCTION:** Postero-lateral spinal instrumentation spanning the entire lumbar spine for treatment of diseases like scoliotic deformation, metastatic spine disease, and unstable fractures are common. Both spinal instrumentation and posterior bone graft provides additional strength to such spines. But what percentage of additional stiffnesses does the spinal instrumentation and the bone graft provide are unknown. Further, the complete union of the bone graft with the spine occurs over a period of time and the effect of this varying union of the graft with the spine is also unknown. We hypothesized that graft fusion has considerable influence in the stresses in the screw and rod and the stresses are highly dependent on the consolidation of the graft. The purpose of the present study is to analyze the biomechanical effect of postero-lateral instrumentation with and without posterior bone graft as well as the effect of varying union of the posterior bone graft.

**METHODS:** A non-linear three-dimensional finite element model of a lumbar spine (L1-S1) was developed from the CT scan of a normal 30-year-old subject. Solid union of the posterior bone graft was modeled by assuming bone allograft properties to the graft material. Non-union and 50% union of the graft were also modeled. Capsular ligaments were removed and facet joints at each level were fused. Posterior instrumentation made of Ti was modeled by 5 mm pedicle screws at all levels and rods with a mean diameter of 5 mm. Moments in all the three physiological directions were applied to the lumbar spine independently in addition to a compressive pre-load of 800 N. Motions of the lumbar spine at each level in all the three physiological loading directions in addition to the stresses in the screws, rods and posterior bone-graft were obtained.

**RESULTS:** Stiffness along the three principal anatomical directions of a normal lumbar spine with a posterior bone graft that had a solid union with the spine was found to be 10 times that of the stiffness of an intact lumbar spine. Posterior instrumentation further increased the stiffness of the spine with fused bone graft by 20 fold. Maximum von-Mises stress was observed at the superior portion of the rods and screws with pedicle screws carrying larger magnitude of stress than rods. As the consolidation of the posterior graft progressed the stresses in both rods and screws gradually reduced. A 50% solid union of the graft reduced the screw-rod maximum von-Mises stress by 40% and a 65% reduction in screw-rod stress was calculated with completely fused graft.

**DISCUSSION:** A fused graft with posterior instrumentation provided a 200 fold increase in stiffness of an intact spine while producing stress shielding to the Ti rod-screw system. Considerable reduction of the maximum von Mises stresses in the postero-lateral rod and screw fusion system (65%) will contribute to prevention of implant failure under repetitive loading highlighting the importance of union of posterior bone graft in reducing the stresses in the posterior instrumentation.

## Dynamic stabilization for prevention of proximal junctional failure in thoracolumbar long fusion

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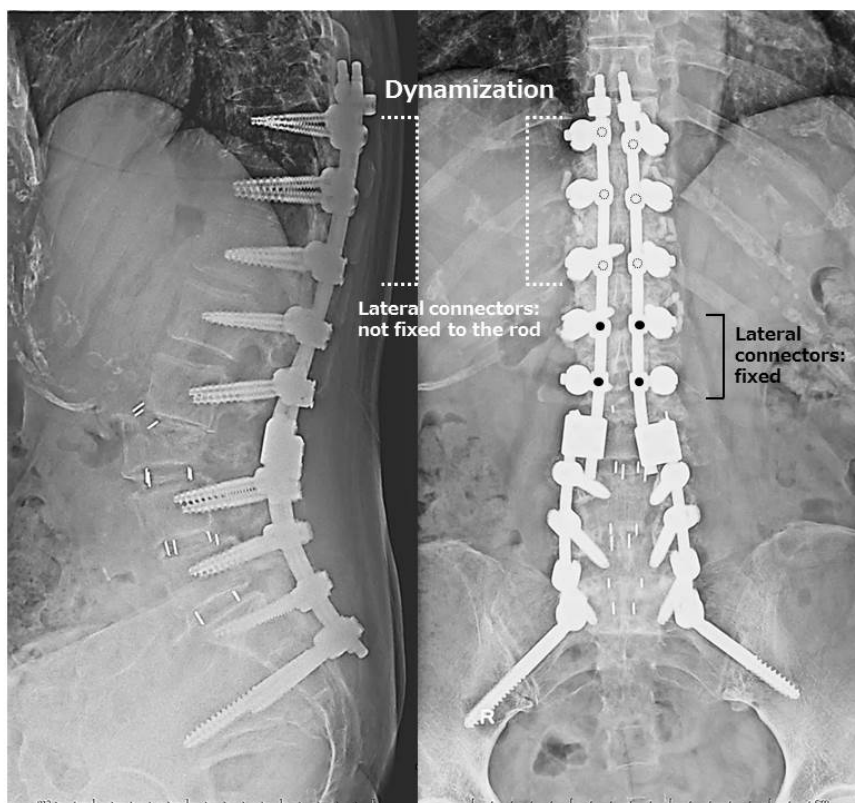
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**Introduction:** In the surgery of adult spinal deformity, too much stiffness of the proximal junctional area is a possible cause of postoperative complications such as junctional fracture and implant failure. To decrease the stiffness of the proximal end of instrumentation, we have devised a dynamic stabilization instrumentation, which allowed small movement of instrumented vertebrae. This study aimed to evaluate the short term result of our dynamization system.

**Methods:** Of 53 patients with adult spinal deformity who underwent thoracolumbar corrective surgery after May 2014, 35 patients with more than 6-month follow-up were included. For dynamic stabilization in proximal end, separate rods were placed medially with use of domino connectors, and the lateral connectors (closed type) of proximal 2 or 3 instrumented vertebrae were not fixed to the rods with set screws. Whole laminae up to uppermost instrumented vertebra (UIV) were bone grafted for posterior fusion at the same time. This construct allowed small movement of the instrumented vertebrae and gradual caudal migration along the rod before completion of bone union in proximal junctional region. Radiographic parameters such as lumbar lordosis (LL), pelvic tilt (PT), sagittal vertical axis (SVA), thoracic kyphosis (TK), proximal junctional angle (PJA) were measured pre- and postoperatively. Postoperative course was evaluated in regard to junctional fracture, proximal junctional kyphosis (PJK), and proximal junctional failure (PJF). The definition for PJK required both of PJA  $>10^\circ$  and PJA at least  $10^\circ$  greater than the preoperative measurement.

**Results:** The mean age was 74 years (range, 64-81), and the mean follow up period was 10.7 months (range, 6-16). Preoperative diagnoses were as follows; PJF after fusion surgery, 15 cases; degenerative kyphoscoliosis, 18 cases; kyphotic deformity after osteoporotic vertebral fracture, 1 case. The treatment included pedicle subtraction osteotomy (PSO), 18 cases; corrective PLIF, 12 cases; others, 4 cases. The most frequent UIV was T10 (range, T7-11), and 28 cases were fixed to ilium distally. The average values of the radiological parameters were as follows (preop/postop); SVA, 153/73mm; PT, 32/24°; LL, -1/34°; PI-LL, 49/16°; TK, 22/41°; PJA, 5/13°. The average postoperative caudal migration of UIV was 3.1mm. Postoperative compression fracture in proximal junctional zone occurred in 10 cases (29%). The numbers of PJK and PJF was 8 cases (24%) and 3 cases (9%), respectively.

**Discussion&Conclusion:** The incidence of PJK is reported to be 20-40%. Considering the higher age of the patients in this study than previous reports, more than 10 years in average, 24% rate of PJK and 9% rate of PJF seemed to be relatively low enough. Although postoperative incidence of compression fracture in proximal junctional zone was high (29%), there was no case of screw backout, which may be attributed to the dynamic property of junctional area. In this study, central structures (spinous process, interspinous ligament, and ligamentum flavum) between UIV and UIV+2 or more were preserved. This possibly served effectively not weakening posterior stabilizer in junctional zone. In conclusion, our dynamization system seemed to be effective for preventing PJF in short term observation.



## Clinical outcomes of pathologic vertebral fractures in patients with multiple myeloma: comparison of reconstruction surgery with adjuvant radiotherapy and radiotherapy alone

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### Introduction

MM is a hematologic malignancy that most commonly causes pathologic vertebral fractures in the spine column. However, the roles of reconstruction surgery on vertebral fractures with neurological deficit remain unclear. We compare the clinical outcomes of reconstruction surgery with adjuvant radiotherapy (RT) and RT alone in patients with pathologic vertebral fractures of multiple myeloma (MM).

### Methods

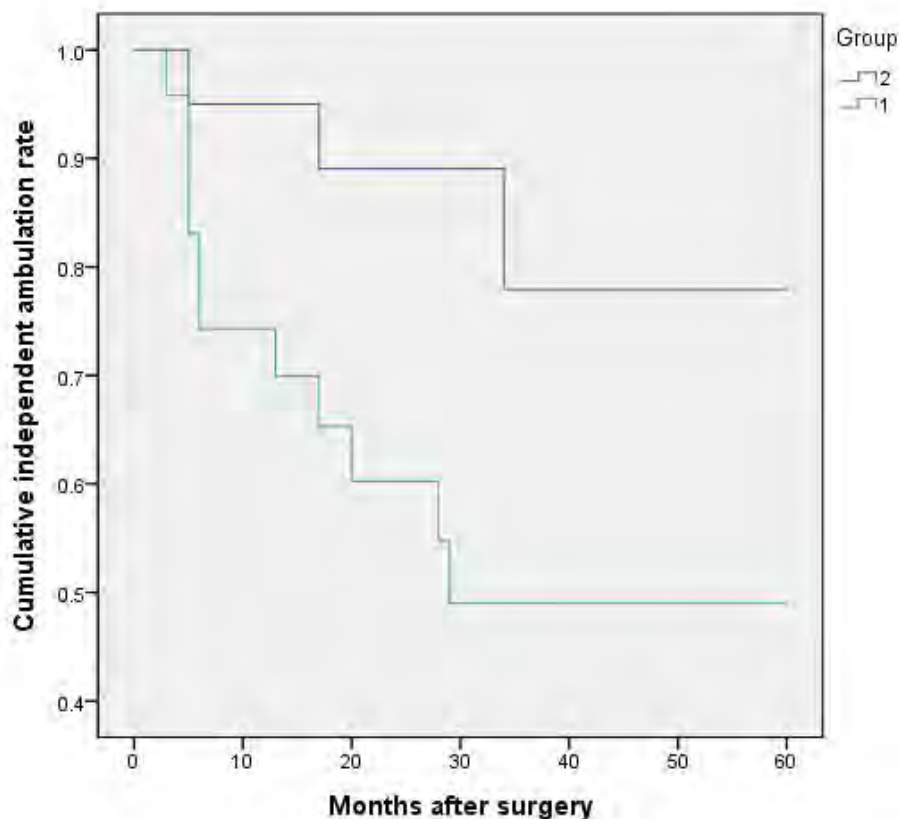
Among the 116 patients with vertebral fractures in MM were that treated by RT at our hospitals from 2008 to 2014, twenty eight patients underwent reconstructive surgery followed by RT (group II). Among the patients who were treated by RT alone, twenty eight patients whose age, performance status (Eastern Cooperative Oncology Group, ECOG) and pathologic conditions of the spine (Spine Instability Neoplastic Score, SINS) matched those of group I were assigned in group I. And twenty eight patients who were treated by RT alone (group I) whose age, performance status (Eastern Cooperative Oncology Group, ECOG) and pathologic conditions of the spine (Spine Instability Neoplastic Score, SINS) were matched to group II. Clinical outcomes including the duration of maintenance of independent ambulation, neurologic outcomes, visual analogue score (VAS) for back pain were assessed.

### Results

Median duration of independent ambulation was longer in group II (median, 51.6 months; 95% confidence interval [CI], 43.0-60.2) than in group I (median, 28.0 months; 95% [CI] 13.4-42.6) (Log rank test;  $p=0.015$ ). Improvement rate of neurological status (group I; 21.4%, group II; 60.7%  $p=0.024$ ) and VAS (group I;  $5.0\pm 2.2$ , group II;  $2.7\pm 2.1$ ,  $p=0.000$ ) were higher in the group II. However, median survival period and treatment related complications were not significantly different between the groups.

### Conclusion

In spinal MM with definite instability, reconstructive surgery may provide an advantage in preserving independent ambulation and neurological function even though it is not associated with median survival.



## Assessment of minimal clinically important differences after microendoscopic laminectomy in patients with lumbar canal stenosis

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### [Background]

Microendoscopic laminectomy (MEL) is one of the useful surgical methods to treat patients with lumbar canal stenosis (LCS). Although many studies have investigated MEL worldwide, minimal clinically important differences (MCIDs) in various outcomes of MEL have not yet been elucidated. This study aimed to evaluate MCIDs in various outcomes after MEL in patients with LCS.

### [Methods]

We enrolled 649 patients who underwent MEL for LCS at our hospital between March 2012 and May 2014. The Oswestry Disability Index (ODI), Roland–Morris Disability Questionnaire (RDQ), SF-36, Japanese Orthopaedic Association (JOA) score, and EuroQol 5 Dimension (EQ-5D) were administered preoperatively and 1 year postoperatively. Each MCID was calculated from the receiver-operating characteristic curve using the outcome of each preoperative and postoperative score.

### [Results]

We followed up 349 patients for 1 year and assessed their scores postoperatively. The scores varied from 40.2 to 22.2 for the ODI, 1.51 to 1.14 for the RDQ, 24.5 to 37.1 for SF-36 for physical functioning, 26.5 to 39.5 for SF-36 for role physical, 10.7 to 15.2 for the JOA score, and 0.59 to 0.74 for the EQ-5D. All scores statistically significantly improved 1 year postoperatively.

The MCID for the ODI was -14 [area under the curve (AUC) = 0.82; sensitivity, 79.6%; and specificity, 71.3%], for the RDQ was -0.20 (AUC = 0.53; sensitivity, 12.7%; and specificity, 92.7%), for SF-36 for physical functioning was +9.3 (AUC = 0.83; sensitivity, 73.5%; and specificity, 81.3%), for SF-36 for role physical was +10.2 (AUC = 0.71; sensitivity, 72.7%; and specificity, 63.3%), for the JOA score was +3.0 (AUC = 0.77; sensitivity, 82.5%; and specificity, 60.7%), and for the EQ-5D was +0.12 (AUC = 0.80; sensitivity, 68.1%; and specificity, 83.1%).

### [Discussion]

In this study, we calculated MCIDs in various outcomes of MEL. In addition, each AUC was generally high, indicating that these scores were valid.



## SSI (Surgical Site Infection) after spinal surgery and nasal MRSA (Methicillin-Resistant Staphylococcus Aureus) colonization

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### Objectives

Several previous reports revealed the nasal MRSA colonization is the risk factor for the SSI after cardiac surgery and gastrointestinal surgery. The objective of this study was to evaluate the relationship with MRSA colonization and SSI after spinal surgery and the effectiveness of the prophylaxis for MRSA SSI.

### Patients and Methods

This study consists of consecutive 436 patients underwent spinal surgery in our institution from March 2011 to December 2015. All of these patients were screened for nasal MRSA before surgery. The MRSA-positive patients received perioperative prophylaxis with nasal mupirocin and a shower with chlorhexidine gluconate solution before surgery from the beginning of 2012.

### Results

There were 17 of 436 patients developed SSI overall.

In 2011, 15 of 75 patients gave a positive screen. 12 patients showed MSSA(methicillin-susceptible Staphylococcus aureus) colonization and 3 patients showed MRSA colonization before surgery in 2011.

From 2012 to 2015, 76 of 361 patients gave a positive screen. 67 patients showed MSSA colonization and 9 patients showed MRSA colonization from 2012 to 2015. There were 6(8.9%) of 67 MSSA-positive patients developed SSI postoperatively. MRSA was isolated from 3 SSI. There were 2(22.2%) of 9 MRSA-positive patients developed SSI. MRSA was isolated from 1 SSI. There were 5(1.7%) of 285 patients with a negative screen developed SSI. MRSA was isolated from 2 SSI.

9(11.4%) of 79 MSSA-positive patients developed SSI postoperatively overall.

The patients with SSI finally got resolution of infection, while 5 patients needed surgical procedure.

### Discussion

Many reports have demonstrated the importance of nasal MRSA screening and decolonization to reduce MRSA-SSI. The patients with a positive screen developed SSI more likely than without a positive screen in 2011 and from 2012 to 2015, respectively.

In 2011, without the prophylaxis, the incidence of MRSA SSI in MRSA-positive patients was significantly higher than in MRSA-negative patients (P=0.04).

From 2012 to 2015, with the prophylaxis, there were only 1 of 9 MRSA-positive patients developed MRSA-SSI. In this period, the incidence of MRSA SSI in MRSA-positive patients was not significantly higher than in MRSA-negative patients (P=0.141)

So, the prophylaxis for MRSA SSI may be effective.

### Conclusion

The patients with a positive screen developed SSI more likely.

9 patients(2.5%) in the consecutive 361 patients underwent spinal surgery showed MRSA colonization before surgery.

The incidence of SSI in MRSA-positive patients was higher than the incidence in others.

Nasal MRSA screening and decolonization reduce the incidence of SSI possibly, regarding with spinal surgery.

In this study, the incidence of SSI in MSSA-positive patients was not low, so MSSA positive patients before spinal surgery also may need some prophylaxis.

Nasal colonization	SSI (2012.Mar~Dec)			
	MSSA	MRSA	others	total
negative (60)	0	0	0	0
MSSA (12)	2	0	1	3(25%)
MRSA (3)	0	1	0	1(33%)
Total (75)	2	1	1	4(5.3%)

Nasal colonisation	SSI (2012~2015)			
	MSSA	MRSA	others	Total
netgative(285)	1	2	2	5(1.7%)
MSSA(67)	2	3	1	6(8.9%)
MRSA(9)	0	1	1	2(22.2%)
Total(361)	3	6	4	13(3.6%)

## An outcomes calculator for informed decision making in spine surgery

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**INTRODUCTION:** We developed and performed a prospective evaluation of an informational web-based calculator for estimating personalized treatment outcomes in spine surgery. Our objective was to evaluate the understandability, usability and impact of a calculator tool for patients with intervertebral disc herniations, spinal stenosis, and degenerative spondylolisthesis who are deciding between surgical and non-surgical treatments. The decision to have back surgery is preference-sensitive and warrants shared decision-making. However, methods for presenting clinical evidence on treatment outcomes in a way that is personalized to an individual patient are needed.

**METHODS:** Using Spine Patient Outcomes Research Trial (SPORT) data, prediction models were developed and integrated into a web-based calculator tool: <http://spinesurgerycalc.dartmouth.edu/calc/>. Consumer Reports subscribers with back related pain were invited to use the calculator via email, and patient participants were recruited to use the calculator in a prospective manner following an initial appointment at participating spine centers. Participants filled out questionnaires before and after using the calculator. Knowledge questions were randomly assigned to be asked either before or after viewing the calculator.

**RESULTS:** Knowledge scores were higher in the post-calculator group compared to pre-calculator group (see Table), indicating that calculator usage successfully informed users. Decisional conflict was lower when measured following calculator use, suggesting the calculator was beneficial in the decision-making process. Participants found the tool helpful and easy to use.

**DISCUSSION:** While the calculator is not a formal decision aid, and focuses only on communicating individualized risks and benefits for the treatment options, it can still benefit the goals of shared decision-making in choosing whether or not to have back surgery. It improved not only knowledge scores but also decreased decisional conflict.

Table 2. Knowledge scores (percentage of correct answers) for pre- and post-calculator groups\*

Condition	Group	Consumers (n = 1256)			Patients (n = 68)		
		N	% correct answers (SE)	P	N	% correct answers (SE)	P
IDH	Pre-calculator	183	24 (2)	<0.001	10	30 (9)	0.101
	Post-calculator	218	32 (2)		20	50 (7)	
SPS	Pre-calculator	340	22 (1)	<0.001	18	25 (6)	0.012
	Post-calculator	364	32 (1)		8	53 (9)	
DS	Pre-calculator	79	21 (2)	0.003	7	21 (7)	0.074
	Post-calculator	72	31 (3)		5	40 (6)	

## The correlation of Scoliosis Research Society questionnaires with biomechanical parameters measured by with gait and balance analyses in patients with adult degenerative scoliosis

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**Introduction:** Patients with adult degenerative scoliosis (ADS) demonstrate an altered gait and balance patterns. Balance is defined as the ability of the human body to maintain its center of mass (COM) within the base of support with minimal postural sway. Self-reported measures are routinely used in the clinical setting to capture data related to function and perceived disability, in the setting of ADS. However, few studies have examined the correlation between patients' self-reported clinical outcome and objective biomechanical gait and balance analyses. The purpose of this study was to determine the correlation between self-reported assessments of function with objective biomechanical measures of function.

**Methods:** Thirty patients with symptomatic ADS who have been deemed appropriate surgical candidates. Gait and functional balance analyses were performed the week before surgery. Spatiotemporal parameters (i.e. gait speed, cadence, stride length, width and time etc.) were calculated during the gait evaluation. The functional balance test was similar to a Romberg's test. COM and head displacements in the sagittal and coronal planes and total sway amount were calculated. Furthermore, Scoliosis Research Society Questionnaires (SRS22r) scores were obtained on the same day of testing. Correlations were determined between the self-report clinical outcome questionnaire measures and objective gait and balance analyses biomechanical data using Pearson's Product Correlation in SPSS. Outcome Measures: Dependent variables included SRS22r scores along with gait spatiotemporal parameters and COM and head sway during functional balance test.

**Results:** The SRS22r total score was correlated with stride length ( $r=0.37$ ,  $p=0.050$ ) during gait and COM total sway ( $r=-0.41$ ,  $p=0.027$ ), horizontal COM sway in the sagittal ( $r=-0.54$ ,  $p=0.002$ ) and coronal ( $r=-0.39$ ,  $p=0.050$ ) planes, and horizontal head sway in the sagittal ( $r=-0.41$ ,  $p=0.029$ ) during the balance test. Detailed analysis was performed on the SRS22r different section scores. The SRS22r function score was correlated with COM total sway ( $r=-0.44$ ,  $p=0.017$ ), horizontal COM ( $r=-0.55$ ,  $p=0.002$ ), and head ( $r=-0.40$ ,  $p=0.030$ ) sway in the sagittal plane during the balance test. The SRS22r pain score was correlated with horizontal COM ( $r=-0.52$ ,  $p=0.004$ ), and head ( $r=-0.36$ ,  $p=0.050$ ) sway in the sagittal plane during the balance test. The SRS22r self-image score was correlated with cadence ( $r=-0.32$ ,  $p=0.040$ ), stride time ( $r=0.36$ ,  $p=0.016$ ), single support time ( $r=0.35$ ,  $p=0.025$ ), and stride length ( $r=0.32$ ,  $p=0.050$ ) during gait. The SRS22r mental health score was correlated with stride length ( $r=0.37$ ,  $p=0.050$ ) during gait and horizontal COM sway in the sagittal plane ( $r=-0.40$ ,  $p=0.033$ ) during the balance test. The SRS22r satisfaction score was correlated with walking speed ( $r=-0.33$ ,  $p=0.027$ ) during gait and base of support width ( $r=0.38$ ,  $p=0.050$ ) during the balance test.

**Discussion:** This study demonstrated a strong correlation between biomechanical parameters as measured with objective gait and balance analyses and functional disability as measured with patient reported outcome measures including the SRS22r. Quantified gait and balance analyses can be a useful tool to evaluate patient outcomes. Objective motor performance measures will improve the evaluation and understanding of the biomechanical effects of spinal disorders on locomotion. Gait and disability are strongly correlated in surgical patients with ADS.

## **Axial loading during MRI reveal insufficient effect of percutaneous interspinous implants on spinal canal area**

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### **Introduction**

Percutaneous interspinous device (IPD) is a less invasive treatment alternative for spinal stenosis compared to open decompressive surgery. Divergent postoperative results of IPD have been reported. With conventional MRI significant increase in cross sectional dural sac area (CSA) has been reported when pre- and postoperative images are compared. However data regarding the IPD effect on the spinal canal during spinal loading are lacking. The objective of the present study was to evaluate the effect of IPD on radiological spinal measures by comparing axial loading during MRI (aMRI) pre- and postoperatively in patients treated with IPD Aperius Aperius PercLID<sup>®</sup>

### **Methods**

19 patients treated with Aperius (28 lumbar levels) due to symptomatic neurogenic intermittent claudication and a MRI verified spinal stenosis ( $< 100\text{mm}^2$  at conventional MRI) were investigated with aMRI pre- and 3 month postoperatively. The CSA, ligamentous interfacet distance (LID), anterior-posterior (AP) lateral recess distance, sedimentation sign, and AP foraminal distance were measured at the operated level as well as at the cranial and caudal adjacent levels at aMRI images. Qualitative estimation of foraminal fat was also made and graded between 0 and 2. Grade 0 representing fat surrounding the whole nerve, grade 1 with the nerve only partly surrounded with fat and grade 2 without any fat. For comparison 13 spinal stenosis patients, operated with decompression at 22 levels, were investigated and differences between the pre- and postoperative aMRIs between the cohorts investigated.

### **Results**

For patients treated with IPD implants the mean CSA at the operated level was  $69\text{mm}^2$  preoperatively compared to  $72\text{mm}^2$  postoperatively ( $p=0.4$ ). The mean CSA at the adjacent levels were  $145\text{mm}^2$  preoperatively and  $135\text{mm}^2$  postoperatively ( $p=0.05$ ). In the decompression group there was a significant increase in CSA, from  $70\text{mm}^2$  preoperatively to  $140\text{mm}^2$  postoperatively ( $p<0.001$ ) at the operated level but also at the adjacent level ( $139\text{mm}^2$  versus  $152\text{mm}^2$ ,  $p<0.01$ ). In the decompression group the LID increased postoperatively with a mean of  $6\text{mm}^2$  ( $p<0.001$ ) and adjacent to the operated level there was a significant change in foraminal fat of the right foramina ( $p=0.05$ ). For the other evaluated parameters there were no significant changes pre-versus postoperatively, neither in the Aperius group nor in the decompression group.

### **Discussion**

With the spine imaged in an axial loaded position, no significant effects of the IPD on radiological spinal measures, such as the CSA, could be proven at the operated level when pre- and postoperative MRI images were compared. Thus, the effect of IPD on the spinal canal must be questioned.

GP030

**BMP vs. alternatives: Cost savings and clinical outcomes data in 137 ALIF patients with 2 yr. Follow-up**

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**Background:** Linking basic science data to clinical results can be difficult. Published studies demonstrate osteogenic properties and low inflammation with micron-textured titanium surfaces, even without the addition of exogenous biologic additives.(1) Interbody implants with these surface characteristics may be able to actively stimulate a portion of the fusion integration, potentially reducing surgeons' reliance on the more expensive and inflammatory biologic additives.

BMP is associated with high fusion rates but authors have published on complications including high inflammation, osteolysis, and heterotopic bone formation. Some demineralized bone matrix products claim increased activity due to retained allograft growth factors (DBM+AGF). Ceramics are usually combined with bone marrow aspiration (Ceramic/ BMA). Finding the proper balance between the biological activities of the bone graft, the host, and the interbody implant would be relevant to clinical fusion outcomes.

**Objectives:** To determine if comparable clinical outcomes and cost savings opportunities can be realized in ALIF fusions with a micron-surface, osteogenic titanium implant, comparing 3 different bone graft substitutes of variable biological potencies.

**Methods:** 137 patients undergoing anterior lumbar interbody fusions were enrolled consecutively and followed for 24 months. All patients received implants with a unique micron-scale textured surface. Group 1: 75 patients received rhBMP-2. Group 2: 62 patients received a bone graft extender (DBM+AGF or ceramic). Clinical outcomes (VAS/ ODI) were collected for 2 years after surgery. Cost savings analysis was performed using manufacturer's list pricing.

**Results:** Both groups achieved similar and clinically significant improvements at all time points compared to pre-op baseline. Although not statically significant, there was a strong trend toward better improvements in VAS and ODI scores at all time points favoring the non-BMP patients (Group 2). Similar outcomes were observed between the DBM+AGF and Ceramic groups. Leg pain was higher at all time points in the BMP cohort (Group 1), compared to the non-BMP cohort (Group 2) reaching statistical significance at 2 years. **Table 1** There were no fusion revisions or non-unions in either group at 24 months. List pricing for biologic graft materials used (per segments fused) are calculated. Cost savings between high and low cost biologics was \$2565 (1 level fusion), \$2373 (2 level fusion), and \$2103 (3 level fusion).

Table 1	VAS Leg		VAS Back		ODI	
	Group 1	Group 2	Group 1	Group 2	Group 1	Group 2
Baseline	5.1	4.9	7.1	7.2	55	49
6 month	2.5	1.9	3.9	3.4	35	32
12 month	2.1	1.7	3.6	3.4	31	27
24 month	2.4	1.3 *	3.5	3	31	25

\*p< 0.001

**Conclusions:** Biological activity of bone graft extenders may be less relevant in the presence of an osteogenic fusion implant. There was no measurable clinical benefit realized by using BMP or DBM+GF with this specific ALIF implant. Results may vary however with other implants. The patients in the non-BMP group, while statistically similar, trended towards better clinical outcomes (VAS/ ODI) at all time points with statistically significant lower residual leg pain at 2 yrs., compared to the BMP group. These results may be related to a reduced inflammatory environment, allowing for a more physiological fusion process with the utilization of this implant surface. This study demonstrates that excellent clinical outcomes and significant cost savings can be achieved in these cases without the need for the most expensive or inflammatory biologics.

1. 1 Spine; 40 (6) 399-404; 2015

## Impaired glucose metabolism is a significant associated factor for radiographic lumbar spinal stenosis

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**Introduction:** Many patients with lumbar spinal stenosis (LSS) also have diabetes mellitus (DM). However, the association with LSS onset is unknown. Since LSS and DM are both common in the elderly, it is possible that age may be a confounding factor. This study aimed to clarify the association between LSS and DM through a cross-sectional analysis of the general population.

**Methods:** This study involved 968 participants (319 men and 649 women) of the primary survey of the Wakayama Spine Study conducted in 2008-2010. T2-weighted cross-sectional magnetic resonance imaging of the lumbar spine was used to evaluate the L1/2-L5/S intervertebral spaces following the four-grade classification criteria of Suri et al. (no stenosis, and mild, moderate, or severe stenosis). The presence of severe stenosis in any of the five intervertebral spaces was considered "Presence of severe spinal stenosis." Basic physical measurements, smoking and drinking habits, HbA1c levels (Japan Diabetes Society value), and the Ankle Brachial Index (ABI) were recorded.

**Statistical analysis:** The collected data were used for an inter-group comparison between subjects with and without severe stenosis. Multivariate regression analysis was performed, with presence or absence of severe stenosis as the response variable and HbA1c level, ABI, presence or absence of smoking or drinking, sex, age, and body mass index (BMI) as the explanatory variables.

**Results:** Of the 968 participants, 288 (30%) had severe stenosis on imaging, 80 (8%) had DM (HbA1c  $\geq 6.1$ ), and 18 (2%) had peripheral artery disease (ABI  $< 0.9$ ). The distribution of HbA1c values (mean  $\pm$  SD) was  $5.2 \pm 0.7$ , and that of ABI values was  $1.10 \pm 0.09$ . The group with severe stenosis had significantly higher age, BMI, smoking rates, HbA1c, and prevalence of DM than the group without severe stenosis. Logistic regression analysis demonstrated that age (unit odds ratio 1.05 [95% confidence interval: 1.04-1.07]), BMI (1.05 [1.00-1.09]), and HbA1c (1.48 [1.19-1.84]) were significant risk factors for severe stenosis. When an HbA1c threshold level of 5.5 (determined through receiver operating characteristic analysis) was substituted in the same model as a binary classifier, the new prevalence odds ratio for severe stenosis was 1.91 [1.4-2.7].

**Discussion:** An HbA1c level of  $\geq 5.5$  corresponds to the threshold value of impaired glucose tolerance. Differential analysis by degree of stenosis on imaging reportedly found that the prevalence of DM was significantly associated with the onset of LSS symptoms, independent of stenosis on imaging. This study suggested that impaired glucose metabolism is involved in anatomical stenosis of the lumbar spinal canal.

## Long-term outcome of targeted therapy for low back pain in elderly *de novo* degenerative lumbar scoliosis

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**INTRODUCTION:** The treatment of low back pain (LBP) with *de novo* degenerative lumbar scoliosis (DLS) is the subject of much debate. We speculate that bone marrow edema (BME) frequently found in the endplates at the concave side of scoliosis on MRI is strongly associated with LBP. We developed a targeting operative therapy; percutaneous intervertebral-vacuum polymethylmethacrylate injection (PIPI) for LBP associated with DLS in the elderly. The aim of this study is to report long-term outcomes of PIPI as a treatment for LBP in the elderly DLS patients.

**METHODS:** We included *de novo* DLS patients aged 65 years and over who had LBP (VAS >50) at least 6 months with intervertebral vacuum phenomenon and BME defined on fat saturated T2-weighted or gadolinium-enhanced T1-weighted MRI. 80 patients who underwent PIPI could be followed more than 2 years. The outcomes were evaluated using Visual analog scale (VAS) of LBP, and the Oswestry Disability Index (ODI). As the objective changes, we measured BME score on MRI. Mean follow-up period was 54.6±21.0 months.

**RESULTS:** The mean VAS and ODI scores were 81.5±14.9 and 52.0±15.3 at the baseline. These scores were significantly improved at 1 month after PIPI (29.9±21.6, 29.3±18.1). These scores were 26.7±24.9, 32.5±17.2 at 2 years after PIPI and 29.7±18.6, 32.9±14.0 at final follow-up. After PIPI, mean BME score was significantly decreased (P<0.001), and correlated with the VAS and the ODI scores (VAS: r=0.502, P<0.001, ODI: r=0.372, P<0.001). During final follow-up, LBP was recurred in 28 patients (mean 32.3 months after PIPI) due to recurrence of BME in the same level of PIPI (10 patients), adjacent level disorder (10 patients), and other level disorders (8 patients). The recurrences of BME were significantly appeared at lateral slip levels (p<0.001). For the salvage surgery, we added PIPI for 18 patients and PIPI and posterior fusion for 1 patient, and the VAS scores were improved from 80.0±12.4 to 34.3±17.8.

**DISCUSSION:** PIPI achieved a positive effect in terms of LBP relief. For the salvage surgery, a secondary PIPI after the initial PIPI was also effective for the recurrence of LBP. PIPI can be recommended as an effective and repeatable treatment for elderly DLS patients.

## Publication trends in spine research: comparison of the Orthopaedic Research Society Spine Section and the International Society for the Study of the Lumbar Spine

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**Introduction** The mission of the Orthopaedic Research Society Spine Section (ORS3) is to advance spine research and improve patient care through enhanced communication and cross-disciplinary collaboration within the ORS and beyond. Dissemination of research findings ensures forward progress and innovation, and recent ORS3 meetings discussed current trends in spine publications and how existing journals are meeting the needs of the ORS3 community. Here, the PubMed database was systematically probed to identify publication trends of ORS3 members and members of the more clinically-focused and global International Society for Study of the Lumbar Spine (ISSLS). In particular, we evaluated whether trends have shifted over the past ten years and if the trends of the two societies were similar. ORS3 and ISSLS member overall publication trends were evaluated with a particular focus on trends in the 'traditional' spine journals (*Spine*, *European Spine Journal*, *The Spine Journal*).

**Methods** We searched PubMed for spine-related articles published over a ten-year span (1/1/2007-12/31/2016) by all principal investigators on the ORS3 and ISSLS membership rosters. Publications were included if an ORS3 or ISSLS member appeared as either the first or last author and if spine-related keywords appeared in the manuscript title. A MATLAB program was developed to read ORS3 and ISSLS membership rosters and create one PubMed search term that included member names, designations for first or last author, and links to spine-related keywords. Search results were downloaded from PubMed, read into EndNote for formatting, and exported to MATLAB for additional analysis.

**Results** Pubmed lists 1,107 articles from 143 ORS3 members (29% Clinician-Scientists, 71% Scientists) spanning 14 countries (top 3: 71% United States, 6% Japan, 5% Canada) and 3,464 articles from 372 ISSLS members (80% Clinician-Scientists, 20% Scientists) spanning 29 countries (top 3: 31% United States, 20% Japan, 7% United Kingdom); 22 researchers belong to both societies. For both groups, the total number of publications and the number of unique journals increased with time [Fig. 1]. Over the ten year span, members of both groups published in hundreds of journals (ORS3 223; ISSLS 494), though ORS3/ISSLS members published five or fewer manuscripts in the majority (ORS 82%; ISSLS 82%) of these journals. Furthermore, both groups published most frequently in the traditional spine journals. In particular, *Spine* was the most prevalent journal for society members, yet *Spine* publications significantly decreased from 2007-2011 to 2012-2016 (ORS3: 24.2% to 9.4%, t-test p=0.03; ISSLS: 24.1% to 15.6%, t-test p=0.0002). Publication trends for *European Spine Journal* and *The Spine Journal* remained unchanged (t-test p>0.05).

**Discussion** We searched the PubMed for spine-related research articles and found that ORS3 and ISSLS have been increasingly productive with time. ORS3 and ISSLS members are publishing in an astonishingly large number of journals, although less in *Spine*. Whether these shifts reflect changes in journal selectivity and/or growing diversity of spine-related research topics remains unclear. Whatever the cause, the increase in distinct journals may suggest that traditional spine journals do not fully serve members' needs.

Figure 1 – Overall Publication Trends

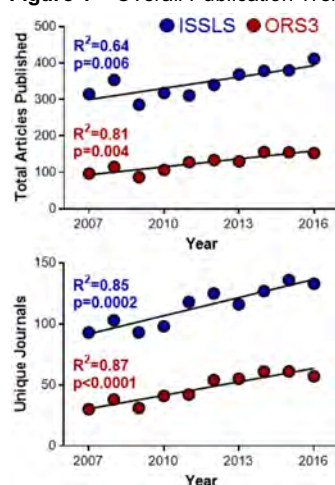


Figure 2 – Publication Trends by Journal

ORS3				ISSLS			
Years 2007-2011		Years 2012-2016		Years 2007-2011		Years 2012-2016	
Total # of Publications		Total # of Publications		Total # of Publications		Total # of Publications	
Total # of Journals		Total # of Journals		Total # of Journals		Total # of Journals	
472		635		1584		1880	
106		168		281		348	
1107		223		3464		494	
Rank	Journal	Count	% Total	Rank	Journal	Count	% Total
1	Spine	114	24.2	1	Spine	60	9.4
2	Spine J	48	10.2	2	Spine J	58	9.1
3	Eur Spine J	28	5.9	3	J Orthop Res	47	7.4
4	J Orthop Res	24	5.1	4	Eur Spine J	42	6.6
5	Arthritis Res Ther	20	4.2	5	J Biomech	36	5.7
6	J Biomech	16	3.4	6	Global Spine J	22	3.5
7	J Bone Joint Surg Am	15	3.2	7	J Biomech Eng	14	2.2
8	J Neurosurg Spine	12	2.5	8	PLoS One	14	2.2
9	Arthritis Rheum	11	2.3	9	J Neurosurg Spine	11	1.7
10	Orthop Clin North Am	10	2.1	10	Arthritis Res Ther	11	1.7



## Relationship between cage design and retropulsion after posterior lumbar interbody fusion

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### Introduction:

Posterior lumbar interbody fusion (PLIF) is a common surgical technique for degenerative lumbar spinal diseases, whereas problems remain regarding implant-related complications. Cage retropulsion might cause neurological deterioration requiring revision surgery. Although several designs of cage are now used, it remains unclear how the cage design affects the rate of cage retropulsion. The objective of this study is to investigate the relationship between cage design and retropulsion.

### Methods:

A total of 500 patients (214 men and 286 women with a mean age of 70.6 years) who had undergone a single or multilevel PLIF between April 2014 and March 2017 were retrospectively reviewed at a minimum of 6-month follow-up. Interbody fusion cages and pedicle screw fixations were used in all patients. Fusion levels was 1.4 segments on average (range, 1-4). Cages were inserted into 699 intervertebral disc spaces (7 in L1/2; 41 in L2/3; 175 in L3/4; 346 in L4/5; 130 in L5/S). Cage shapes were box-type in 231 patients and boomerang-type in 269 patients. Cage retropulsion was defined as cage migration beyond posterior margin of vertebral body. The rates of cage retropulsion were compared between box-type group and boomerang-type group. In those with cage retropulsion, the rates of revision surgery and pseudarthrosis were also analyzed. Pseudarthrosis was defined as the absence of bridging bone across the disc space on CT. Vertebral bone mass was assessed by the percentage of young adult mean (% YAM) in bone mineral density (BMD) of lumbar vertebra.

### Results:

Cage retropulsion occurred in 2.4% (12 of 500 patients); 3.9% in box-type group (9 of 231 patients) and 1.1% in boomerang-type group (3 of 269 patients). The incidence of cage retropulsion in boomerang-type group was significantly lower than that in box-type group ( $p=0.043$ ). Mean period to cage retropulsion was 3.3 weeks (range, 2-8 weeks). Cage retropulsion occurred in 1.1% at L3/4 (2 of 175 segments), 2.0% at L4/5 (7 of 346 segments), 2.3% at L5/S (3 of 130 segments); the differences were not significant among the operative levels. Revision surgery for cage retropulsion was required in 3 of 12 patients within 5 postoperative weeks. Cage retropulsion resulted in pseudarthrosis in all except revision cases. Mean vertebral bone mass (% YAM of lumbar vertebral BMD) was 93.0% (range, 40%–167%) in the patients without cage retropulsion, and 92.8% (range, 65%–129%) in those with cage retropulsion; the difference was not significant.

### Discussion:

The current study Properties of boomerang-type cage, which could be inserted more forward and provide larger segmental lordosis, might reduce the incidence of cage retropulsion. Although cage retropulsion did not entirely cause neurological symptoms requiring revision surgery, it was likely to result in pseudarthrosis. As well, the current results suggested that low vertebral bone mass might not be a risk factor for cage retropulsion.

## Load-sharing through elastic micro-motion accelerates bone formation and interbody fusion

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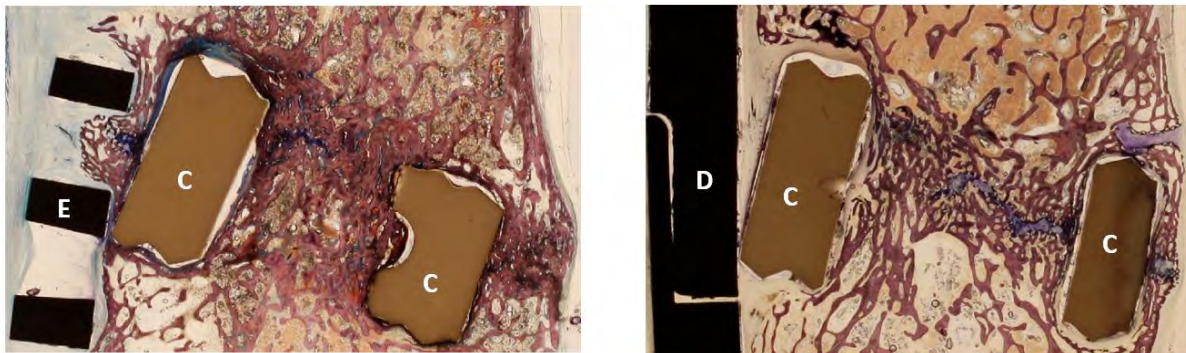
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**Introduction:** Achieving a successful spinal fusion requires the proper biologic and biomechanical environment. The biomechanics of spine fusion is similar to fracture healing which demonstrates that rigid fixation leads to primary bone formation, less rigid fixation leads to secondary bone formation, and more compliant fixation results in fibrous non-union. Following anterior cervical discectomy and fusion (ACDF), the biomechanics of fusion is largely dictated by the properties of the plate. The ideal cervical plate stabilizes a motion segment sufficiently to facilitate bone formation and at the same time fosters load-sharing and eliminates stress-shielding. The purpose of this study was to evaluate the efficacy of a novel elastically deformable, continuously load-sharing anterior cervical spinal plate for promotion of bone formation and interbody fusion in a large animal model *in vivo*.

**Methods:** The elastically deformable plate design is analogous to a serpentine spring with double struts supporting each transverse member of the spring. The plate is designed to promote a favorable load-sharing environment with the with the cage/graft through the entire range of physiologic motion. After IACUC approval, fourteen goats underwent an ACDF and received either a translationally dynamic or elastically deformable plate. Animals were followed out to 18 weeks and were evaluated by plain x-ray, CT scan, and undecalcified histology to evaluate the rate and quality of bone formation and interbody fusion.

**Results:** Results showed that animals treated with the elastically deformable plate demonstrated superior early bone formation, earlier bony bridging, and superior rates of fusion relative to the translationally dynamic plate in all measures and at all time points from 8 to 18 weeks post-operatively. As shown in the figure, bone formation within the cage (c) of the elastically (e) deformable treated levels (left) was superior to dynamic (d) plate treated levels (right) for all animals at 14 weeks post-operatively.

**Discussion:** Results demonstrate that the elastically deformable plate which allowed micro-motion is efficacious for achieving earlier bone formation, earlier bridging bone, and faster fusion relative to a dynamic plate in the challenging goat ACDF model. Results suggest that the combination of continuous load-sharing and stability through the entire range of physiologic loading promotes faster bone formation and better fusion. While the optimal implant stiffness is not yet characterized, results from this study demonstrate that load-sharing through elastic micro-motion accelerates bone formation and interbody fusion. A more comprehensive understanding of these relationships may be paradigm-shifting with respect to the design of next-generation implants and other therapeutic approaches to spine fusion.



### Microendoscopic foraminotomy for the lumbosacral junction: two year's outcome and risk factors for poor results

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**Introduction:** Microendoscopic spine surgery may be an ideal procedure for the treatment for extraforaminal stenosis at the lumbosacral junction, because it can reach to a deep layer and provide a bright and magnified visual surgical field with minimal invasion for surrounding structures. The purpose of this study was to estimate the 2 years surgical outcome and to clarify the risk factors for the poor results in patients surgically treated with this procedure for extraforaminal stenosis at the lumbosacral junction.

**Methods:** A total of 122 patients (65 men, 57 women, average age 67.4 years), who received microendoscopic decompression for the extraforaminal stenosis at lumbosacral junction and completed a follow-up at 2 years after surgery, were included in this case series. Clinical outcomes were evaluated according to the Japanese Orthopaedic Association score for low-back pain (JOA score: 0-29 points) and the visual analog scale (VAS: 0-100mm) for low-back pain, leg pain, and leg numbness, and Japanese Orthopaedic Association Back Pain Evaluation Questionnaire (JOABPEQ) including a domain of psychological disorders.

**Statistical analysis:** 1) Postoperative change of evaluated items were observed. Based on the JOA score recovery rate (RR), RR of 50%≤ and RR of <50% was defined as good results and poor results, respectively. Minimal clinically important difference of VAS was defined as 20mm. 2) To clarify the risk factors for poor results, a multiple logistic regression analysis was conducted with possible risk factors as explanatory variables (ex. age, sex, preoperative JOA score, VAS, psychological disorders in JOABPEQ).

**Results:** During the follow-up period, 12 patients required revision surgery. The remaining 110 patients were conducted clinical evaluation. The mean JOA score was significantly improved from 14.2 points to 20.5 points, and the average improvement rate was 42.7%. The mean VAS scores for low-back pain, leg pain, and leg numbness were also improved from 53.6, 72.3, and 57.7 to 29.9, 28.3, and 28.2, respectively. The patients' rates improved more than minimal clinically important difference were 63.4%, 78.2%, and 59.4% in low-back pain, leg pain, and leg numbness, respectively. Based on the logistic regression analysis, female sex (odds ratio 3.8), preoperative psychological disorder (unit odds ratio 1.04) were significant risk factors for poor results.

**Discussion:** The JOA recovery rate in this case series was 42.7%, which is significantly less than our experience in the microendoscopic decompression surgery for the patients with central type LSS (Minamide, et al. J Neurosurg Spine 19: 664-71, 2013). Without doubt, microendoscopic spine surgery has a significant advantage for the patients from the stand point of minimum invasive. The physicians may still need to clarify the pathology of the extraforaminal stenosis at lumbosacral junction. Female sex and psychological disorder were found to be risk factors for poor surgical results. We speculate there is a confounding factor which relates to both of sex and poor results. Older age or preoperative lower JOA score were not risk factors in this case series. We are planning to evaluate radiological features of the patients because it should be a limitation of this study.

## Two different type of stooping posture after iliac screw fixation for degenerative adult spinal deformity

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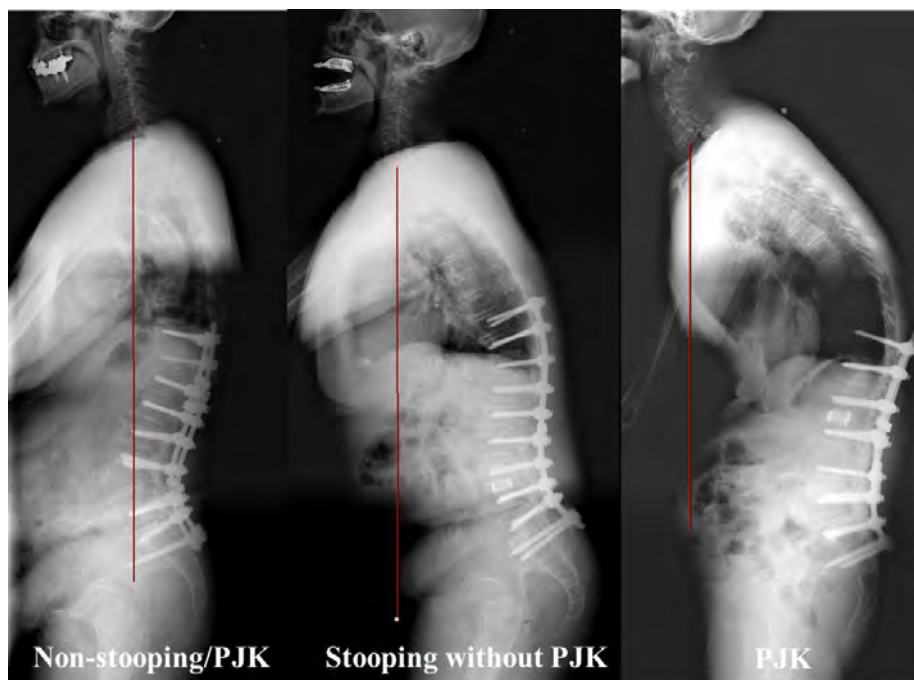
**Introduction** Proximal junctional kyphosis (PJK) is a segmental deformity that occurs after correction of the sagittal deformity above the upper end instrumentation. However, stooping posture could develop without PJK after surgical correction. They showed the different sagittal imbalance that increases the mechanical demands of pelvis extension. However, many studies that have addressed this issue have focused on PJK. Therefore, the objective of this study is to investigate different risk factors between post-operative stooping posture without and with PJK after iliac screw fixation in degenerative adult spinal deformity (ASD).

**Methods** 80 patients who had undergone surgical correction for degenerative ASD were enrolled. Patients with degenerative sagittal imbalance who were more than 60 years old at the time of index surgery were included for homogeneity. All those who had more 5 levels fusion from upper instrumented vertebra (UIV) of L1 and above were included. Univariate and multivariate analysis for clinical, surgical and radiological factors including paravertebral muscles were conducted for respective risk factors between stooping posture and PJK. In addition, clinical outcomes were evaluated.

**Results** 40 patients without stooping or PJK were compared with patients who had stooping posture (n=18) and PJK (n=22), respectively. Univariate analysis for stooping posture without PJK revealed that more fusion levels, fusion at thoracolumbar junction, lesser correction of lumbar lordosis (LL), sacral slope (SS), pelvic tilt (PT), thoracic kyphosis (TK), and less ratio of cross-sectional area (CSA) of paravertebral muscles to disc were the significant risk factor. More fusion levels (odds ratio (OR)=3.109, p=0.044), less correction of SS (OR=1.221, p=0.003) and TK (OR=1.264, p=0.049) were the independent risk factors for stooping posture in multivariate analysis. In PJK group, the significant risk factors were higher body mass index (BMI), greater post-operative PT, and lesser correction of SS in univariate analysis. The greater post-operative PT (OR=1.105, p=0.026), and lesser correction of SS (OR=1.084, p=0.036) were the independent risk factors for PJK in multivariate analysis.

In subgroup analysis among non-stooping/non-PJK, stooping/non-PJK, and PJK groups, there were significant differences concerning correction of SS (9.7° vs. 2.8° vs. 4.6°, p=0.010) and PT (-11.1° vs. -4.1° vs. -7.6°, p=0.015), and ratio of CSA of paravertebral muscles to disc (0.90 vs. 0.76 vs. 0.96, p=0.017), respectively. Regarding the clinical outcomes, patients in non-stooping/non-PJK group reported significant improvement of VAS for back (7.1 vs. 4.1, p=0.0001) and leg pain (6.4 vs. 4.3, p=0.001), and ODI (57.3 vs. 45.5, p=0.002) while only significant improvement of VAS for back pain (7.5 vs. 5.3, p=0.022) was observed in stooping group and no significant improvement in PJK group.

**Discussion/conclusion** This study revealed that less correction of sagittal parameters was a risk factor of stooping posture (correction of SS and TK) and PJK (post-operative PT, correction of SS) compared to non-stooping/non-PJK group. In patients with stooping posture, less correction of LL, greater post-operative pelvic incidence (PI)-LL mismatch and SVA, combined with paravertebral muscle weakness were significant risk factors directly compared to PJK group. Clinical outcomes were also significant different between two groups.



## Spinal correction surgery enables longterm relief of gastroesophageal reflux disease symptoms in adult spinal deformity

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**Introduction:** Gastroesophageal reflux disease (GERD) is reported to be one of the complications for adult spinal deformity especially in patients with thoracolumbar kyphosis due to vertebral fracture. We previously reported the impact of spinal correction on GERD symptom relief (Sugimoto, Dig Endosc 2016). However the longterm effect of the spinal correction on GERD symptom is yet to be revealed.

**Methods:** We investigated 381 adult spinal deformity patients over the age of 18, who underwent at least 5 vertebrae levels of spinal correction and fusion during 2010-2015 in our hospital. We used F-scale questionnaire (FS) with GERD 62% sensitivity and 59% specificity for GERD diagnosis at the cut-off value 8 points (Kusano, J Gastroenterol 2004). Preoperatively 132 patients had over 8 points examined by FS. Patients with the preoperative value of 8 points or more showing any recovery within 6 months from surgery were defined as correction effective group. Among the correction effective group, 85 patients were followed for at least for 2 years and was examined for their FS scores on their first and second postoperative year. These patients were further divided in to subgroups. Patients with the FS score improvement of more than 5 points were categorized as maintained group and patients with the FS score of less than 5 was categorized as worsened group. Using standing whole spine X ray, the relationship between the FS scores and the changes in sagittal vertical axis (SVA), thoracic kyphosis (TK), lumbar kyphosis (LL), proximal junctional angle (PJA) and coronal Cobb angle were investigated. ANOVA, Bonferroni and t-test was used for statistical analysis.

**Results:** Among the 132 patients with the FS value of over 8, 111(84%) showed improvement of the score at 6 months postoperatively. The preoperative values significantly improved from 16.0 to 4.8 immediately after operation and was maintained at the first and second postoperative year with the scores of  $8.6 \pm 7.1$  and  $8.6 \pm 7.5$  ( $p < 0.0001$ ). However the first and second postoperative year scores were significantly worse in comparison with the immediate postoperative value ( $p = 0.002$ ). The X ray analysis showed that there was a significant difference in the changes of SVA between the FS maintained group and the worsened group (35mm vs 4.7mm SVA change,  $p = 0.01$ ). There were no significant differences in another local area X-ray parameters.

**Discussion:** This study showed the impact of spinal correction on GERD symptoms in adult spinal deformity, any improvement was seen in 84% of GERD (+) patient. The interesting finding in our study was that the reprogression of the GERD symptom was not influenced by the worsening of the spinal global alignment as these changes were greater in patients with the improved FS scores. Further investigation is required to reveal the factors with direct influence on the GERD symptoms.

**Conclusion:** In adult spinal deformity patients, GERD symptoms are immediately improved directly after operation and the improvement is maintained throughout the second postoperative year. Thus patients with GERD symptoms due to adult spinal deformity have good operative indication for deformity correction.

## Behavioural, radiologic and morphologic long-term consequences of an acute single lumbar intervertebral disc injury in mice

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**Introduction:** Low Back Pain (LBP) is a difficult and complex condition that affects millions of lives but is still difficult to diagnose and treat. Many anatomical components of the spine are involved, including intervertebral discs (IVDs, aka discogenic pain). To investigate the underlying mechanisms of discogenic pain, mechanical lumbar disc injury models have been developed in various species; these injuries result in persistent disc pathology. In contrast, studies addressing physical impairment and behavioral signs of LBP report transient changes that resolve during the first months following disc injury. Discrepancies therefore exist between transient behavioural changes following mechanical disc injury, the persistence of disc pathology, and the long term behavioural consequences of progressive disc degeneration. To improve therapeutic options, clinically-relevant animal models that integrate both pathological and behavioral changes need to be used. The goal of this study was to investigate the long term behavioural and physiological consequences of an acute single intervertebral disc injury in mice.

**Methods: Animals:** Female 20g CD1 mice (Charles River Laboratories, St-Constant, QC, Canada). **Surgical procedure:** A ventral longitudinal incision was performed under deep anesthesia (isoflurane 2.5%) and the ventral aspect of the L4/L5 intervertebral disc was visualized (sham animal) or punctured (injured animal) by a slow single penetration with a 30G needle. Animals were evaluated 0.5-12 months post-surgery. **Behavioural Measures:** Motor performance was assessed by measuring spontaneous wheel running over a 60 min test period. Axial Low Back Pain: The grip force, FlexMaze, and tail suspension assays were used as measures of axial discomfort. Radiating Leg Pain: Hindpaw sensitivity to mechanical (von Frey) and cold (acetone test) stimuli were used. Radiological Assessment: Disc Height Index (DHI) was quantified using *In vivo* X-ray images for L1-L6. Morphologic Changes: *Ex vivo* assessment of disc degeneration by T2-MRI using 7T-Bruker machine with a spatial resolution 80×80×500 µm.

**Results:** Injured animals presented significantly increased body weight compared to sham mice, but no motor disturbances were observed. Consistent with our previous studies, a subset of animals developed cold but not mechanical plantar hypersensitivity that we interpret as a sign of radiating pain. Behavioral signs of axial discomfort were transiently observed around 6 month post-injury. Injured discs were significantly narrower upon X-ray examination. Interestingly, the analysis of MRI images revealed that 12 month post-injury, uninjured IVDs directly adjacent to injured discs started to show signs of degeneration including disc narrowing.

**Discussion:** Disc injury results in severe disc degeneration that persists for up to 1 year post-injury. Behavioural signs of discomfort developed in a delayed fashion and peaked 3 to 9 months post-injury. In contrast, spines continue to degenerate beyond that time window. In the present study, we also demonstrate that disc degeneration spreads to discs adjacent to the initially injured disc.

GP040

**Low back pain prognostic factors for time receiving wage replacement benefits.**

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**Introduction.** Recent systematic reviews have identified only a few back pain studies that utilize “time-to-event” data. This study addresses that oversight with a unique and original approach data analysis approach using survival analysis, calculated by the method of Cox regression.

The objective was to develop a prognostic model that predicts time receiving workers’ compensation benefits for low back pain claimants enrolled in any one of 20 post injury rehabilitation clinics across Ontario.

**Methods.** A retrospective review of prospectively collected data was used to identify an inception cohort. To obtain the outcome and predictor variables, patient data from two separate resources were linked: a clinical (physiotherapy) and an administrative (Ontario workers’ compensation) database. Those with back pain claims filed between 2011 and 2015 were included and followed for 1 year from the date of accident (n=1652).

The independent variables that were assessed for predictive value were a back pain questionnaire, clinical, demographic and administrative factors. The outcome variable was cumulative number of calendar days receiving wage-replacement benefits.

**Results.** Multivariable Cox proportional hazards regression revealed 8 significant predictors of shorter time on benefits:

- 1) symptom duration less than 31 days (hazard rate (HR)=0.879)
- 2) attending early intervention rehabilitation (HR=1.51)
- 3) not working in the construction industry (HR=1.89)
- 4) high Low Back Outcome Score (higher perceived function) (HR=1.025)
- 5) younger age (HR=0.992)
- 6) higher wage-replacement benefit rate (HR=1.00)
- 7) intermittent (not constant) pain (HR=1.15)
- 8) no sleep disturbance (HR=1.15)

A predictive score was calculated to categorize claimants as at high or low risk for chronicity; 23% were at high risk.

**Discussion.** Building a predictive model should focus on the identification of key variables that can be easily identified and reliably collected in a clinical setting.

Clinicians need to be aware of what factors differentiate people who become chronically disabled from those who do not. This study identifies 8 significant factors associated with shorter time on wage-replacement benefits. This multivariable model indicates a robust and reasonably accurate clinical prediction capacity.

## Health related quality of life improvement after spinal fusion for degenerative low back pain vs adult spine deformity

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**INTRODUCTION:** Adult Spine Deformity (ADF) requires more extensive surgical intervention compared to Degenerative Spine (DS) patients without deformity, with greater risks and complications. Clinical improvement in ADF should justify the need for more extensive surgery, compared to DS patients.

**Study design** - Self-reported HRQOL data from prospective cohorts of ADF and DS patients were compared by independent observers, to assess improvement after surgery in each group.

**METHODS:** Consecutive patients operated between 2004-2011, satisfying the inclusion criteria with minimum 2 yr followup were enrolled. DS cohort had instrumented fusion of  $\leq 4$  segments, with or without decompression. ADF cohort were treated with  $\geq 5$  segments instrumented fusion with/without decompression/osteotomy. Data were prospectively collected at pre-op and at 3, 6, 12 and 24 months post-op; SF-36 and ODI scores were compared between the groups.

**RESULTS:** DS group had 610 patients, (M=312, F=298) and mean age 48.7 yr (+/-14 SD). ADF group had 93 patients (M=33, F=60) and mean age 57.7yr (+/-15.5 SD). Mean ODI score in the DS and ADF groups were 55.1 vs. 49.38 (pre-op,  $p=0.003$ ), 38.74 vs. 33.6 (at 6 mo) and 39.05 vs. 27.96 (at 24 mo,  $p=0.005$ ) respectively. Both the groups improved significantly over baseline ( $p<0.05$ ). Mean MCS score in the DS and ADF groups were 44.27 vs. 47 (pre-op) and 48 vs. 46.65 (at 24 mo) respectively, and there was no significant difference between the groups or within the group at different follow-up period. The PCS scores in the DS and ADF groups were 27.5 vs. 28.9 (preop), 34.8 vs. 35.6 (at 6 mo), and 32.9 vs. 35.3 (at 24 mo). Both the groups improved significantly compared to pre-op ( $p<0.05$ ) but there was no significant difference between the groups at any follow-up period. The mean Bodily Pain (BP) component of the SF 36 score in the DS and ADF groups were 27.6 vs. 30.16 (pre-op,  $p=0.005$ ), 36.5 vs. 39.8 (at 6 mo,  $p=0.03$ ) and 34.9 vs. 42.81 (at 24 mo,  $p=0.0001$ ). Both the groups improved significantly ( $p<0.05$ ) over baseline.

**CONCLUSION:** Pain scores (ODI and BP), and physical function (PCS) improved significantly in both the groups compared to pre-op. DS group had increased pain scores compared to the ADF group at baseline. The ADF group showed significantly better improvement in the pain scores compared to the the DS group at 2 year follow-up period.



## Effect of peri-operative adverse events on long-term patient reported outcomes after lumbar spine surgery

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**Introduction.** Peri-operative adverse events lead to patient disappointment, resource utilization and increased healthcare costs. There is a paucity of data on how complications affect long-term patient reported outcomes. The purpose of this study was to examine peri-operative adverse events and their long-term impact on patient reported outcomes.

**Methods.** There were 3621 consecutive patients analysed who had elective spine surgery for degenerative lumbar spine disorders and were enrolled in the Canadian Spine Outcomes and Research Network (CSORN) prospective database. Peri or immediate postoperative adverse events were divided into Major and Minor for lumbar disc herniation, degenerative spondylolithesis, and spinal stenosis. Outcomes at 3 and 12 months for disability score, VAS leg and back, and SF-12 were assessed using univariate and multivariable linear regression.

**Results.** There were 109 major complications (3.01%). Patients that experienced major complications were significantly older ( $64.41 \pm 11.59$  vs.  $57.26 \pm 14.87$ ), were more likely to have experienced their condition for >2 years (47.7% vs. 32.85%), had longer surgical times (177.6 vs. 134.3 mins.) and had higher rates of comorbidities (all  $p < 0.05$ ).

Major complications were associated with higher disability score at 3 months ( $p < 0.015$ ) but not at 1 year ( $p < 0.7$ ), and lower SF12 Physical Component Score at 3 months ( $p < 0.005$ ) but not at 1 year ( $p < 0.16$ ). Length of stay was longer after an adverse event ( $12.15 \pm 20.7$  vs.  $3.72 \pm 16.9$  days,  $p < 0.0001$ ). In multivariable linear regression (after controlling for significant variables in univariate analysis), no single adverse event was significantly associated with a poorer disability score at 3 months.

**Discussion.** Major adverse events during hospital admission led to significantly worse outcomes at 3 months but not at 1 year after surgery for degenerative lumbar disease.

## Lumbar surgery in octogenarians. Really?

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**Introduction.** Lumbar decompression for spinal stenosis is the most common spine surgical procedure performed. With our aging population, elective spine surgery is becoming more common in the elderly. The aim of this study was to identify if age, specifically being 80+, influences effects of lumbar decompression surgery on leg pain at one-year follow up.

**Methods.** Retrospective analysis of prospectively collected data on elective lumbar surgery patients in the Canadian Spine Outcomes and Research Network (CSORN) database. Consecutive surgical patients with a pathological diagnosis of lumbar stenosis were dichotomized into <80 years old and ≥80 years groups. The impact of age on one-year improvement in health related quality of life (HRQL) was assessed using ANCOVA, adjusting for significant confounders identified in univariate analysis.

**Results.** One-year HRQL data was available on 1507 patients (<80 n=1414, ≥80 n=93). Median patient age was 61 years (range 18-90 years) with 49% female. Adjusting for confounders demonstrated that the older patients were more likely to have a higher ASA score, less likely to smoke, less likely to be receiving insurance payments, less preoperative narcotic use and had a lower BMI.

The two groups were similar in gender distribution, exercise status, pre-operative neurological deficit, symptoms duration, number who had a fusion and prior lumbar surgery.

After adjusting for confounders, there was no statistically significant difference in one-year improvement on disability score (-18.90 vs -21.27, p<0.798), EQ5D (-0.06 vs 0.01, p<0.072), SF-12 Mental Component Score (0.60 vs 3.54, p<0.067), Numeric Rating Scale back pain (-3.88 vs -3.45, p<0.16) and Numeric Rating Scale leg pain (-4.31 vs -3.69, p<0.28). The ≥80 group experienced statistically less improvement on SF-12 Physical Component Score (PCS) (5.96 vs 10.78, p<0.027) at one year compared to their younger counterparts, although the difference did not reach minimal clinically important difference for PCS.

**Discussion.** At one-year post-operative follow-up, change in Numeric Rating Scale leg pain and SF-12 PCS score showed statistically significantly less improvement in those 80+ years old, although these observed differences were not clinically significant. The remaining patient reported outcomes appeared similar between the older and younger patient groups. When considering patient reported outcomes, lumbar surgery in those 80+ years old may be a reasonable choice.

## Spinopelvic sagittal alignment after minimally invasive decompression surgery without fusion in patients with lumbar degenerative spondylolisthesis

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### INTRODUCTION

Spinopelvic sagittal balance is important in managing lumbar diseases and low back pain (LBP). Anterior translation of the C7 plumb line, high pelvic incidence (PI), and pelvic retroversion were reportedly marked in degenerative spondylolisthesis (DS) patients compared with a normal population. The purpose of this study was to evaluate the change in spinal sagittal alignment after decompression alone in patients with low-grade DS.

### METHODS

We retrospectively reviewed the records of 87 patients (48 men, 39 women; mean age  $69.2 \pm 9.3$  years) who underwent microendoscopic laminotomy. We enrolled 35 patients with DS and 52 patients without DS. Spinopelvic parameters were evaluated, including the sagittal vertical axis (SVA), lumbar lordosis (LL), sacral slope (SS), pelvic tilt (PT), and PI. Primary outcome was a change in spinopelvic alignment between the baseline and latest follow-up values (DS group versus non-DS group). Secondary outcomes were the relations between the improved global sagittal alignment and the preoperative spinopelvic parameters.

### RESULTS

Both groups showed significantly alleviated LBP, leg pain, and leg numbness. There were no significant intergroup differences in the JOA score or VAS at the latest follow-up. Preoperative SVA and PI were significantly higher in the DS group than in the non-DS group ( $p < 0.05$ ). SVA significantly decreased and LL significantly increased in the DS group ( $p < 0.05$ ), whereas those parameters did not differ significantly from before to after surgery in the non-DS group (Fig). No significant differences existed between the groups for SS, PT, or  $PI - (= \text{minus}) LL$ . In both groups, the SVA improvement correlated significantly with the preoperative SVA (DS:  $r = 0.702$ , non-DS:  $r = 0.397$ ). There was also a significant intergroup difference in the correlation coefficient ( $z = 1.98$   $r = 0.048$ ).

### DISCUSSION

In the present study, the results in the DS group, SVA and LL did not significantly improve in the non-DS group, indicating that the preoperative kyphotic compensation to avoid neuralgic symptoms is greater in DS patients than in those without DS. Our results suggest that global sagittal imbalance in patients with DS can be treated by decompression without requiring a corrective procedure in some patients whose malalignment was induced by compensatory reduction of the LL. In conclusion, SVA and LL significantly improved after microscopic laminotomy in patients with low-grade DS and neurologic symptoms. SVA improvement in the DS group was correlated with preoperative spinopelvic sagittal imbalance. It should be noted that the strength of those correlations was greater than for those in the non-DS group.

## Do preoperative psychological factors affect patient satisfaction with surgery for lumbar spinal stenosis?

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### Introduction

Some reports have focused on the relationship between patient satisfaction and psychological factors, and most have used the VAS or NRS as a measure of patient satisfaction. However, there are no clear cutoff values for VAS or NRS ratings of patient satisfaction, which makes it difficult to judge patient satisfaction with the outcome. The Zurich claudication questionnaire (ZCQ), which includes symptom, function, and satisfaction domains, is used to rate patient-reported outcomes for patients with lumbar spinal stenosis (LSS). The cutoff values for the subdomains have been reported and accepted. The purpose of the present study was to examine whether preoperative psychological factors affect patient satisfaction with surgery for LSS as measured by the ZCQ satisfaction score.

### Patients and Methods

A total of 157 LSS patients who were planning to undergo surgery at our institute were involved in this survey between September 2010 and November 2016. The mean age ( $\pm$  SD) at the evaluation was  $70 \pm 8.43$  years. The following instruments were used to evaluate preoperative psychological factors: Pain Catastrophizing Scale, Pain Anxiety Symptoms Scale-20, Hospital Anxiety and Depression Scale (HADS), Self-Rating Questionnaire for Depression. The ZCQ and VAS were used to assess low back pain, leg pain, and leg numbness preoperatively and 1 year postoperatively. Patients were divided into two groups according to the absolute ZCQ patient satisfaction score: satisfaction responders (score  $\leq 2.5$ ) (SR) and nonresponders (score  $>2.5$ ) (NR). Prospectively collected data were analyzed statistically to determine whether preoperative psychological factors were related to patient satisfaction with surgery for LSS. The data were analyzed using the Mann-Whitney *U* test and multiple regression analysis. A *P*-value  $<0.05$  was considered to be significant.

### Results

The SR and NR groups included 113 and 44 patients, respectively. Age at the time of surgery, gender, preoperative VAS, and ZCQ scores did not differ between the two groups. The changes in the ZCQ score after surgery were larger in the SR group than in the NR group (symptom severity:  $1.19 \pm 0.13$  vs.  $0.37 \pm 0.01$ ; physical function:  $1.09 \pm 0.04$  vs.  $0.37 \pm 0.05$ ;  $P < 0.05$ ). The depression and anxiety scores on the HADS questionnaire were significantly higher in the NR group than in the SR group (depression:  $7.33 \pm 3.72$  vs.  $5.14 \pm 3.37$ ; anxiety:  $6.50 \pm 3.49$  vs.  $5.09 \pm 3.77$ ;  $P < 0.05$ ). However, multiple regression analysis showed no significant relationships.

### Discussion and Conclusions

Patients who indicated satisfaction with the surgery on the ZCQ showed evidence of less anxiety and depression preoperatively. Our data suggest that preoperative anxiety and depression may affect patient satisfaction with surgery for LSS. The multiple regression analysis showed no significant relationship between preoperative psychological state and patient satisfaction. Therefore, it is likely that psychological factors as well as other factors such as postoperative physical function and quality of life contribute to patient satisfaction. Collectively, these results suggest that evaluation of preoperative psychological state and preoperative care for anxiety and depression may lead to improved patient satisfaction with surgery for LSS.

## Beneficial effects of regular exercise prior to thoracolumbar spinal surgery

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**Introduction.** "Prehabilitation" (or "prehab") has been promoted as a preoperative intervention purported to improve patient outcomes, especially in the context of arthroplasty surgery; however, there is currently little evidence to support this theory following spine surgery. Our objective was to determine if there is an association between self-reported preoperative exercise and postoperative outcomes after thoracolumbar spinal surgery.

**Methods.** Retrospective multivariable analysis of prospectively collected data in the Canadian Spine Outcomes and Research Network (CSORN) database. All thoracolumbar surgery patients with degenerative pathology only were identified. Fracture or tumour patients were excluded. Multivariable logistic regression was used to adjust for possible confounding effects of age, gender, number of operated levels, instrumentation, revision surgeries, current smoking status, and Charlson Comorbidity Index. Patients who reported that they exercised regularly (i.e. at least twice per week) for at least 6 weeks prior to surgery were compared to those not exercising regularly.

**Results.** There were 1,105 patients in the regular exercise group compared to 2,788 in the not exercising control group. There was no significant difference in improvement in disability score at 12 months follow-up between the two groups. In univariate analyses, the regular exercise group trended towards having lower adverse events (5.5% vs. 7.3%,  $p=0.0532$ ), as well as significantly shorter length of stay above expected (0.3 days vs. 1.0 days,  $p<0.0001$ ). In multivariable analysis, the regular exercise group had fewer adverse events (adjusted odds ratio (OR): 0.695 (95% CI: 0.51-0.95)), and were less likely to have a length of stay greater than expected for their procedure (OR: 0.690 (95% CI: 0.57-0.84)).

**Discussion.** After adjusting for confounding, we demonstrated that patients who exercised regularly before surgery had significantly shorter length of stay and fewer post-operative adverse events. Further study is required to determine if a "prehab" program is effective, although our results suggest that cost savings from reduced length of stay may justify the expense.

## Accuracy of two major scoring systems for prediction of metastatic spine tumor prognosis: analysis of revised Tokuhashi and Katagiri scores

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### INTRODUCTION

Two major scoring systems, the revised Tokuhashi (Tokuhashi score) and Katagiri scores, were reported together in 2005 and have been widely used to predict the prognosis in patients with metastatic spine tumor. Because the prognosis has improved in recent years, we suspected that these scores are unsuitable for current treatments. We aimed to investigate the accuracy of the Tokuhashi and Katagiri scores in patients with metastatic spine tumor who underwent spine surgery.

### METHODS

Study subjects included 84 patients with metastatic spine tumor who underwent spine surgery from May 2009 to April 2017. Of these, 22 patients with unknown prognosis, 15 who remained alive, and one who underwent kyphoplasty were excluded. Forty-eight (male, 26 and female, 22) patients were included in the final analysis. The average age was 61.1 (range, 26-79) years, and average time between spine surgery and death was  $397.2 \pm 481.3$  (range, 16-2201) d. The of the primary tumor were breast cancer in 12 patients, lung cancer in seven, renal cell carcinoma in six, prostate cancer in five, and other origins in 18. These patients were classified into three groups according to the points obtained in the Tokuhashi and Katagiri scores. For the Tokuhashi score, the short-term group (0-8 points) comprised 32 patients, the mid-term group (9-11 points) comprised 14 patients, and the long-term group (12-15 points) comprised two patients. For the Katagiri score, the short-term group (6-10 points) comprised 26 patients, the mid-term group (3-5 points) comprised 19 patients, and the long-term group (0-2 points) comprised three patients. The accuracies both scores were investigated in the three groups. Statistical data were analyzed using analysis of variance, and the level of significance was set at 5%.

### RESULTS

The accuracies of the Tokuhashi score were 65.6% in the short-term group, 57.1% in the mid-term group, and 100% in the long-term group. No significant difference was observed among the groups ( $P = 0.70$ ). The overall accuracy of the Tokuhashi score was 64.6%, and the inaccuracy was due to 11 (22.9%) patients who lived longer than predicted and six (12.5%) patients who lived shorter than predicted. The accuracies of the Katagiri score were 80.8% in the short-term group, 10.5% in the mid-term group, and 100% in the long-term group. A significant difference was observed among the groups ( $P < 0.01$ ). The overall accuracy of the Katagiri score was 54.2%, and the inaccuracy was due to 16 (33.3%) patients who lived longer than predicted and six (12.5%) patients who lived shorter than predicted.

### DISCUSSION

The accuracies of predictions were 64.6% and 54.2% for the Tokuhashi and Katagiri scores, respectively. Thus, the two major scoring systems for predicting the prognosis of metastatic spine tumor were imprecise. Because of rapid progress in cancer therapy in the recent years, one third of the patients have lived longer than predicted by these systems. Thus, our study suggests that patients with metastatic spine tumor live longer than predicted by scoring systems, particularly in surgically treated patients.

## Sagittal spinopelvic alignment in patients with hip osteoarthritis

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### Introduction

Recently, sagittal spino-pelvic angular (SSPA) parameters have been considered important factors in the determination of treatment and evaluation of pathophysiology. The pelvic incidence (PI) is a particularly useful parameter. Since the introduction of the PI, studies on the sagittal spine alignment and pelvic orientation have been increasing. PI has been reported to be a useful morphological parameter, which is not affected by posture and which remains constant after a subject reaches skeletal maturity. Rivière et al. classified the sagittal spine balance and lumbo-pelvic complex (LPC) according to the PI. However, while many investigators have studied the PI, there are a few reports describing the relationship of the PI and hip osteoarthritis. We therefore evaluated the relationship of the PI and hip osteoarthritis in Japanese subjects.

### Methods

A retrospective analysis was conducted on 763 patients with hip osteoarthritis (HOA) who underwent primary total hip arthroplasty (THA) in our hospital (HOA group). A control group was also established, consisting of 47 patients with avascular necrosis of the femoral head (ANF) who underwent primary THA. We excluded patients with high dislocation of the hip. These two groups were then divided into 4 subgroups by age ( $\leq 59$ , 60-69, 70-79,  $\geq 80$  years of age). We classified the patients into spine type 1+2 ( $PI < 40^\circ$ ), spine type 3 ( $40^\circ < PI < 60^\circ$ ), and spine type 4 ( $PI > 60^\circ$ ) groups according to the report of Rivière. We also classified the patients into an LPC type 1 ( $PI < 40^\circ$ ) group called "hip users", and an LPC type 2 ( $PI > 40^\circ$ ) group, called "spine users". Lateral standing radiographs of the pelvic, thoracic, and lumbar spine were obtained. The SSPA parameters that were analyzed were lumbar lordosis (LL), sacral slope (SS), and the PI. A Kruskal-Wallis analysis was used to identify correlations among the features. A P value  $< 0.05$  was considered statistically significant.

### Results

Statistical analyses showed that the HOA group had a significantly higher PI and SS ( $54^\circ$  and  $41^\circ$ ) than the control group ( $47^\circ$  and  $33^\circ$ ). Regarding the spine type classifications, fewer patients in the HOA group belonged to spine type 1+2 and more belonged to spine type 4 than did those in the control group. In both groups, older patients tended to show a stable PI, lower LL, and higher SS compared with younger patients.

### Discussion

The HOA patients had a higher PI than the control patients, which is consistent with similarly selected patients in other Japanese study. Therefore, the common genetic factors affecting the gestational development may lead to the development of a pelvic and acetabular morphology.

As the ability of the pelvis to adapt to spinal changes is related to PI, because PI is determined by SS and PT, both the small PI and large PI group were called "hip users" and "spine users", respectively, according to the classification of Rivière. Therefore, the HOA patients may be more likely than the control patients to belong to the "spine user" group. "Spine user" indicates subjects that mainly their spine to carry out normal daily activities, instead of using their hip joint

## Postoperative loss of lumbar lordosis affects clinical outcomes in patients with pseudoarthrosis after PLIF using cortical bone trajectory screw fixation

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**Introduction:** Pseudoarthrosis after PLIF is one of the major complications. However, in some patients with pseudoarthrosis after PLIF, clinical symptoms improved satisfactorily after surgery. This retrospective study thus aimed to investigate relationships between clinical outcomes and radiographic parameters in patients who developed pseudoarthrosis after single-level PLIF.

**Methods:** Among 263 patients who underwent single-level PLIF with cortical bone trajectory screw fixation (CBT-PLIF) for degenerative lumbar disorders between September 2012 and October 2015 and were followed for at least 2 years after surgery, 27 patients who were diagnosed as pseudoarthrosis using dynamic radiographs of the lumbar spine in the standing position and computed tomography were enrolled in this study. Clinical outcomes were measured using Oswestry Disability Index (ODI) preoperatively and at 2 years postoperatively. These 27 patients were divided into 2 groups based on postoperative improvement of ODI. The group G consisted of 15 patients with greater improvement of ODI than the mean improvement of ODI, and the group P consisted of the others (12 patients). As radiographic parameters, lumbar lordosis (LL), segmental lordosis (SL), segmental range of motion (Seg-ROM), the extent of subsidence, and screw loosening were compared between the 2 groups.

**Results:** The mean ODI improved from 19.9 points before surgery to 9.6 points at 2-year follow-up visit in all 27 patients (mean improvement: 9.9 points). None of age at the time of surgery, sex, BMI, fused areas and preoperative ODI showed significant differences between the 2 groups. No significant differences were found in immediate postoperative SL (group G:  $-6.9^\circ$  vs group P:  $-9.5^\circ$ ,  $p=0.3$ ), postoperative 2-year SL (group G:  $-6.0^\circ$  vs group P:  $-6.9^\circ$ ,  $p=0.6$ ), and the changes of SL during postoperative 2 years (group G:  $-2.8^\circ$  vs group P:  $-2.5^\circ$ ,  $p=0.9$ ). Seg-ROM at postoperative 2-year follow-up did not significantly differ between the 2 groups (group G:  $4.8^\circ$  vs group P:  $5.8^\circ$ ,  $p=0.4$ ). None of the extent of subsidence and the incidence of screw loosening showed statistical differences. Postoperative 2-year LL tended to improve more in the group G than in the group P, although no significant difference was found (group G:  $-36.9^\circ$  vs the group P:  $-28.3^\circ$ ,  $p=0.06$ ). Whereas the changes of LL from before surgery to immediately after surgery showed no significant difference between the 2 groups (group G:  $-1.7^\circ$  vs group P:  $-4.1^\circ$ ,  $p=0.3$ ), the changes of LL from before surgery to postoperative 2-year follow-up and these changes during postoperative 2 years were significantly better in the group G (the mean changes of LL:  $-3.5^\circ$  and  $-5.1^\circ$ , respectively) than in the group P (the mean changes of LL:  $+4.6^\circ$  and  $+0.5^\circ$ , respectively) ( $p<0.05$ ).

**Discussion:** Of the 27 patients with pseudoarthrosis after single-level CBT-PLIF, the lumbar spine had been becoming more lordotic during postoperative 2 years in 15 patients with better improvement of ODI, whereas 12 patients with less improvement of ODI had been losing LL during postoperative 2 years. These results indicate that there is a significant correlation of clinical outcomes and LL even in patients with pseudoarthrosis after single-level CBT-PLIF.



## Prospective multicenter surveillance and risk factor analysis of surgical site infection after lumbar laminectomy and/or herniotomy in adults

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**INTRODUCTION:** Surgical site infection (SSI) is a serious and significant complication after spinal surgery, and it is associated with high morbidity rates, high healthcare costs, and poor patient outcomes. The accurate identification of risk factors is essential for developing strategies to prevent devastating infections. The purpose of this study was to identify independent risk factors for SSI in adults undergoing posterior lumbar spinal decompression surgery using a prospective, multicenter, surveillance research method.

**METHODS:** From July 2010 to June 2014, we performed a prospective surveillance study in adult patients who had developed SSI after undergoing lumbar laminectomy and/or herniotomy at 10 participating hospitals. Patients who underwent lumbar fusion surgery were excluded. Detailed preoperative and operative patient characteristics were prospectively recorded using a standardized data collection form. The recorded preoperative patient characteristics included age at time of surgery, sex, body mass index (BMI), smoking, diabetes mellitus, the patient's American Society of Anesthesiologists (ASA) score and steroid use. The recorded operative patient characteristics included operating time, estimated blood loss, anatomic location of spinal surgery (cervical, thoracic, lumbar), emergency surgery, iliac crest bone grafting, dural tear and use of intraoperative fluoroscopy. Identification of SSI was based on the Centers for Disease Control and Prevention definition. Data were analyzed using multivariate regression analysis with  $P < 0.05$  set as the significance level.

**RESULTS:** A total of 4,146 consecutive adult patients were enrolled, of whom 26 (0.63%) developed postoperative surgical site infections. Multivariate regression analysis indicated 2 independent factors: smoking ( $P = 0.024$ ,  $OR = 2.7$ ,  $95\%CI: 1.1-6.3$ ) was a statistically significant independent risk factor for developing SSI, while surgery using endoscopes ( $P = 0.007$ ,  $OR = 0.22$ ,  $95\%CI: 0.075-0.66$ ) was statistically significant independent protective factor against developing SSI.

**DISCUSSION:** Smoking was an independent risk factor, and surgery using endoscopes was an independent protective factor for SSI after lumbar laminectomy and/or herniotomy in adult patients. Identification of these correlating factors for SSI could be used to develop protocols to decrease the risk of SSI.

## **Risk factors for incidental durotomy during posterior spine surgery for degenerative diseases in adults: a prospective single-center observational study**

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**INTRODUCTION:** Incidental durotomy (ID) is a common intraoperative complication of spine surgery. It may lead to persistent cerebrospinal fluid leakage, which may cause serious complications including severe headache, pseudomeningocele formation, nerve root entrapment and intracranial hemorrhage. The purpose of this study is to clarify the independent risk factors for ID during posterior open spine surgery for degenerative diseases in adults.

**METHODS:** Between July 2010 and December 2016, We conducted a prospective observational study of adult patients (>17 yrs) who underwent posterior open spine surgery for degenerative diseases in our hospital. We set up various factors, which include age, gender, body mass index, American Society of Anesthesiologists (ASA) physical status classification, diabetes, hemodialysis, smoking, steroid intake, location of the surgery, the type of procedure, instrumentation, and past surgical history in the operated area. Multivariate logistic regression analysis was performed to identify the risk factors. Significance was set at  $P < 0.05$ . In addition, odds ratio (OR) and 95% confidence interval (CI) were calculated for each of the variables.

**RESULTS:** A total of 4,652 consecutive patients were enrolled (mean of the age: 66.2yrs). The total incidence of ID after surgery was 5.7% (49 cases). The results of the analysis suggest that older age ( $P=0.016$ ,  $OR=1.03$ ,  $95\%CI: 1.01-1.06$ ), and revision surgery ( $P=0.043$ ,  $OR=2.10$ ,  $95\%CI: 1.03-4.30$ ) were the significant risk factors for IDs during posterior open spine surgery for degenerative diseases. In addition, the multipel regression analysis showed that cervical surgery was identified as a independent protective factor against ID ( $P=0.016$ ,  $OR=0.31$ ,  $95\%CI: 0.12-0.81$ ). Therefore, we identified 2 independent risk factors for and a protective factors against ID.

**DISCUSSION:** These results may contribute to making surgeons aware of the risk factors for ID and can be used to counsel patients on the risks and complications associated with posterior open spine surgery for degenerative diseases.

## Discrepancy of clinical outcome and postoperative magnetic resonance imaging after percutaneous endoscopic lumbar discectomy

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### INTRODUCTION:

It is known that postoperative magnetic resonance imaging (MRI) of lumbar disc herniation often has a residual mass. Although there were some reports on longitudinal change in postoperative MRI of open surgery (Love's procedure) and micro endoscopic discectomy (MED), there is no report on percutaneous endoscopic discectomy (PED). A prospective study was undertaken to establish the normal spectrum of early MRI findings in patients who had resolution of symptoms after PED surgery. In this study, we examined to change the postoperative MRI and clinical symptoms.

### METHODS:

Thirty-three patients underwent PED surgery under local anesthesia from 2014 to 2016,

Clinical assessments and MR examinations were conducted preoperatively and immediately postoperatively (within 1 week) and late postoperatively (3 months and 12 months). Clinical assessments were performed using visual analogue scale (VAS) for low back pain and leg pain, the Japanese Orthopaedic Associations scale score (JOA score), respectively. The residual disk bulging after surgery was classified into four grades compared with preoperative MR images. (Grade A:none, B:25%<, C:25-75%, D:75%>)

### RESULTS:

For classification of MRI at postoperative 1-week, 9 patients had a grade B, 8 patients a grade C, 16 patients a grade D. Postoperatively, at postoperative 3 months, 18 patients had a grade A, 10 patients a grade B, 5 patients a grade C, at postoperative 12 months, 29 patients had a grade A, 3 patients a grade B, 1 patient a grade C.

In addition, the high intensity change in the residual mass was seen in 78% of patients 1 week after surgery and in 18% of patients after 3 months.

Mean VAS scores of low back pain at preoperative, postoperative 1 week, 3 months, 12 months were  $5.5 \pm 2.8$ ,  $1.9 \pm 1.8$ ,  $1.0 \pm 1.5$ ,  $0.9 \pm 1.4$ , respectively. Mean VAS scores of leg pain at preoperative, postoperative 1 week, 3 months, 12 months were  $6.5 \pm 2.6$ ,  $2.1 \pm 1.9$ ,  $0.7 \pm 1.3$ ,  $0.5 \pm 1.0$ , respectively. The mean values of JOA score were at preoperative, postoperative 1 week, 3 months, 12 months were  $12.8 \pm 5.1$ ,  $23.8 \pm 2.8$ ,  $26.6 \pm 2.9$ ,  $27.9 \pm 1.7$ , respectively.

There was significantly statistical difference of VAS and JOA score at 1week, 3months and 12 months after surgery.

### DISCUSSION and CONCLUSION:

Both opinions have been reported that there is correlation or no correlation between postoperative findings and clinical outcome. In this study, postoperative MRI findings within one week had residual mass of grade C and D in 24 patients (73%). In the early postoperative period, clinical symptoms improved even if there is the residual mass. High intensity change was shown in the excision site, there is a possibility that the residual mass which show high intensity change on MRI will regress during time course. In conclusion, the residual mass in the early stage following the surgery may not correlate to the clinical symptoms.

## Actual state of surgical site infection after spine surgery in our department - what seen from the data in recent 16 years -

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STUDY DESIGN: A retrospective study.

OBJECTIVE: The purpose of this study was to analyze the data regarding surgical site infection (SSI) after thoracic and lumbar spine surgery in our department in recent 16 years and consider its risk factors.

METHODS: Patients who underwent thoracic or lumbar spine surgery between January 2001 to December 2016 were included in this study. Of these patients, 25 patients (16 males and 9 females) were detected postoperative SSI. 27 re-operations were done. We examined SSI, instrument use or not, month of initial surgery, operative time of initial surgery, the amount of intraoperative bleeding, time and finding of SSI, pathogenic bacteria, and methods of treatment.

RESULTS: A total of 1894 patients were included. The incidence of SSI was 1.4%. Infection rate was significantly higher in lumbosacral spine operation group than another group: 1.7% in thoracic spine (4/241), 1.0% in lumbar spine (13/1324), 2.0% in thoracolumbar spine (4/204), and 4.8% in lumbosacral spine (6/125). The incidence of SSI was 1.8% (15/837) in instrument group and 1.1% (12/1057) in none-instrument group respectively, and there was no significant difference between two groups. The rate of season of initial surgery in SSI group was higher in Summer and Winter than another seasons. 0 case was found from March to May (Spring), 11 cases from June to August (Summer), 6 cases from September to November (Autumn), and 10 cases from December to February (Winter). The mean operative time of initial surgery was 193 min (55-439 min) in SSI group and it was significantly longer than that of noninfection group. The mean amount of intraoperative bleeding was 762ml (100-2335ml) in SSI group and it was significantly more than that of noninfection group. The local sign of SSI (discharge from wound, fever, pain or redness or swelling of wound) was found 36.7 days (5-382 days) after initial operation. Pathogenic bacteria was identified 23 of 27 cases. MSSA was detected in 7, S.epidermidis in 3, MRSA in 2, Staphylococcus haematolyticus in 2, E.coli in 2, Enterococcus faecalis in 2, MRSE in 1, Enterobacter cloacae in 1, S.capitis in 1, Propionibacterium acnes in 1, Peptostreptococcus magnus in 1. All patients underwent debridement and drainage, and antimicrobial agent by intravenous injection until inflammatory reaction was normalized. After this treatment all of 12 patients was cured in instrument unused group, but 7 of 15 instrument group (47%) was unable to preserve instrument.

CONCLUSIONS: We found that the incidence of SSI was higher in operation that was done in summer and winter than in other season. Longer operative time and large amount of bleeding were risk factors for SSI.

## Stand-alone lateral lumbar interbody fusion is an effective intervention for adjacent segment disease following previous lumbar fusion surgery

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### Introduction:

Adjacent segment disease (ASD) following previous lumbar spine fusion is a common clinical problem that can cause back pain, lower extremity radiculopathy, or neurogenic complaints. Lateral lumbar interbody fusion (LLIF) is an attractive option for surgical treatment of this pathology as it provides a minimally invasive solution to achieve interbody fusion and indirect neural decompression while avoiding a posterior approach in the face of previously placed hardware and resulting scar tissue. We sought to characterize outcomes of stand-alone LLIF for ASD following previous lumbar fusion surgery.

### Methods:

We retrospectively reviewed patients between 2007-2016 with a prior posterior instrumented fusion who underwent a subsequent stand-alone LLIF for ASD by a single surgeon. Demographic variables and patient-reported outcomes were obtained on all patients. Radiographic parameters (lumbar and segmental lordosis, total and segmental coronal angulation, and intervertebral disc heights) were compared between preoperative, initial post-operative appointment and at final follow-up. Patients were also followed for symptomatic pseudarthrosis or subsidence that required re-operation. Appropriate statistical tests were performed to calculate relationships between the pre-operative and post-operative measurements and outcomes.

### Results:

A total of 25 consecutive patients met inclusion criteria. Average follow-up was 30.2 months (range 6-101 months). There were 18 men and 7 women with a mean age of  $62.0 \pm 11.3$  years. Of the 25 patients, 13 (60%) radiculopathy and/or neurogenic claudication, and 25 (100.0%) with severe back pain. The mean surgical time was  $108 \pm 51.4$  minutes and estimated blood loss was  $63 \pm 65.4$  ml.

Segmental and regional lordosis as well as intervertebral height were restored and maintained by the surgery. Oswestry Disability Index ( $46.6 \pm 16.4 \rightarrow 30.4 \pm 16.8$ ;  $p=0.002$ ) and Back Visual Analog Scale ( $8.4 \pm 1.0 \rightarrow 5.2 \pm 1.9$ ;  $p<0.001$ ) significantly improved from preoperative to postoperative assessments. Five patients experienced anterior thigh pain/dythesias post-operatively and 1 patient presented with 4+/5 hip flexor weakness post-operatively, that all resolved within 6 weeks. Three patients required additional surgery (2 for worsening lower back and buttock pain, while one experienced recurrent radicular symptoms), all of who were revised to include posterior instrumentation (at 1, 3, and 8 months after the stand-alone LLIF).

### Discussion:

Traditional posterior surgical approaches for patients requiring decompression and fusion adjacent to prior instrumented posterior fusion are associated with high morbidity and complication rates related to exposure and extension of prior posterior instrumentation as well as challenging decompression in the face of epidural scar tissue. The current study supports that in a majority of patients, stand-alone LLIF with real time, directional neural monitoring, is a safe and effective approach with low morbidity and acceptable complication rates for patients with symptomatic ASD following previous lumbar fusion.

## Does persistent back pain in patients with delayed vertebral collapse differ with methods of surgical treatment?

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### INTRODUCTION

Various surgical procedures have been proposed in the management of delayed vertebral collapse, however, the optimal surgical procedures remain controversial. In this study, we examined on persistent back pain after surgery in patients treated at two university hospitals.

### METHODS

This study involved 29 patients who underwent surgery for osteoporotic delayed vertebral collapse with apparent motor deficit with a minimum 1-year follow-up. Patients were divided with Visual Analogue Scale (VAS) scores below the mean with persistent back pain at final follow-up (group P) and those with VAS scores higher than the mean (group G). We examined surgical methods, age, bone density, operation time, blood loss, modified Frankel Classification, ADL, JOA score, change in local kyphotic angle, and implant complications between the two groups.

### RESULTS

There were 12 patients in group P and 17 in group G. Surgical procedures in group P included posterior spinal fusion without osteotomies (n = 6), posterior fusion with grade 3 osteotomies (n = 4), and vertebral column resection (VCR) (n = 2), whereas those in group G included posterior spinal fusion without osteotomies (n = 4), with osteotomies (n = 3), posterior spinal fusion with vertebroplasty (n = 7), and VCR (n = 3). There were no significant difference in age, bone density, operation time and blood loss between the 2 groups. The improvement rate for JOA scores of groups P and G were  $45.5 \pm 26.2$  and  $53.2 \pm 22.8\%$ , respectively, indicating a trend of improvement in group G. The modified Frankel classification scores increased  $1.6 \pm 1.3$  and  $2.7 \pm 1.3$  points, and ADL scores improved by  $1.6 \pm 1.1$  and  $2.5 \pm 0.9$  points in groups P and G, respectively, indicating significantly better improvement in group G than in group P ( $p < 0.05$ ). Kyphotic angles measured preoperatively, postoperatively, and at the final follow-up showed no difference between the 2 groups. New vertebral fractures were observed in 33.3% and 35.3% of patients, whereas implant loosening was found in 50% and 23.5% of patients in groups P and G, respectively. A significantly higher number of patients underwent anterior column manipulation by vertebroplasty or VCR in group G (n = 10, 58.8%) than in group P (n = 2, 16.6%).

### DISCUSSION

Patients in group G who had better postoperative VAS scores showed greater improvement in motor function and ADL. More number of patients received vertebral anterior column manipulation in Group G than in group P. Imaging findings revealed no differences between new vertebral fractures or local kyphotic angles, but the incidence of implant loosening tended to be lower in group G than in group P. Manipulation of anterior column may have contributed to prevent significant implant loosening and to a better VAS scores for postoperative lower back pain.

## Establishment of a novel measurement technique for pedicle screw stability -LASER resonance frequency analysis-

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### INTRODUCTION:

Insertion torque<sup>1</sup> and pull-out strength<sup>2</sup> are the installation strengths generally used for evaluating pedicle screw stability at the laboratory level. However, it is difficult to use these techniques clinically because these techniques are measured bone-invasively. A non-invasive and repeatable measurement technique: resonance frequency analysis (RFA) has been performed for evaluating implant stability in dentistry field by vibrating the magnet attached to the implant with a magnetic pulse<sup>3</sup>. This magnetic-RFA needs to install a special device with magnet directly to the implant. We developed the novel technique to perform RFA by Laser which is non-invasive, non-contact and repeatable technique for application to the field of spinal surgery.

We examined the relationship among three installation strengths: insertion torque, pull-out strength and Laser-RFA with model bones and human fresh cadaveric vertebrae.

### METHODS:

Three different densities of cancellous model bones (10, 15 and 20pcf, three by three, a total of nine materials) and sixty-two fresh non-frozen cadaveric lumbar vertebrae of human were tested. We installed the pedicle screw: Associa (Kyocera Medical Corporation, Osaka, Japan). Only for model bones, screw removal and re-insertion were repeated for four times at the same insertion path in order to have a variation in more conditions. Three kinds of installation strengths: Insertion torque (Nm), pull-out strength (N) and Laser-RFA (Vibrating Laser: Q-Swch Nd:YAG Laser, measurement Laser of resonance frequency: Laser Doppler Vibrometer) (Hz) were performed respectively (Figure 1). About Laser-RFA, the obtained signals were spectrally analyzed by fast Fourier transformation, and the frequency with the largest amplitude was defined as the resonance frequency.

Pearson's correlation coefficients (R) were used to evaluate the relationships among the three installation strengths of model bone and vertebrae.

### RESULTS:

Model bones: there was strong correlation between insertion torque and pull-out strength ( $R=0.901$ ,  $p<0.001$ ). On the other hand, Laser-RFA showed moderate correlations with insertion torque ( $R= 0.712$ ,  $p<0.001$ ) and pull-out strength ( $R=0.698$ ,  $p<0.001$ ). To repeat the screw removal and re-insertion, all installation strengths decreased. However, Laser-RFA tended to be preserved especially in high-density material, unlike insertion torque and pull-out strength (Figure 2).

Vertebrae: there was strong correlation between insertion torque and pull-out strength ( $R=0.723$ ,  $p<0.001$ ). Laser-RFA showed moderate correlation with insertion torque ( $R=0.421$ ,  $p<0.05$ ) and pull-out strength ( $R=0.392$ ,  $p<0.05$ ). Overall, the results of vertebra tended to have a lower correlation coefficient than the results of model bones.

### DISCUSSION:

In the field of dentistry, it has been reported that, unlike insertion torque and pull-out strength which reflected the stability when pulling out the implant along the longitudinal direction, RFA reflected the stability when the implant was tilted sideways: closer to the stress applied to the implant in vivo<sup>4</sup>. There is a possibility that the result of Laser-RFA indicates the correct pedicle screw installation strength than insertion torque and pull-out strength.

For the development of instrumentation surgery, the establishment of the quantitative, repeatable and non-invasive method to measure the implant stability is necessary. This is the first report of Laser-RFA and there is a possibility that Laser-RFA can be replaced the conventional methods.

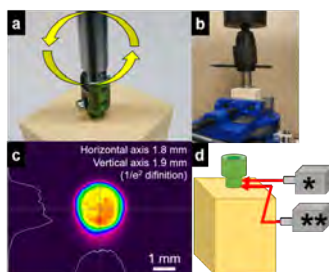


Figure 1: (a) Insertion torque. (b) Pull-out strength (c and d) Concentrated Laser profile. \* Vibrating Laser \*\* Measurement Laser

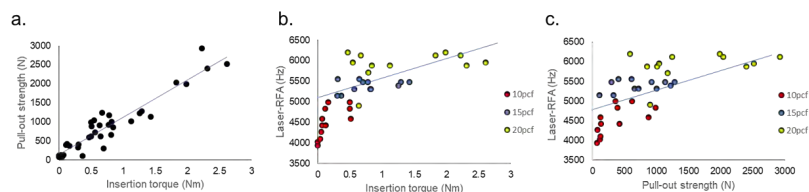


Figure 2: Scatter plots and best fit lines of linear regression between (a): Insertion torque vs. Pull-out strength, (b): Insertion torque vs. Laser-RFA and (c): Pull-out strength vs. Laser-RFA. About (b) and (c), the colors of the scatter plots change in accordance with material density. Laser-RFA tends to be preserved in the high density material (20pcf) compared to insertion torque and pull-out strength even if screw removal and re-insertion were repeated.

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## Relationship between facet joint osteoarthritis and spinal segmental motion in degenerative spondylolisthesis

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### [Introduction]

Degenerative spondylolisthesis (DS) causes an unstable lumbar spine due to degeneration of the lumbar intervertebral disc and facet joints with age and laxity of the anterior longitudinal, posterior longitudinal and yellow ligaments. There are no radical treatments to prevent progression of DS in patients with lumbar spinal canal stenosis (LSS) associated with DS. Lack of knowledge about the pathophysiology of DS makes it impossible to prevent its progression. Therefore, it is important to clarify the pathology of this disease and develop effective treatments. We compared findings from *in vivo* three-dimensional imaging analysis of lumbar dynamic CT images in patients who underwent surgery for LSS without DS and for LSS with associated fourth DS (the most frequent form of this disease). We aimed to analyze the influence of FJOA on the pathology of DS using *in vivo* three-dimensional image analysis.

### [Method]

The subjects were 50 patients with a chief complaint of radicular or cauda equine symptoms caused by LSS including L4/5 and in whom conservative therapy was ineffective who underwent CT (anterior/posterior flexion in the supine position). Based on lumbar lateral plain X-ray, the subjects were divided into groups the spondylolisthesis (Sp) group (slippage  $\geq 5\%$ ) (n=26, mean age 74 years) and the non-spondylolisthesis (non-Sp) group (n=24, mean age 70 years). Imaging findings and *in vivo* 3D segmental motions were evaluated. The disc height index (DHI), interspinous distance, height of the intervertebral foramen, height of the facet joint and dynamic changes in these distance were measured. Differences in data for the Sp and non-Sp groups were examined by Mann-Whitney U-test and Fisher exact test ( $\alpha=0.05$ ).

### [Result]

In the Sp group (mean slippage 16%), there was a significantly lower DHI in the anterior flexion position ( $p<0.05$ ). Interspinous distance and dynamic changes in this distance did not differ significantly between the two groups. In the Sp group, the heights of the intervertebral foramen in anterior and posterior flexion positions and on the right and left sides were significantly lower ( $p<0.001$ ), but there were no differences in dynamic changes. In the Sp group, the height of the superior articular process tended to be lower, the height in anterior flexion was significantly lower, and dynamic changes on the right and left sides were significantly larger relative to the non-Sp group ( $p<0.001$ ). The degeneration level of the facet joint was significantly higher and the axial and total translational motion were significantly larger in the Sp group ( $p<0.05$ ).

### [Discussion]

In this study, progressive FJOA and larger segmental motion in the distance between the craniocaudal edges of the facet joints were found in the Sp group. These findings clarify for the first time that slippage induces ligament laxity in the facet joint due to progressive FJOA and affects spinal segmental motion *in vivo*. This study showed the importance of the evaluation method and therapy targeting the facet joint in DS. The *in vivo* three-dimensional imaging analyses employed in this study were useful for new insights into the pathology of DS.



## Risk factor analysis of surgical site infections after posterior instrumentation fusion surgery for spinal trauma, prospective multicenter study

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**Introduction:** Surgical site infection (SSI) is a serious complication after spinal surgery, and it is associated with high morbidity rates, high healthcare costs, and poor patient outcomes. The accurate identification of risk factors is essential for developing strategies to prevent devastating infections. High quality studies based on a prospective design and a large sample size are required to identify precise independent risk factors for SSI following spinal surgery.

**Methods:** From July 2010 to December 2014, we performed a prospective multicenter study in patients who had developed SSI after surgery for spinal trauma at 10 participating hospitals. Detailed preoperative and operative patient characteristics were prospectively recorded using a standardized data collection form. The recorded preoperative patient characteristics included age at time of surgery, sex, body mass index (BMI), smoking, diabetes mellitus, the patient's American Society of Anesthesiologists (ASA) score and steroid use. The recorded operative patient characteristics included operating time, estimated blood loss, anatomic location of spinal surgery (cervical, thoracic, lumbar), emergency surgery, iliac crest bone grafting, dural tear and use of intraoperative fluoroscopy. Identification of SSI was based on the Centers for Disease Control and Prevention definition. Data were analyzed using multivariate regression analysis with  $P < 0.05$  set as the significance level.

**Results:** A total of 592 consecutive patients (313 males, 279 females, mean age 62.0 [15-97]) were enrolled, of whom 18 (3.0%) developed postoperative wound infections (1 superficial and 17 deep SSI). Multivariate regression analysis indicated that ASA score  $\geq 3$  ( $P=0.017$ ; Odds Ratio [OR] =3.41, 95% confidence interval [CI] 1.25-10.0) was a statistically significant independent preoperative risk factor for developing SSI.

**Discussion:** ASA score  $\geq 3$  was an independent preoperative risk factor for SSI in the present study. Identification of these risk factors can be used to develop protocols aimed at decreasing the risk of SSI following surgery for spinal trauma in the future.

## Investigation of the combinations of loading and facet joint contributions to lumbar disc herniation

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### Introduction.

Lumbar disc herniation (herniation) can compress nerve roots, cause a localised inflammatory response and consequently lead to sciatica. Numerous *in-vitro* studies have been conducted in an attempt to characterise herniation and it has been well established that it can occur by fatigue loading or sudden overload most frequently at the L4-L5 or L5-S1 levels. Despite the significant role of the facet joints in restricting axial rotation, extension and anterior shear, several studies have removed these joints prior to testing, which may compromise the physiological conditions that occur *in-vivo*. Therefore, the aim of this study was to compare the modes of failure between sheep functional spinal units (FSUs) with or without facet joints under three directions of sudden overload.

### Methods.

Twenty-seven L4-L5 FSUs were dissected from sheep lumbar spines and extraneous soft tissue was removed. Specimens were classified as 'intact FSU' where facet joints were preserved or 'isolated disc' where facet joints were removed. Before testing, each FSU was subjected to a 0.1 MPa compressive preload in 0.15 M phosphate buffered saline for at least four hours to reach equilibrium. Specimens were then tested in one of three postures: 13° flexion (FL), 10° lateral bending (LB) or 13° flexion and 10° lateral bending (FL+LB) (Intact FSUs: 4 x FL, 4 x LB, 4 x FL+LB, Isolated Discs: 5 x FL, 5 x LB, 5 x FL+LB) and compressed at 400 mm/min to 3 mm was reached in the hexapod robot [1]. Failure mode was classified as a) herniation b) herniation and endplate-vertebral shear fracture c) endplate-vertebral shear fracture or d) vertebral damage. Load-displacement curves were analysed to determine failure stress and modulus. A chi-squared test was used to determine significant differences between failure modes, while a two-way ANOVA was performed on failure stress and modulus with two within-subjects factors of loading direction and a between-subjects factor of facet joint ( $p < 0.05$ ).

### Results.

Chi-squared tests indicated a significant difference between modes of failure in intact FSUs and isolated discs ( $p = 0.001$ ). A two-way ANOVA revealed that intact FSUs had a significantly higher stress at failure compared to isolated discs in flexion ( $p = 0.003$ ), lateral bending ( $p = 0.000$ ) and combined flexion and lateral bending ( $p = 0.027$ ) (Figure 1). There was only a significant difference in modulus between intact FSUs and isolated discs in lateral bending ( $p = 0.003$ ), where intact FSUs had a higher average modulus.

### Discussion.

Modes of failure varied significantly between intact FSUs and isolated discs. Generally, intact FSUs failed by herniation, while isolated discs failed predominantly by shearing at the endplate-vertebra junction with or without herniation. This suggests that the facet joints protect the annulus-endplate-vertebra junction rather than the disc. These failure modes differ to previous findings that reported herniation in both intact FSUs and isolated discs [2]. Stress at failure was significantly higher in intact FSUs compared to isolated discs, indicating facet joint contribution to failure mode. Furthermore, these results suggest the facet joints should be intact during mechanical testing of an FSU due to differences in stress and failure modes in isolated discs.

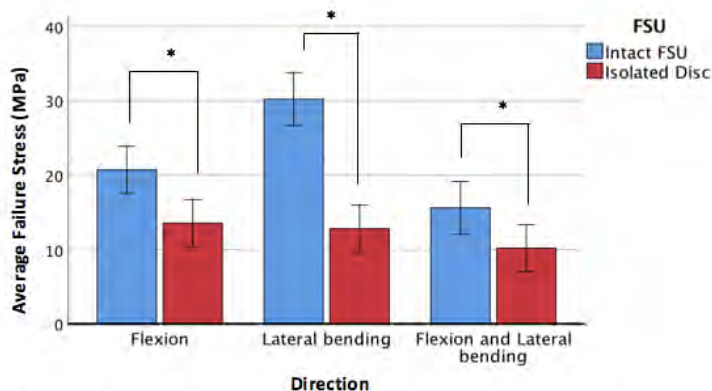


Figure 1. Bar graph of average stress at failure in intact FSUs and isolated discs. Error bars: 95% confidence interval. Asterisk:  $p < 0.05$ .

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## Prediction rule for determining discharge destination post posterior thoracolumbar spinal fusion procedures using the Canadian spine outcomes and research network

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**Introduction.** Patients unable to be discharged home after spinal operations may require prolonged hospitalization while awaiting placement at rehabilitation facilities; thus, creating considerable economic burden on the health care system. Prognosis of discharge destination could have a tremendous health economic contribution. The objective of this study was to create a prediction rule of pre-operative clinical factors in those who get discharged home after thoracolumbar posterior spinal fusion procedures.

**Methods.** Utilizing multicentre prospectively collected data from the CSORN database, a retrospective analysis was conducted of patients who underwent posterior thoracolumbar fusion between 2008 and 2017 (n=1,988). Multivariable logistic regression was used to identify predictors of patient discharge destinations: home (n=1,807) versus other facilities (n=181) using a backward selection procedure. A data-splitting technique was utilized to develop and test the multivariable models (80% for model development and the full sample for model validation).

**Results.** The mean age of the cohort was 59.9 years with 52.6% females. Regression analyses identified 9 significant predictors; after adjusting for all other covariates in the model, pre-operative predictors of discharge home were:

-age <65 years (odds ratio [OR]=2.349, 95% confidence interval [CI]=1.492-3.697, p<0.001)

-not living alone (OR=2.48, 95% CI=1.573-3.917, p<0.001)

-lower disability score (OR=0.96, 95% CI=0.945-0.975, p<0.001)

-diagnosis of deformity (OR=1.96, 95% CI=1.001-3.850, p<0.05)

-diagnosis of spondylolisthesis (OR=2.1, 95% CI=1.261-3.486, p<0.004)

-no ASA score of III (OR=1.6, 95% CI=1.028-2.492, p<0.037)

-MIS procedure (OR=2.8, 95% CI=1.169-6.719, p<0.021)

-levels of fusion <3 (OR=4.4, 95% CI=2.693-7.199, p<0.001)

-absence of preoperative neurologic deficit (OR=1.26, 95% CI=0.805-1.958, p<0.315).

The final model was internally validated and confirmed the same predictors. ROC curve analysis revealed area under the curve of 0.846, confirming that the model has significantly better discrimination than chance; sensitivity=90%, specificity=45%.

A clinical prediction rule for the final model is represented by the following equation:  $\text{Log}(\text{odds of success}) = 1.097 - 0.711(\text{age}<66) + 0.797(\text{living not alone}) - 0.029(\text{ODI score}) + 0.391(\text{Diagnosis of deformity}) + 0.817(\text{Diagnosis of spondylolisthesis}) + 0.367(\text{not ASA III}) + 1.40(\text{MIS procedure}) + 1.41(<3\text{levels}) + 0.485(\text{no neuro def})$

**Discussion.** Using the CSORN database, we constructed a prediction rule that can be easily applied to patients in a clinical setting to assess their likely post operative discharge destination following posterior thoracolumbar instrumented fusion.

## The effect of cage geometry on segmental lordosis in posterior lumbar interbody fusion: hyper-lordotic box cages versus boomerang cages

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### Introduction:

The preservation of segmental sagittal alignment is crucial in spinal reconstructive surgery. In this study, we compared the surgical outcome of posterior lumbar interbody fusion (PLIF) cases using the hyper wedged cages (HC) or boomerang cages (BC).

### Methods:

Between October 2014 and March 2016, 22 patients underwent instrumented PLIF for lumbar degenerative disease that included L4-5 level at a single center. All patients were followed for at least 1 year. HC (CAPSTONE CONTROL; Medtronic Sofamor Danek) with 12-degree angle was used in 7 men and 5 women (mean age 71 y/o). BC (MILESTONE PEEK; Medtronic Sofamor Danek) with 6-degree angle was used in 6 men and 4 women (mean age 64 y/o). All the cages were made of PEEK and all pedicle screws were poly axial screw. Laminectomy and bilateral facetectomy were performed, and the local bone obtained during decompression was morselized and impacted in the cages. Clinical outcomes were evaluated using the JOA score. Radiographic findings, L4-5 segmental lordotic angle, correction angle, and %anterior and posterior disc height (%ADH and %PDH) were measured. Additionally, existence of the end-plate injury by the cage rotation in HC group was evaluated.

### Results:

There was no significant difference in clinical outcomes between the two groups. L4-5 segmental lordotic angle changed from 13.8°(pre-op) to 19.5°(1 year post-op) in HC group and from 16.7°(pre-op) to 21.9°(1 year post-op) in BC group. Correction angle was 5.7°in HC group and 5.2°in BC group. %ADH changed from 21.0% to 27.0% in HC group and from 21.9% to 25.0% in BC group. There was no significant difference between the 2 groups in terms of the L4-5 segmental lordotic angle, corrections angle and %ADH. On the other hand, %PDH changed from 12.5% to 11.9% in HC group and from 12.3% to 8.2% in BC group. %PDH was significantly reduced in BC group ( $p=0.041$ ). In addition, the end-plate injury was recognized in three patients which was assumed to be related to cage rotation maneuver in HC group.

### Discussion:

Despite the initial difference in angulation of cage geometry, segmental lordotic angle did not differ between the two groups. Radiographic analyses demonstrated that placement of boomerang cages in the anterior interbody space with bilateral facetectomies led to effective compression maneuver proved by significantly smaller %PDH in comparison to hyper wedged box type cages. The end-plate injury was identified in cases using hyper wedged box type cages accompanying rotational maneuver, which elicit concerns for potential end-plate damage in cases with disc narrowing. Thus, boomerang cages offer similar segmental lordotic angle with minimal risk of end-plate damage in PLIF surgery.

## Associations between determinants of socioeconomic status, beliefs about back pain, and exposure to a mass media back pain campaign

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**Introduction** Socioeconomic status (SES) has been shown to be associated with morbidity, mortality, and health inequality. SES is often investigated in health disparities research, but little is known about the relationship between socioeconomic factors and low back pain (LBP). Considering that LBP is one of the most prevalent disorders worldwide with an enormous economic and societal burden, it is important to identify factors that relate to known modifiable risk factors for persistent LBP, such as back pain beliefs. This could provide additional insight into public education interventions that might help reduce the prevalence of LBP by targeting specific determinants, such as socioeconomic factors like education, occupation, or income. This study aims to examine the relationship between SES and the belief that one should stay active through LBP, and between SES and self-reported exposure to a mass media health education campaign undertaken in Alberta, Canada.

**Methods** Over the past decade, a mass media campaign designed to improve back beliefs has been undertaken among the general public of the province of Alberta. From 2010 through 2014, annual data on public beliefs were gathered using cross-sectional surveys. Between 2010 and 2014, 9,572 randomly selected Alberta residents aged 18-65 years were surveyed. The sample appeared representative of the overall population of adult Albertans based on region, sex, and age information available in the most recent Statistics Canada census information. Data were collected using Computer-Assisted Telephone Interviews web-based surveys. The surveys asked for the respondents' beliefs regarding staying active through an episode of LBP, and whether they remembered hearing/seeing the LBP campaign. Several determinants for SES, including education, employment status, occupation, and annual household income were included in univariate and multivariate logistic regression modeling to test associations between these determinants and the outcomes.

**Results** Most respondents were females older than 44 years. The average household consisted of 2.7 people, and one third of respondents reported an annual household income of \$100,000CDN or more. Furthermore, 67.6% of respondents reported agreeing with the statement "If you have back pain you should try to stay active", and 42% of respondents reported exposure to campaign advertising. Univariate analysis showed that language, education, employment, marital status, and annual household income were significantly associated with the belief that one should stay active through LBP. In multivariate analysis, income was the strongest determinant of this belief ( $p=0.002$ ). Univariate analysis for exposure to the campaign showed language, education, employment, and occupation were significantly associated with self-reported exposure, while only education remained significant in multivariate analysis ( $p=0.01$ ), with more education leading to lower exposure.

**Discussion** Respondents with a higher annual income were more likely to believe that one should stay active through LBP, while respondents with more education were less likely to report exposure to campaign advertising. To fully understand the association between socioeconomic factors and LBP, and to target campaigns accordingly, more research is needed. Future research should focus on identifying specific SES groups that are vulnerable for LBP, and evaluating the SES factors that are most suitable for intervention.

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## Supine vs. upright weight bearing MRI in the evaluation of patients with lumbar spondylolisthesis

Richard D. Guyer, Donna D. Ohnmeiss

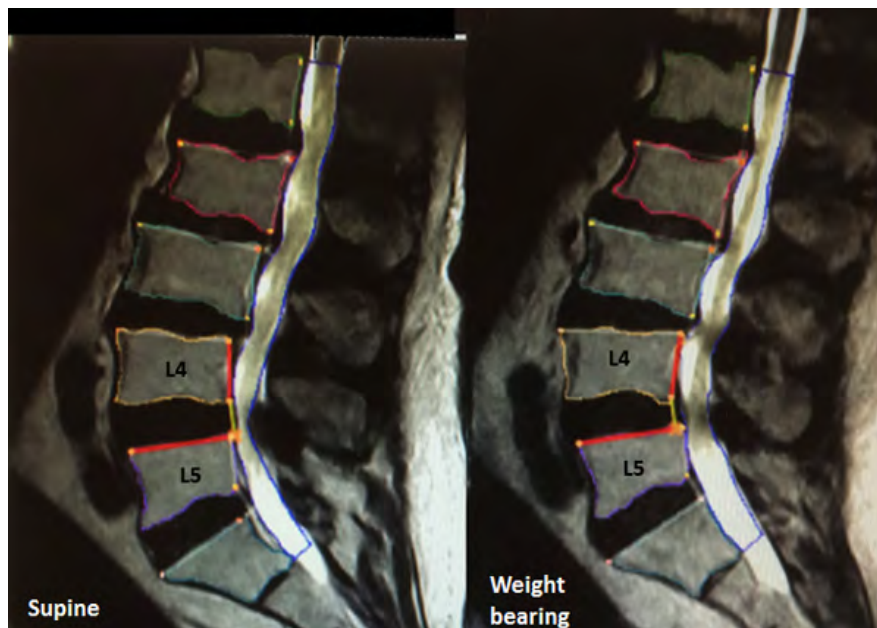
**INTRODUCTION:** The severity of the slip in patients with spondylolisthesis is often evaluated with imaging studies, including MRI. One potential problem is the imaging being performed with the patient lying supine in the scanner, usually with a support under the legs. This creates imaging the spine in a somewhat unnatural and unloaded position. Use of upright MRI provides imaging in a weight bearing, normal position. The purpose of this study was to determine if there were differences in the severity of spondylolisthesis seen on MRIs made in the supine vs. weight bearing positions.

**METHODS:** MRIs in the supine and upright weight bearing positions were made on 28 patients with spondylolisthesis. All scans were performed using the Esaote G-scan. This is an open scanner in which the table rotates with the patient on it, so the supine and upright weight bearing images (table rotated 84° vertically) were obtained during the same scanning session. The imaging parameters used for the study was the T2 fast spin echo sequence. MRIs from both positions were measured using semiautomated Q-Spine software in which each vertebral body from L1 to S1 is registered allowing various measurements be to made automatically. Measurements made for the current study included as the primary measure, the listhesis at level of the spondylolisthesis (difference in the inferior posterior margin of the superior vertebrae). Also analyzed were the vertebral body translation (difference in the location of the midpoint of the vertebral body), segmental angle (angle of the disc space at the level of the slip), and the overall lumbar lordosis (L1-L5).

**RESULTS:** In the weight bearing position, the mean listhesis value was 4.2 mm, which was significantly greater than the value of 3.1 mm recorded for the supine position (paired t-test  $p < 0.01$ ). The figure below shows the supine and upright MRIs with the vertebral segmentation and the listhesis measurement that changed 4.4 mm at L4-5 when comparing the images made with the patient in the two positions.

Among the secondary outcome measures assessed, the vertebral body translation increased significantly at the level of the slip in the upright position (4.3 mm vs. 5.3 mm;  $p < 0.01$ ). Lumbar lordosis was significantly greater in the weight bearing position (57.6° vs. 55.3°;  $p < 0.05$ ) while there was a trend for the angle at the level of the spondylolisthesis to be less in the weight bearing position (7.8° vs. 9.1°;  $0.05 < p < 0.075$ ) compared with supine.

**DISCUSSION:** There were statistically significant differences in the severity of listhesis, vertebral body translation, and lordosis when comparing MRI scans made in the supine and weight bearing positions. These results support that body position during MRI can effect the images. This may have implications on evaluating severity of spondylolisthesis.



## Lumbo-sacral alignment and deformity in patients with adult spine deformity deteriorate in standing compared with supine position

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3. Orthopaedic Surgery, Niigata University Hospital, Niigata, Japan

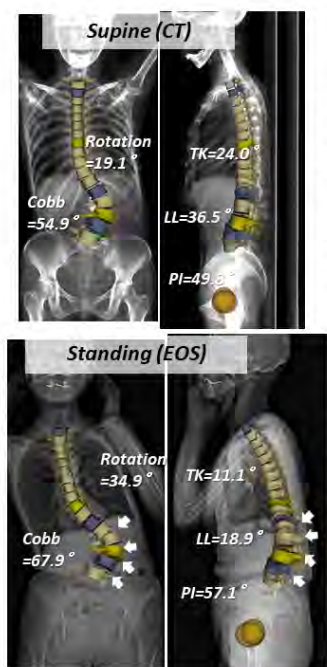
**Introduction.** To understand a pathology of lumbar spine disease, it is important to know the difference of the spinopelvic alignment between supine and standing positions. A precise comparison of the positional difference has, however, not been reported in the patients with adult spinal deformity (ASD) using the same modality and measurement method.

**Purpose.** To establish a method for comparing whole spine alignment between supine and standing, and to clarify the difference of the alignment in ASD patients.

**Methods.** Twenty-four patients with ASD (mean age: 60.1 years, range 20-80 years; 24 women) were evaluated. A slot-scanning three-dimensional X-ray imager (EOS) was used to assess the whole spine in the standing position. Computed tomography (CT) was used to assess the whole spine in the supine position. The computed tomography DICOM dataset of the whole spine in the supine position was transformed to two-dimensional (coronal and sagittal) digital reconstructed radiography (DRR) images. The DRR images were input for three-dimensional measurement by the EOS software. Then, the spinopelvic alignment of supine (CT) and standing (EOS) positions were compared after confirmation of repeatability of the measurement.

**Results.** The mean intraclass correlation coefficients (supine, standing) of intra-rater / inter-rater reliabilities for the measured parameters were 0.981, 0.984 / 0.970, 0.986, respectively. The Cobb and rotation angles of the major curve, mostly the thoracolumbar area, were significantly greater in the standing position than in the supine position. Lumbar lordosis during standing was significantly kyphotic. With respect to the pelvic parameters, the sacral slope was significantly smaller in the standing position than in the supine position. Pelvic tilt and pelvic incidence were significantly greater in the standing position than in the supine position (Table.1).

**Discussion and Conclusions.** We established a method for comparing spinopelvic alignment between the supine and standing positions by converting CT DICOM data into DRR images. Comparison revealed that lumbar lordosis in the standing - weight-bearing - position was significantly less lordotic and the pelvis was significantly more retroverted, with a smaller SS, greater PT, and even greater PI, compared with that in the supine position in ASD patients. The results of the present study is compatible with the symptom that the patients are aware of when standing and tend to stoop with back pain / fatigue, whereas the symptoms disappear when lying on a bed.



**Table 1. Comparison of the whole spine alignment between supine and standing positions**

Parameters (°)	position	Image modality	Mean	Range (min/max)	SD	p-value
T1-T12 Kyphosis	supine	CT	24.4	-2.2 / 44.7	10.9	0.8581
	standing	EOS	24.0	-6.8 / 56.2	15.5	
Lumbar Lordosis	supine	CT	33.1	-11 / 55.9	17.5	<0.0005
	standing	EOS	21.8	-32.6 / 63.3	25.5	
Sacral Slope	supine	CT	34.1	11.1 / 48.5	10.5	<0.0005
	standing	EOS	27.0	0 / 60.4	14.1	
Pelvic Tilt	supine	CT	19.2	5.2 / 37	7.5	<0.0001
	standing	EOS	30.7	3.8 / 48	10.6	
Pelvic Incidence	supine	CT	53.4	32.2 / 68.1	9.2	<0.005
	standing	EOS	57.7	33.6 / 80.8	10.9	
Cobb angle	supine	CT	31.0	6.8 / 57	15.3	<0.0005
	standing	EOS	39.5	12.2 / 74.2	20.1	
Rotation	supine	CT	11.7	0.1 / 25.0	7.6	<0.05
	standing	EOS	14.7	0.7 / 34.9	10.2	

## Clinical results of facet fusion using a ligamentum flavum floating method for degenerative lumbar spondylolisthesis

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**Introduction:** On the basis of clinical studies of instrumented facet fusion (FF) as a decompression procedure for degenerative lumbar spondylolisthesis (DLS), we devised a new method for facet fusion that is less invasive to the dura matter than traditional FF. Facet fusion using a ligamentum flavum (LF)-floating method (LFF-FF) was used instead of removing the LF for cauda equina syndrome caused by unstable DLS. We sought to evaluate clinical outcome and MRI findings.

**Methods:** In the present study, we included 31 consecutive patients with unstable DLS, who underwent LFF-FF. The surgery used a 5-cm midline skin incision, and bilateral laminar fenestration around the LF using high-speed drills, allowing a floating LF. The thickened LF was not removed, but remained floating on the dural sac. FF was achieved using autologous bone harvested from the spinous process. Percutaneous pedicle screws were then inserted through the fascia. The following variables were compared between patients in the LFF-FF group and a group of 44 patients who underwent conventional FF: operating time; intraoperative bleeding; drain bleeding volume 2 days after surgery (DBV); the early clinical outcomes at 6 months after surgery assessed using a visual analogue scale (VAS) of buttock and lower limb pain (BLP-VAS) and buttock and lower limb numbness (BLN-VAS); and Japanese Orthopaedic Association Back Pain Evaluation Questionnaire (JOABPEQ). Furthermore, thickness of the LF at the thickest point (LFT), and cross-sectional area of the thecal sac (CSATS) were measured on MR images preoperatively, at a week, and at a month postoperatively in all LFF-FF group patients.

**Results:** The mean operative time was 148 min, blood loss was estimated to be 63 g, and DBV was 118 mL in patients of the LFF-FF group. The patients in the LFF-FF group had significantly lower DBV than patients in the FF group. All LF floating phenomena occurred a week after surgery, and no presence of hematoma in contact with the dura was found. The mean CSATS increased significantly from 153% a week after surgery to 215% within a month. The mean LFT became significantly thinner than before surgery, by 81% within a month after surgery. In patients in the LFF-FF group, JOABPEQ category scores demonstrated therapeutic effectiveness in 83% for low back pain, and 75% for walking ability. BLP-VAS and BLN-VAS scores were reduced to 19% and 28% of their preoperative values, respectively. There were no significant differences in any preoperative scores, postoperative scores, or therapeutic effectiveness between the two groups.

**Discussion:** The results indicate that the thecal sac begins to expand just after LFF-FF and enlarges to a sufficient size with LFT thinning within a month after surgery. The LF floating method is considered to lead to effective decompression of the dural sac because of good clinical outcomes of LFF-FF as comparable to FF. A decrease of DBV using this method may lead to a decrease of postoperative epidural hematoma. LFF-FF may reduce the risk of dural tears and postoperative epidural hematomas because this method does not expose the dura matter.



## Pressure-induced end-plate fracture in the porcine spine: is the annulus fibrosus susceptible to damage?

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**Introduction:** End-plate fractures, particularly along the apophyseal ring of the vertebra, are common in the adolescent population. It has been hypothesized that this is due to the weakened state of the apophyseal ring in these skeletally immature individuals, the relatively high water content in the intervertebral disc (IVD), and the fact that the apophyseal ring is not yet fully fused. Previous work created clinically similar end-plate fractures in the porcine spine, which also lacks a fused apophyseal ring, via nucleus pulposus (NP) pressurization, and noted that no macroscopic damage to the annulus fibrosus (AF) was detected<sup>1</sup>. However, given that previous research has identified a link between vertebral fracture and subsequent herniation<sup>2</sup>, it's likely that the AF may also become damaged following endplate fracture. Therefore, the purpose of this study was to determine if the mechanical properties of the AF are altered following end-plate fracture.

**Methods:** The current study employed a high-rate IVD pressurization model to create end-plate fractures in the porcine cervical spine. Specifically, 28 functional spine units were isolated from the cervical region of fourteen porcine spines. In 14 specimens, a standard high pressure inflation needle was inserted through the anterior wall of the IVD into the NP. Each IVD was then slowly injected with hydraulic fluid until resistance to further injection was detected. Additional fluid was then injected in a rapid manner until an audible pop sound was heard indicating fracture of the end-plate. The remaining 14 specimens did not undergo fracture testing. Two samples were then dissected from each IVD and mechanical testing was performed. The first sample consisted of two adjacent outer layers of the posterior region of the AF which were subjected to uniaxial tensile testing in the circumferential direction. The second sample was a multi-layered tissue sample dissected from the approximate outer ten layers of the posterior-lateral AF adjacent to the bilayer sample location. This sample was dissected such that delamination was initiated between the two middle-most layers in order to perform a peel test thereby isolating the laminate adhesive bond. AF mechanical properties and laminate adhesion strength were quantified in both the fractured and un-fractured specimens.

**Results:** All specimens which underwent the rapid pressurization fractured in the end-plate (Figure 1). In these spines, AF laminate adhesion strength was 31% lower compared to the un-fractured spines. This finding was anecdotally corroborated by an increased ease of dissection and manual delamination in the specimens obtained from the fracture group. No other differences were observed between the fracture and un-fractured spines for any other measured mechanical variables.

**Discussion:** The decrease in laminate adhesion strength suggests that end-plate fracture damage is not isolated to the vertebra and instead also results in micro damage to the laminate adhesion or interlamellar matrix of the AF. This may increase in the risk of progressive delamination of the AF, which is associated with IVD herniation.

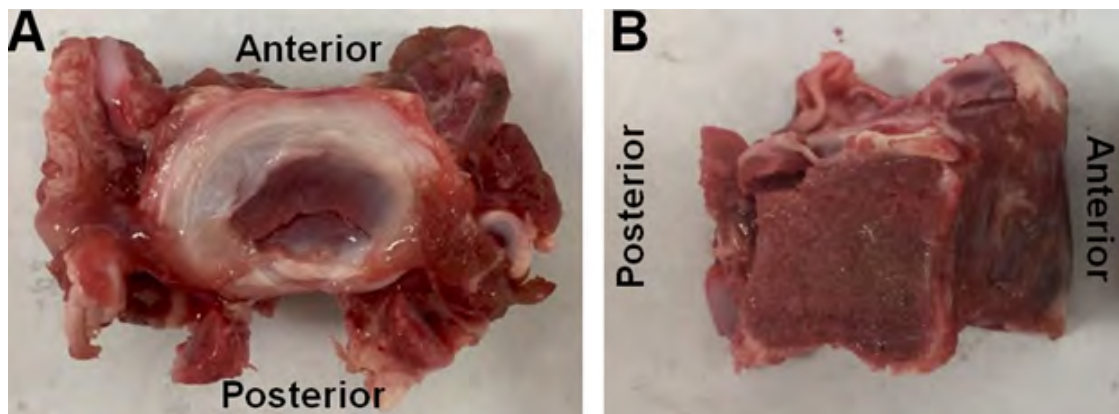


Figure 1. Typical fracture pattern on the inferior end-plate of the superior vertebra; transverse (A) and sagittal (B) view.

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## The relationship between compensatory mechanisms of residual kyphotic deformity after osteoporotic vertebral fractures and health-related quality of life

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### Introduction:

Thoracolumbar kyphotic deformity after osteoporotic vertebral fractures (OVFs) may cause persistent back pain and adverse effects on health-related quality of life (HRQOL). However, the influence of radiographic parameters after OVFs on HRQOL is still unknown. The aim of this study is to assess the relationship between compensatory mechanisms of residual kyphotic deformity after OVFs and HRQOL.

### Material and methods:

A total of 95 patients with residual kyphotic deformity after osteoporotic vertebral fractures were enrolled in this study. Patients with painful new (within three months) OVFs, nonunion, pathological fracture, and a previous history of spine surgery were excluded from the study. The mean age was 78 years, and there were 8 males and 87 females. Radiographical parameters included thoracic kyphosis (TK), lumbar lordosis (LL), lower lumbar lordosis (LLL), thoracolumbar kyphosis (TL), sagittal vertical axis (SVA), T1 pelvic angle (TPA), pelvic tilt (PT), and pelvic incidence (PI). Compensatory mechanisms were categorized based on pelvic inclination into three types: Group A, no compensation (PT <20°); Group B, compensated by pelvic retroversion (PT >20°, SVA <50mm); Group C, decompensation (PT >20°, SVA >50mm). Clinical outcomes including Oswestry Disability Index (ODI), Japanese Orthopedic Association Back Pain Evaluation Questionnaire (JOABPEQ), and visual analogue scale (VAS) of low back pain (LBP) were compared among the 3 groups.

### Results

The median ODI (Group A: 20, Group B: 22, Group C: 44, P=0.002) and LBP VAS (Group A: 21, Group B: 22, Group C: 50, P=0.006) were significantly worse in Group C than in Group A and Group B. The pain-related disorders (Group A: 71, Group B: 71, Group C: 43, P=0.029) and gait disturbance (Group A: 71, Group B: 64, Group C: 29, P<0.001) in JOABPEQ were significantly worse in Group C than in Group A and Group B. There were no significant differences in social life dysfunction (Group A: 62, Group B: 54, Group C: 49, P=0.055) and psychological disorders (57 vs 51 vs 50, P=0.262) among the 3 groups. The TL was significantly greater in Group C than in Group A and Group B (Group A: 30°, Group B: 27°, Group C: 38°, P=0.028). The LLL was significantly greater in Group A than in Group B and Group C (Group A: 41°, Group B: 34°, Group C: 33°, P=0.002). The PT (Group A: 18°, Group B: 25°, Group C: 32°, P<0.001) and TPA (Group A: 16°, Group B: 22°, Group C: 33°, P<0.001) were significantly different among three groups. ROC curve analysis showed that the optimal cut-off value of the TPA was 26° (AUC=0.685, sensitivity=63%, specificity=67%).

### Discussion:

Global sagittal alignment of Group A was compensated by hyperlordosis of the lower lumbar spine, and Group B was compensated by thoracic hypokyphosis and pelvic retroversion. Clinical outcomes were significantly worse in the decompensation group.

## Efficacy of prevention program using delirium risk scoring system for postoperative delirium after spine surgery

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### Introduction:

With the increasing elderly population in Japan, delirium after spinal surgery is an important complication. Our previous study revealed that psychiatric disorders, benzodiazepines use, age >70 years, hearing loss, and admission to the ICU are independent risk factors associated with postoperative delirium. A delirium risk scoring system was implemented based on risk factors to predict postoperative delirium. The aim of this study is to determine the efficacy of a prevention program using a delirium risk scoring system for postoperative delirium after spine surgery.

### Method:

A historical cohort study was conducted to compare the incidence of postoperative delirium in a pre-intervention group (Group A, n=293) versus a post-intervention group (Group B, n=265). The intervention consisted of preoperative patient education, change in medical protocol, early removal of catheter, and consult with the psychiatric liaison team. The delirium risk scoring system ranged from 0 to 36 points, and it was divided into three groups (Low risk: 0 to 4 points, medium risk: 5-9 point, high risk: 10 points or more.). An interventional prevention program was implemented for medium and high-risk groups. The outcomes were compared with the incidence and adverse outcomes of postoperative delirium in Group A and Group B. The adverse outcomes of delirium included combative behavior and self-removal of vascular or urinary catheters.

### Results:

After interventions, the incidence of delirium significantly decreased (Group A 22% vs Group B 13%, P = 0.008). The incidence of delirium was 0% in the low-risk group (n=45), 10% in the medium-risk group (n=124), and 24% in the high-risk group (n=96). The occurrence of combative behavior significantly decreased from 66% in Group A to 40% in Group B (P = 0.02). Self-removal of catheters tended to decrease from 19% in Group A to 9% in Group B (P = 0.245).

### Discussion:

This scoring system provides a useful tool for early detection of postoperative delirium. The prevention program using a delirium risk scoring system decreases the incidence as well as adverse outcomes of postoperative delirium after spine surgery.

## Delirium risk score

Factors	Total
Psychiatric disorder	10
Age >84 years	5
75-84 years	3
65-74years	2
Hearing loss	3
ICU, HCU	3
Benzodiazepines use	3
Central nervous system disorder	3
ASA grade 3	2
grade 2	1
Preop Alb <3.5 g/dl	2
Preop Hb <11 g/dl	2
Cervical	1
Diabetes mellitus	1
Steroid use	1
H2 blocker use	1

## 5-hydroxytryptamine (serotonin) in human intervertebral disc: preliminary in vitro study

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**INTRODUCTION:** 5-hydroxytryptamine (5-HT: serotonin) is a monoamine neurotransmitter derived from the essential amino acid tryptophan. In peripheral tissues, 5-HT, released from platelets and mast cells in response to peripheral inflammation or injury, is considered to have the potential to induce hyperalgesia (nociceptive pain), including sciatica from lumbar disc herniation. In addition, 5-HT released in injured tissues induces an inflammatory response. Several studies have shown that 5-HT receptor antagonist showed anti-inflammatory effects in human articular chondrocytes. Therefore, we hypothesized that 5-HT and its receptors exist in human intervertebral discs (IVDs), and are responsible for the pathogenesis of disc degeneration and associated pain. However, whether human IVDs express 5-HT receptors and have the potential to synthesize 5-HT remains unknown.

In the process of 5-HT biosynthesis, tryptophan hydroxylase 1 (TPH-1) catalyzes the monooxygenation of tryptophan to 5-hydroxytryptophan; therefore TPH-1 is a rate-limiting enzyme in the biosynthesis of 5-HT. The purpose of this study was (1) to examine the expression of 5-HT receptor (5-HT<sub>1A</sub>) and TPH-1 by human IVD cells and (2) to evaluate those expressions with/without proinflammatory cytokine IL-1 $\beta$  stimulation *in vitro*.

**METHODS:** Institutional Review Board approval was obtained for this study, which used human IVD tissues obtained from spine surgeries. Annulus fibrosus (AF) and nucleus pulposus (NP) cells were separately isolated by sequential enzyme digestion. Isolated cells were cultured in monolayer in DMEM/F12 containing 10% fetal bovine serum (FBS). The expression of 5-HT<sub>1A</sub> and TPH-1 was examined using real-time polymerase chain reaction (PCR) and immunohistochemistry. To evaluate the effect of IL-1 $\beta$  stimulation, AF or NP cells were cultured with or without recombinant human IL-1 $\beta$  (rhIL-1 $\beta$ ) at 0.1, 1.0 or 10 ng/ml in DMEM/F12 containing 0.3% FBS for 24 hours. Differences in quantitative outcome measures were established using one-way ANOVA with Fisher's Least Significant Difference test ( $p < 0.05$ ).

**RESULTS:** Immunoreactivity to 5-HT<sub>1A</sub> was clearly identified in monolayer cultures of AF and NP cells. Immunoreactivity to 5-HT<sub>1A</sub> was found in cell membranes of both AF and NP cells. mRNA expressions of 5-HT<sub>1A</sub> and TPH-1 were clearly identified by both AF and NP cells. IL-1 $\beta$  significantly stimulated the mRNA expression of 5-HT<sub>1A</sub> and TPH-1 in a dose-dependent manner by NP cells ( $P < 0.05$  vs. control, respectively); however no significant differences were identified for AF cells.

**DISCUSSION:** The results of this study showed, for the first time, that one of the 5-HT receptors (5-HT<sub>1A</sub>) and TPH-1 were expressed by human IVD cells. This suggests that human IVD cells have the potential to biosynthesize 5-HT and respond to 5-HT through 5-HT receptors in an auto and/or paracrine manner. Since these expressions are upregulated by IL-1 $\beta$ , 5-HT and its receptors may have the possibility to be associated with the progression of IVD degeneration. Further studies are needed to clarify the metabolism and function of 5-HT in human IVDs.

## Clinical outcomes and prognosis after spinal surgery for patients on hemodialysis

**TAKASHI CHIKAWA, Fumitake Tezuka, Yoichiro Takata, Toshinori Sakai, Koichi Sairyō**

### **Background:**

The impact of dialysis dependence on perioperative risk of spinal surgery is not fully understood. This study sought to examine clinical outcomes and prognosis after spinal surgery for patients undergoing hemodialysis.

### **Methods:**

Subjects were 87 patients (48 men and 39 women) who underwent spinal surgery. Mean age at surgery was 64.9 (48-82) years. Mean follow-up period was 15.9 (0.5-41) years. We investigated the level of spinal surgery, surgical method, number of surgeries, Japanese Orthopaedics Association score, recovery rate (Hirabayashi method), postoperative complications, and mortality and morbidity. We chose the indication of surgery as possible spinal fusion for cases with progressive destructive changes and instability.

### **Results:**

Of 48 patients who underwent cervical surgery, anterior fusion was performed in 4 patients, simultaneous posterior and anterior surgery (anterior body fusion with laminoplasty) in 5, laminoplasty in 27, and posterior fusion with laminoplasty in 12. Of 9 patients who underwent thoracic surgery, decompression surgery and spinal fusion were performed in 3 and 6 patients, respectively. Of 53 patients who underwent lumbar surgery, lumbar decompression, posterior fusion, and lateral lumbar interbody fusion were performed in 9, 12, and 2 patients, respectively. Multiple operations were performed in 21 patients (47 operations), all of which developed a concomitant disorder or lesion at another spinal level requiring further surgery (excluding revision surgery due to infection and nonunion). Two surgeries were performed in 17 cases, three in 3, and four in 1. These cases all developed a concomitant disorder or lesion at another spinal level, leading to further surgery. Surgical site infection occurred in 9 cases; infection rate was high at 8.2% (9/110 cases). With meticulous debridement and continuous irrigation, healing was achieved in all but 2 cases without hardware removal. Mean recovery rate was 49.6%, 31.9%, and 56.9% in the cervical, thoracic, and lumbar spine, respectively, and was 48.0% in cases of multiple surgeries, with favorable outcomes. There were 28 mortalities; death within 1 year after surgery occurred in 9 cases and death in the perioperative period within 3 months after surgery occurred in 5 cases. In the remaining 19 deaths, the patients initially survived for more than 1 year after surgery, and death was due to dialysis-related complications or underlying disease. In total, 50 cases were successfully followed up for more than 2 years after surgery; Kaplan-Meier analysis showed no difference in survival rate between the two groups with destructive spondyloarthropathy (DSA) type and non-DSA type lesions.

### **Conclusions:**

The results of this study indicate that spinal surgery for patients undergoing hemodialysis can reliably ameliorate neurological impairment, with resultant improvement in quality of life, and a high level of satisfaction despite the high complication rate. Surgery should be performed as soon as possible after appropriately explaining the potential risks and complications.

### Variation of C-reactive protein and white blood cell counts in spinal operation: primary fusion surgery versus revision fusion surgery

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**INTRODUCTION:** Serum C-reactive protein (CRP) concentrations and white blood cell (WBC) count are commonly used to identify postoperative wound infections. We investigated whether changes in serum CRP levels and WBC counts actually differed between patients undergoing revision spinal fusion surgery and those undergoing a primary fusion.

**METHODS:** Patients who underwent posterolateral fusion (PLF) surgery between October 2013 and April 2015 were considered for this study. Sixty-seven patients with primary lumbar PLF (pPLF) and 21 with revision PLF (rPLF) were enrolled. A retrospective assessment of preoperative and postoperative CRP levels and WBC count was undertaken. Also, we gathered peak CRP day, and CRP normalization days. Co-morbidity data were also obtained to evaluate any effects on the course of CRP and WBC count post-operatively.

**RESULTS:** CRP levels peaked at 3 days after surgery. The maximum CRP values recorded for each group: 4.17 (standard deviation [SD], 4.18) mg/dL and 4.88 (SD, 3.03) mg/dL for pPLF and rPLF. This difference was not statistically significant (p=0.24). A rapid fall in CRP within 5-9 days was observed for both groups.

**DISCUSSION:** Out of our expectation, changes in CRP levels after spinal fusion surgery follow the same course regardless of whether it is a revision operation or not. Because of this result, both the primary PLF surgery and revision PLF surgery should be monitored using CRP in the similar way and the antibiotic administration should be determined.

Table 2. Mean values of preoperative and postoperative CRP and leukocyte profiles

Variable	pPLF (n=67)	rPLF (n=21)	p-value <sup>†</sup>
CRP (mg/dL)			
Preoperative	0.18±0.30	0.13±0.17	0.501
Day 3	4.17±4.18	4.88±3.03	0.242
Day 6	1.59±1.45	2.13±2.03	0.250
Day 9	1.27±2.66	0.86±0.58	0.419
Normalization days	9.68±7.12	10.61±3.36	0.260
p-value <sup>†</sup>	<0.001	<0.001	
WBC (×10 <sup>9</sup> /μL)			
Preoperative	6.61±1.78	6.67±2.41	0.663
Day 3	9.31±3.47	8.37±2.88	0.384
Day 6	8.73±3.58	6.97±2.11	0.081
Day 9	7.99±3.72	7.00±2.63	0.279
p-value <sup>†</sup>	0.046	0.145	

Values are presented as mean±standard deviation.

pPLF, primary posterolateral fusion cases; rPLF, revision posterolateral fusion cases; CRP, C-reactive protein; WBC, white blood cell. Normal CRP value: <0.5 mg/dL; Normal WBC value: <12 ×10<sup>9</sup>/μL

<sup>†</sup>The p-values were derived from Wilcoxon rank-sum tests. <sup>‡</sup>Longitudinal differences were obtained by using Kuruskal-Wallis test.

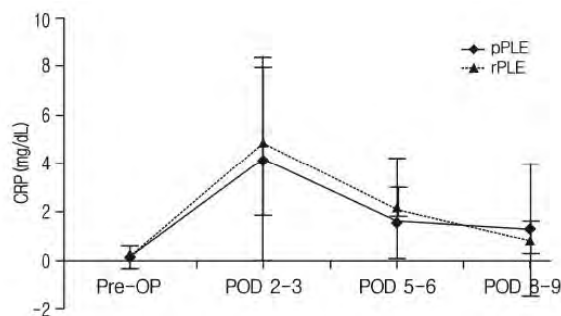


Fig. 1. Kinetics of postoperative C-reactive protein (CRP) levels (mg/dL); primary fusion operation (pPLF) vs. revision fusion operation (rPLF). Values are mean and standard error. Pre-OP, preoperation; POD, post-operative day.

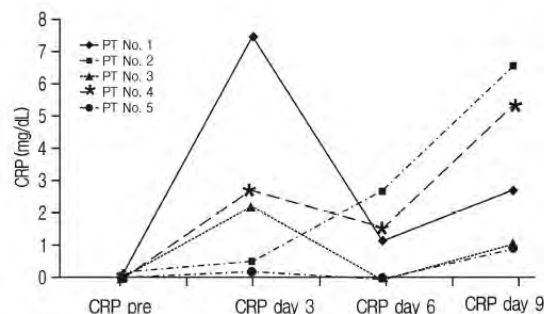


Fig. 3. C-reactive protein (CRP) profiles of infection complication cases (mg/dL); infection patient (PT) numbers 1 and 2 had primary fusion surgery. Infection PT numbers 3, 4, and 5 had revision fusion surgery.

## Spinal deformity and depression symptoms -locomotive syndrome and health outcomes in aizu cohort study (LOHAS)

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### INTRODUCTION

Of the spinal deformity, sagittal imbalance can cause low back pain and difficulty to walk. In addition to physical symptoms, mental health can be deteriorated by sagittal imbalance of the spine. However, it is not clear about relationship between spinal deformity and mental health in adult. The purpose of this study was to clarify the relationship between spinal deformity and depression symptoms in general population.

### METHODS

This study design is cross sectional study using data from Locomotive Syndrome and Health Outcomes in Aizu Cohort Study (LOHAS) in 2010. The LOHAS is a cohort study starting in 2008 and involves residents aged 40 to 80 years who participated in annual health check-up among 2 communities (Tadami and Minamiaizu) in Fukushima Prefecture, Japan. The participants were received whole-spine radiography assessment. We identified the sagittal vertical axis (SVA) as indicator of spinal deformity. Depressive symptoms were assessed using the 5-item version of the Mental Health Inventory (MHI-5). We defined a score of 60 as cut-off points for having depressive symptoms according to the previous study<sup>1</sup>. Potential confounding factors assessed in the present study were sociodemographic characteristics including age and gender, and status of employment, living alone and bodily pain by self-reported questionnaire. The timed up and go (TUG) test was used to assess the comprehensive physical function. Bodily pain was assessed using subscale SF-12. We classified participants into three categories based on SVA: mild deformity category (under 40 mm), moderate (40 to 95 mm) and severe (over 95mm), in accordance with clinical meaning<sup>2</sup>. To estimate relationship between spinal deformity and depression symptom, we calculated adjusted risk ratio (RR) as indicator of effect, and 95% confidence interval [CI] using generalized linear model with poisson link.

### RESULTS

786 (86.6%) participants were included for statistical analysis. Overall, the mean age of the participants was 68.1 (standard deviation, 8.8) years, and 39.4% were male. Among these participants, 21.0% were identified as having depression symptom and 18.6% were classified into mild deformity category, 28.9% were into moderate and 4.1% were into severe category. The prevalence of depression symptom by SVA categories were 18.6% in mild, 23.8% in moderate and 40.6% in severe category, respectively. In the multivariable analysis with adjustment for age, gender, status of employment, living alone, bodily pain and TUG, the RR of SVA for depression symptom against mild category were 1.12 [95%CI, 0.74-1.70] in moderate category and 2.29 [1.01-5.17] in severe category.

### DISCUSSION

We found that there was significant relationship between spinal deformity and depression symptom in general population. The spinal deformity has been newly identified as risk factor of depression in present study. This observed finding could provide the evidence that adults with severe spinal deformity should be paid more attention to possibility of having depression symptom in clinical practice.

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## Functional role of mechanosensitive ion channel Piezo1 in Modic changes, and the effect of *Propionibacterium acne*

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**Introduction** Piezo1 is an ion channel involved in mechanotransduction in bony and cartilaginous tissue. Being a weight-bearing structure, endplate and its pathological status, MC, are mechanical-linked. Yet, the function of Piezo1 in intervertebral discs hasn't been studied. Our study is to evaluate the function role of mechanosensitive Piezo1 ion channel in tissue and cells of MC.

**Methods** For the in-vivo part, animal specimens of motion segments with or without MCs were obtained from rabbits that revived intradisc injection of *P. acnes* for 6 months. Immunostaining and qPCR were performed to detected Piezo1 level. For the in-vitro part, rat nucleus pulposus cells (NPC) and endplate cells (EPC) were used. Cells were applied with 0.4MPa compressive force, in the presence or absence of *P. acnes* supernate. Cell viability were tested by CCK-8 assay, Piezo1 distribution were investigated with immunofluorescence, and Cytokine expression were measured by western-blot and qPCR.

**Results** By immunostaining, the specimens from MC model segments showed more Piezo1 positive staining in endplate region than control segments, and increased Piezo1 expression was confirmed by qPCR. When compressed without *P. acnes* supernate, both EPC and NPC showed higher Piezo1 concentration at the cell membrane, while Piezo1 expression (by qPCR) are not evaluated. When *P. acnes* supernate was added, the cell membrane Piezo1 expression maintained elevated, and the expression of Piezo1, together with inflammatory cytokines, were also up-regulated. The results suggest that compression can induce Piezo1 to membrane, where the ion channel functions, and more Piezo1 were synthesis by the stimulation of *P. acnes* supernate.

**Discussion** Piezo1 is expressed and functioning in disc cells with MCs, and its function can be regulated by *P. acnes* and force stimulation.

*Key words: Modic changes, intervertebral disc endplate, Propionibacterium acne, Piezo1, inflammation.*



## Validation of clinical CT against $\mu$ CT to measure lumbar facet joint width

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**Introduction:** The human lumbar vertebrae bear a significant portion of body weight and thus, have the greatest risk of injury and degeneration. One of these critical load-bearing components is the lumbar facet joint which not only withstands compressive loads, but also sustains shear loads in torsion. Facet joint osteoarthritis is often implicated as a cause of low-back pain in the elderly. In detriment of load-bearing ability, facet joint osteoarthritis is characterized by a narrowing of the facet joint width [1]. This condition is often diagnosed through the use of clinical computed tomography imaging, but the spatial resolution of this technique is usually thought to be sub-optimal [2]. This study aims to compare the facet joint width data collected using clinical computed tomography imaging with the data collected using micro computed tomography ( $\mu$ CT) imaging, which is considered the gold standard due to its higher spatial resolution.

**Methods:** Ten fresh, lumbar spines from deceased donors (6F/4M) were used in this study. The L3/4, L4/5, and L5/S1 facet joints were isolated bilaterally for analysis due to higher incidence of facet joint osteoarthritis resulting from their inferior position along the spine. Once isolated, the spines were potted in translucent silicone rubber to preserve the position of the facet joints. After curing completely for 24 hours, they were scanned separately using a micro computed tomography scanner (Scanco  $\mu$ CT 50, Scanco GmbH, Brütisellen, Switzerland). The  $\mu$ CT scan settings were as follows: 45 kV, 200  $\mu$ A, at a resolution of 48.4  $\mu$ m voxel size and a matrix size of 1024  $\times$  1024. A custom-written Visual C++ routine was used to determine the facet joint width by finding the least distance from an individual point on the superior facet joint to a point on the corresponding inferior facet joint surface (Fig. 1). Data is presented as mean  $\pm$  SD. A paired Student's t-test was employed to compare data by level.

**Results:** The mean width values calculated using the  $\mu$ CT images were larger than the corresponding values calculated using the computed tomography images at all spinal levels bilaterally except for the left side L5/S1 (Table 1). In general, both  $\mu$ CT and computed tomography values followed a similar pattern: the largest width measured at L4/5 and the smallest width measured at L5/S1. The only exception to this pattern was the right-side  $\mu$ CT data.

**Discussion:** The described pattern of mean facet joint width could be attributed to the differing facet joint anatomical orientation or position [1]. The differences in facet joint width between both imaging modalities were insignificant (t-value >2); therefore validating the use of clinical computed tomography as a tool to diagnose facet joint osteoarthritis. The  $\mu$ CT allowed visualization of more subtle changes in the articular surfaces due to its increased resolution. Nonetheless, this study demonstrated the mean facet joint width could be evaluated with sub-voxel level using multiple data points by means of clinical computed tomography.

**Table 1: Facet joint width by imaging modality (mm, mean $\pm$ SD)**

Level	$\mu$ CT		CT	
	L	R	L	R
L3/4	1.10 $\pm$ 0.28	1.08 $\pm$ 0.20	0.96 $\pm$ 0.10	1.00 $\pm$ 0.17
L4/5	1.12 $\pm$ 0.19	1.05 $\pm$ 0.29	1.04 $\pm$ 0.26	1.03 $\pm$ 0.20
L5/S1	0.87 $\pm$ 0.22	0.98 $\pm$ 0.15	0.92 $\pm$ 0.15	0.89 $\pm$ 0.17

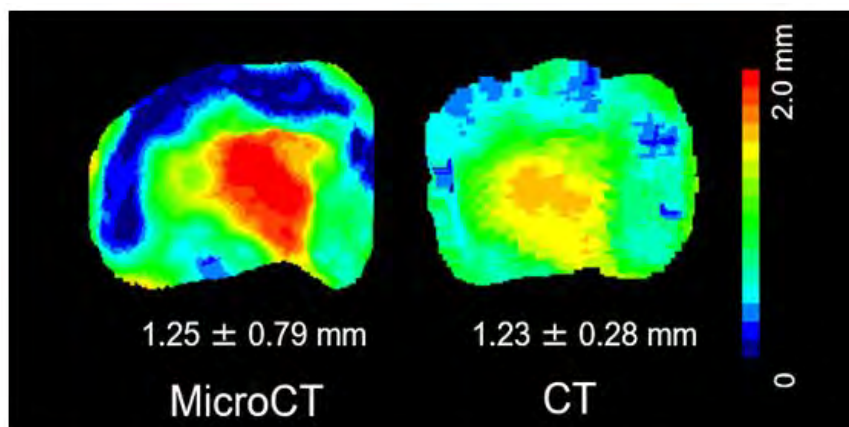


Figure 1: FJW Distribution: Comparison Between  $\mu$ CT and CT in the same specimen.

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- [2] Gellhorn A, et al. Nature Rev. Rheumatol. 2013; 9(4):216-24.

**GP075**

**Simple predictor of postoperative neurologic status in patients with metastatic spinal cord compression - Cord compression ratio on MRI**

**Sang-Il Kim<sup>1</sup>, Kee-Yong Ha<sup>1</sup>, Hyung-Youl Park<sup>1</sup>, Joo-Hyun Ahn<sup>1</sup>, Hyung-Ki Min<sup>1</sup>, Ki-Hyun Kwon<sup>1</sup>, young-Hoon Kim<sup>1</sup>**

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Publish consent withheld

## Skeletal muscle cell oxidative stress as a possible therapeutic target for denervation-induced sarcopenia

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**Study design:** A basic study using a rodent model of sarcopenia.

**Objective:** To elucidate the contribution of oxidative stress to muscle degeneration and the efficacy of antioxidant treatment for sarcopenia using an animal model of neurogenic sarcopenia.

**Introduction:** Oxidative stress has been reported to be involved in a number of pathologies, including musculoskeletal disorders. Its relationship with sarcopenia, one of the potential origins of lower back pain, however, is not yet fully understood.

**Methods:** Myoblast cell lines (C2C12) were treated with H<sub>2</sub>O<sub>2</sub>, an oxidative stress inducer, and N-acetyl-L-cysteine (NAC), an antioxidant. Apoptotic effects induced by oxidative stress and the antioxidant effects of NAC were assessed by western blotting, immunocytochemistry, and 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) cell viability assays. An animal model of sarcopenia was produced via axotomy of the sciatic nerves to induce muscle atrophy. Eighteen male Sprague-Dawley rats were divided into sham, axotomy, and axotomy+NAC groups. Rats were provided water only or water containing NAC (1 g/L) for two weeks. The gastrocnemius muscle was isolated and stained with hematoxylin and eosin (H&E) two weeks after axotomy, from which muscle cells were harvested and protein extracted for evaluation.

**Results:** Mitogen-activated protein kinases (MAPKs) were significantly activated by H<sub>2</sub>O<sub>2</sub> treatment in C2C12 cells, which was ameliorated by NAC pretreatment. Furthermore, H<sub>2</sub>O<sub>2</sub> induced apoptosis and death of C2C12 cells, which was prevented by NAC pretreatment. The weight of the gastrocnemius muscle was reduced in the axotomy group, and this was also prevented by NAC administration. Lastly, although muscle specimens from the axotomy group showed greater reductions in muscle fiber, the oral administration of NAC significantly inhibited amyotrophy via antioxidant effects.

**Discussion and Conclusion:** The current *in vitro* and *in vivo* study demonstrated the possible involvement of oxidative stress in sarcopenic pathology. NAC represents a potential anti-sarcopenic drug candidate, preventing amyotrophy and fatty degeneration.

## The characteristics of endplate fractures in the thoracolumbar fracture with fixation

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### Introduction

Endplate is known to be an important structure for disc degeneration because it provides mechanical stability and nutrition to the adjacent disc. Endplate fracture is frequently found in thoracolumbar fracture, which may cause adjacent disc degeneration. However, endplate fracture and subsequent disc degeneration in thoracolumbar fracture have not been studied yet. In this study, we investigated the changes of endplate fracture after healing of thoracolumbar fractures.

### Methods

This study involved consecutive 37 patients who had a traumatic thoracolumbar fracture and were treated with posterior instrumentation and fusion. All patients had successful fusion and underwent the implant removal surgery at  $20.5 \pm 12.3$  months after the index surgery. Computed tomography (CT) and magnetic resonance images (MRI) at the time of injury and at the implant removal surgery were used to evaluate the change of endplate fracture and disc degeneration. The severity of endplate fracture or defect was evaluated using total end plate defect score (TEPS). Disc degeneration was evaluated using Pfirrmann grade. McNemar's test was adopted to compare endplate defect scores. Kendall's tau-b was used to reveal the relationship between demographical and radiological parameters.

### Results

Of the 61 fractured vertebrae in the 37 patients, 87 discs and 174 endplates were examined. At the time of injury, there were 53 (60.2%) upper endplate fractures and 23 (26.2%) lower endplate fractures. At the implant removal, there were 50 (56.8%) upper endplate defects and 34 (38.6%) lower endplate defects ( $P=0.014$  and  $0.160$  for upper and lower endplate, respectively). TEPS changed significantly on McNemar's test ( $P<0.001$ ). At injury, all discs were normal disc (grade I or II). Disc degeneration following endplate fracture was found in 40 (46.0%) discs, in which 36 discs changed to grade III (41.4%), and 4 discs changed to grade IV (4.6%). Correlation analysis showed that TEPS at the injury was correlated with the adjacent disc degeneration at the follow-up. ( $r=0.270, 0.388$  and  $0.525$  vs.  $0.531, 0.540$ , and  $0.707$ , respectively; all  $p < 0.001$ ). All the grade IV discs at follow-up had TEPS of more than 6 at the time of injury.

### Discussion

In the course of fracture healing in thoracolumbar fracture, severe endplate defect made significant disc degeneration even under the circumstance of stabilization using instrumentation. Severity of endplate defect changed significantly. The severity of endplate defect was highly associated with disc degeneration. In all cases with grade IV disc, TEPS at injury was more than 6, which means TEPS at injury equal or greater than 6 can be a risk factor for disc degeneration in surgically treated thoracolumbar fracture.

## Psychological factors are central to understanding chronic low back pain

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**INTRODUCTION:** Low back pain (LBP) is a bio-psycho-social condition and LBP patients are treated by various health professionals with different training and presumed beliefs. Considering that theoretical foundations and emphases vary among health disciplines, it is possible that these professionals (e.g., researchers and clinicians from different disciplines) possess different “mental models” of what and how various factors relate to LBP. A novel way to investigate individual thinking about particular processes is through the development and analysis of fuzzy-logic cognitive maps (FCM). FCMs are particularly useful for modeling interactions between variables in complex systems, such as LBP. This study aimed to use this approach to describe similarities and differences by which different health professionals think about LBP.

**METHODS:** Participants from different disciplines (n=28), who have contributed significantly to the understanding of LBP (e.g., publications, contributions to societies, etc.), were selectively recruited for this study and represented the following disciplines: 1) Basic Science (n=6), 2) Chiropractic (n=4), 3) Spine Surgery (n=2), 4) Physical Medicine & Rehabilitation (n=2), 5) Physical/Exercise Therapy (n=12), and 6) Psychology (n=2). Each participant underwent a structured one-on-one interview to construct an FCM that represented the individual's understanding (mental model) of how factors related to LBP using *Mental Modeler* software ([www.mentalmodeler.org](http://www.mentalmodeler.org)). This process involved nomination of factors contributing to patients' outcomes (i.e., pain, disability, and quality of life) and the weighting of the connections (strength of the effect) between these factors. Factors from each model were tabulated and categorized into eight domains: 1) Nociceptive Detection & Processing, 2) Behavioral/Lifestyle 3) Tissue Injury/Pathology, 4) Contextual, 5) Psychological 6) Social/Work, 7) Biomechanical, and 8) Individual Factors. To determine the importance of each factor expressed in the FCM, centrality was computed as:  $Centrality = |a| * (\# \text{ of connections in}) + |b| * (\# \text{ of connections out})$ , where a and b are the weighting/strength of the connections. Based on this definition, centrality of a factor increases by the number of connections to and from the specific factor in the FCM, as well as by the weighting of these connections. Centrality of each domain (sum of centrality for each factor within the designated domain) was expressed as a percentage of the eight domains and grouped by discipline.

**RESULTS:** 263 factors were generated from the 28 FCM. Psychological Factors was the most prominent domain accounting for 33% of the centrality across all six participant groups, and was the most “central” domain for four groups (Figure 1). Tissue Injury/Pathology accounted for 14.7% of the centrality across all groups and was the most “central” for the remaining two groups (Basic Science and Spinal Surgery) (Figure 1).

**DISCUSSION:** Psychological factors were considered to be the most central/important to understanding LBP across disciplines, yet many of these professions do not specialize in the psychology of LBP. Although the selection of individuals and the relatively small sample size representing each discipline may bias the results, such findings support the notion that multi-disciplinary interventions (which includes consideration of psychological factors) to treating patients with LBP is sensible.

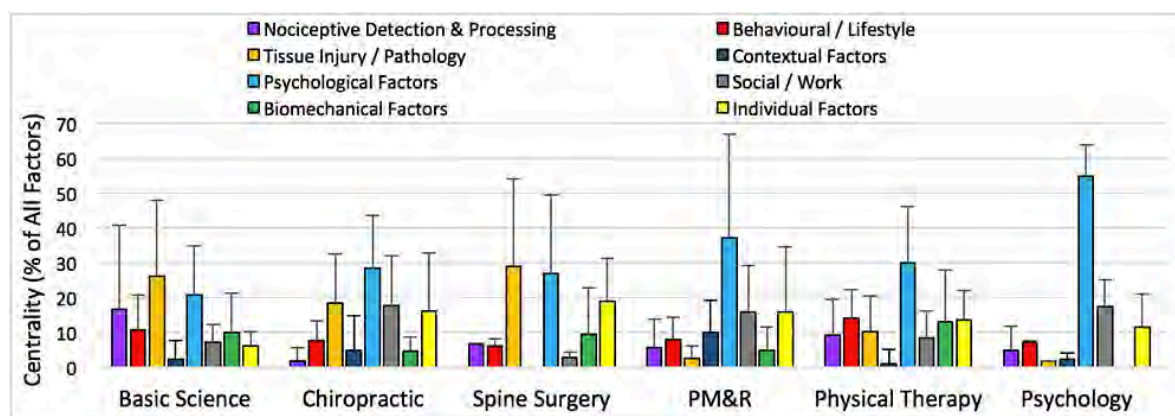


Figure 1. Centrality of domains across disciplines.

## Comparison of intraoperative fluoroscopic and postoperative radiographic measurement of lumbar lordosis in flatback syndrome

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**INTRODUCTION:** Intraoperative confirmation of adequate lumbar lordosis (LL) is necessary to avoid postoperative flatback syndrome. We used the computer software, NuvaMap (NuVasive, San Diego, CA, USA) which enables the intraoperative measurement of LL from 2 separate spliced fluoroscopic images. The correlation with the intraoperative final fluoroscopic measurement and postoperative standing radiographic measurement of LL is not reported, thus we reported the relationship of those 2 parameters in flatback surgery.

**METHODS:** Consecutive patients with flatback syndrome who underwent corrective fusion surgeries were included in this study. Intraoperative lumbar lordosis was measured using fluoroscopic imaging and the NuvaMap software. We measured spinopelvic parameters from postoperative first standing radiograph. LL discrepancy between intraoperative fluoroscopic and postoperative radiograph measurement was evaluated with dependent t-test. Multivariate logistic regression analyses were used to identify associations between risk factors and LL discrepancy ( $R^2=0.55$ , 95%CI  $p<0.05$ ). Predictors included demographic information (age, gender, body mass index, primary diagnosis), surgical procedure (operative procedure, number of fusion segment), and preoperative radiographic findings (preoperative LL, Pelvic incidence, Sagittal vertical axis). Pearson's correlation analysis was performed to assess the correlation coefficient between intraoperative fluoroscopy and postoperative radiographic measurement of LL. P-value less than 0.05 was considered statistically significant difference.

**RESULTS:** A total of 32 patients (7 males and 25 females, mean age 66.7 years) were included in this study. Twenty-eight posterior spinal fusions, 13 extreme lateral interbody fusion surgeries and/or 11 anterior spinal fusions were performed. Radiographic analysis showed a mean intraoperative LL of  $57.3\pm 8.9^\circ$ . The mean LL in postoperative radiographs was  $53.5\pm 9.7^\circ$ . The LL discrepancy was  $3.9\pm 8.3^\circ$ . The number of fusion segments of lumbar spine were independently associated with higher risk for intraoperative and postoperative LL discrepancy. Moderate correlation existed between intraoperative LL and first standing LL ( $r=0.60$ , 95%CI: 0.32-0.78,  $p=0.0003$ ). In case of 1 or 2 segments fusion, there were no significant correlation ( $p>0.05$ ), however strong correlation existed between intraoperative and postoperative LL in case of 3, 4, and 5 segments fusion ( $r=0.90$ , 0.94, 0.78 respectively,  $p<0.05$ ).

**DISCUSSION:** Intraoperative fluoroscopic measurements of LL could provide reliable information about the final restoration of LL. Intraoperative final LL is useful parameter to predict postoperative first standing LL especially during 3 or more level fusion surgeries, however intraoperative LL measurement in 1 or 2 segment fusion surgery should be used with more caution when making intraoperative decisions regarding lumbar correction.

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## Quantitative MRI correlates with histological grade in a percutaneous needle injury mouse model of disc degeneration

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**Introduction:** Low back pain due to disc degeneration is a major cause of morbidity and health care expenditures worldwide. Most current treatments neither address the underlying pathophysiology of disc degeneration, nor restore disc function. While stem cell-based therapies are promising, there is an urgent need to develop reproducible *in vivo* animal models to further develop and validate these potential treatments. Moreover, quantitative imaging tools suitable for *in vivo* application that correlate with disease state will be critical in assessing the impact of these therapies on disc degeneration. In the present study, we investigated the utility of quantitative magnetic resonance imaging (MRI) and micro computed tomography (mCT) in predicting histological grade in a percutaneous needle injury mouse model of disc degeneration.

**Methods:** In this IACUC approved study utilizing 30 male C57BL/6 mice aged 6-8 months, we performed fluoroscopic guided percutaneous needle injury of caudal mouse discs (C7-8, C9-10) using varying needle sizes (27G, 29G, and 31G) and either single (unilateral) or double (bilateral) annulus fibrosus (AF) puncture (n=10/group) as well as 30 intervening controls. Mice were euthanized 4 weeks post-injury, and post-mortem MRI (4.7T) and mCT (10mm resolution) was performed on all discs. Average T2 relaxation times of the nucleus pulposus (NP) from MRI and volumetric disc height index (DHI) from mCT were calculated [1]. Disc segments were then fixed and decalcified, and paraffin sections were stained with hematoxylin and eosin or Alcian blue and picrosirius red. Semi-quantitative histologic assessment was performed (average from three blinded assessors) using an adapted grading scheme [2].

**Results:** MRI analysis demonstrated that that 27G and 29G double puncture groups had significantly lower NP T2 values compared with controls, while 31G double puncture trended towards lower T2 values (Fig 1A). Conversely, DHI, as assessed using mCT, was similar among experimental groups. Blinded quantitative histological assessment revealed significantly worse histologic scores for both 27G and 29G double puncture groups compared with control (Fig 1B). There was a significant, strong, linear, inverse relationship between histological grade and NP T2 relaxation time, and a weak, but still significant, inverse linear relationship between histological grade and DHI (Figs 1C and D).

**Discussion:** In the present study, we demonstrate that quantitative MRI can detect disc degeneration in the mouse after percutaneous needle injury, specifically after 29G and 27G double AF puncture, when compared with uninjured controls. Histological grading confirmed MRI findings and was strongly correlated with NP T2 relaxation time, suggesting that *in vivo* T2 time may serve as a surrogate for histology in longitudinal studies of both disc degeneration and regeneration in the mouse. Interestingly, DHI was not significantly affected by any injury type, suggesting that this injury technique results in mild to moderate degrees of degeneration and may be well-suited for studying cell based therapies in which residual host NP cells are present and paracrine signaling is still possible. **Acknowledgements:** Funding from the NIH (R21AR070959, P30AR069619), the Department of Veteran's Affairs (I01RX001321) and the Sharpe Foundation.

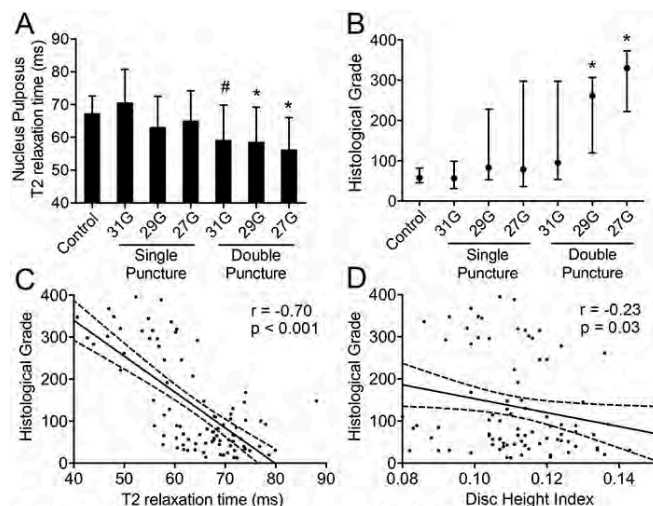


Figure 1. A. NP T2 relaxation time (mean $\pm$ SD). B. Overall histological grade (median and IQR). C. Strong, linear, inverse correlation between NP T2 relaxation time and histological grade. D. Weak, linear, inverse correlation between Disc Height Index and histological grade. \* $p < 0.05$  and # $p < 0.1$  vs control.

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## The effect of nicotine on human bone marrow stem cell proliferation and differentiation

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### Introduction:

Cigarette smoking has been correlated with intervertebral disc degeneration, imbalance in bone formation and increased pseudarthrosis rates. Although in vitro studies have shown that nicotine influences stem cell proliferation and osteogenesis, data on smoking cessation is still sparse. Therefore, the aim of this study was to understand the effect of the nicotine cessation period on the osteogenic differentiation of bone marrow derived stem cells (BMSCs), which are the key player in bone regeneration and repair.

**Methods:** Commercially available human BMSCs were expanded and cultured as three-dimensional spheres ( $3.5 \times 10^5$ ) to mimic tissue environment. Human BMSC spheres were cultured in the presence or absence of nicotine extracts (750 $\mu$ M) for a period of 5 days. To simulate durations of nicotine cessation, stem cells were then returned to normal growth media for a period of 5 days. After the cessation period, BMSC were differentiated for 21 days in defined osteogenic media. Four groups were studied based on the initial treatments before osteogenesis: 1) BMSC pre-treated with nicotine and nicotine cessation (Nicotine+ and Cessation+: N<sup>+</sup>C<sup>+</sup>), 2) BMSC pre-treated with nicotine and no cessation (N<sup>+</sup>C<sup>-</sup>), 3) BMSC cultured in growth media only no nicotine exposure with the same time frame as group 1 (control1, N<sup>-</sup>C<sup>+</sup>), and 4) BMSC cultured in growth media only no nicotine exposure with the same time frame as group 2 (control2, N<sup>-</sup>C<sup>-</sup>). After the three weeks of osteogenic differentiation, spheres were collected and analyzed for proliferation using pico-green staining, calcification using Alizarin red staining, and gene expression using real time polymerase chain reaction (RT-PCR). Gene expression values were calculated using the  $\Delta\Delta$ CT-method and GAPDH as housekeeping gene. One-way analysis of variance and Mann-Whitney U test with Bonferroni adjustment (if needed) were used for statistical analysis.

**Results:** Nicotine exposure reduced the number of cells in both groups with and without cessation when compared to controls (N<sup>+</sup>C<sup>+</sup>:  $4.73 \times 10^4$ , control1:  $6.56 \times 10^4$ , N<sup>+</sup>C<sup>-</sup>:  $5.59 \times 10^4$ , control2:  $6.52 \times 10^4$ ). In terms of the calcification area, nicotine without cessation group had significantly less than the control (N<sup>+</sup>C<sup>-</sup>:  $14.2 \pm 9.3\%$  vs. control2:  $27.6 \pm 4.3\%$ ,  $p=0.026$ ). A similar trend was observed in the nicotine cessation group (N<sup>+</sup>C<sup>+</sup>:  $28.3 \pm 2.0\%$  vs. control1:  $31.3 \pm 3.4\%$ ,  $p=0.941$ ). The gene expression of ALP, OCN, BSP, RUNX and OPN showed tendency to be higher in the Cessation group compare to the noCessation group, although the p-value did not reach the significance. In contrast, the gene expression of COL1 was higher in the noCessation group than Cessation group.

**Conclusion:** Our initial data indicated that nicotine had an inhibitory effect on osteogenic differentiation of hBMSCs, and that the cessation period reversed the effect to some extent. Further steps include electron microscopy, histological and immunohistochemistry analysis.



## Mild (and not severe) disc degeneration is implicated in the progression of L5 spondylolysis to spondylolisthesis

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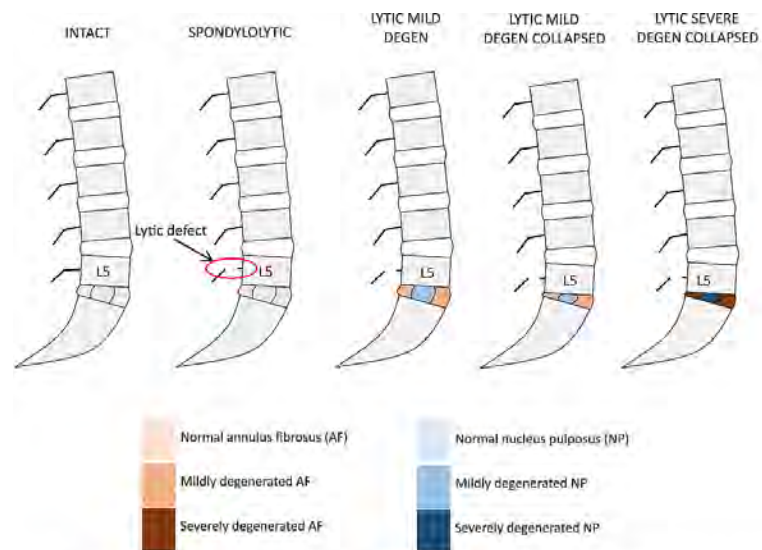
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**INTRODUCTION:** The pathomechanism for the progression of a L5 spondylolytic defect to spondylolisthesis remains unclear despite viable qualitative theories supported with clinical radiographic evidence. Lytic spondylolisthesis is often associated with disc degeneration at the level below defect; however, it is not clear whether disc degeneration is the cause or consequence of lytic spondylolisthesis [1]. Here we use computed tomography (CT) data and nonlinear finite element (FE) modelling to create a three-dimensional model of lumbosacral spine to investigate the role of different grades of disc degeneration in the progression of L5 bilateral lytic defect to spondylolisthesis.

**METHODS:** High-resolution lumbosacral CT data (437 axial cuts, 512 x 512 pixels) from an anonymised healthy male subject (26 years) were segmented in image processing software Avizo Standard (vers. 8.1) to build a geometrically accurate 3D model of an intact lumbosacral spine (L1-S1). The 3D model of spine was manipulated to generate four more models representing different states of L5-S1 disc degeneration in the presence of a bilateral L5 lytic defect (Figure 1). Models were then imported into FE modelling software Strand7 (vers. 2.4.6) for pre-processing, running nonlinear static solves, and post-processing of the results per published protocols [2]. The material property data (shear, compressive and bulk modulus) for mild and severely degenerated L5-S1 discs were obtained from the literature [3]. Disc height collapse was modelled as a 50% reduction in disc height measured in the mid-sagittal plane. Models were loaded in sagittal bending plane with pure moments of 10Nm and the sacral mass fixed in space. A separate pilot study comparing in vitro kinematics data with numerical results from a FE model of L3-L4 motion segment was conducted in order to calibrate material property values assigned to various elements in the FE model [4].

**RESULTS:** Compared with the baseline INTACT state, the greatest increase in Flexion (Fx) and Extension (Ex) range of motion (ROM) at L5-S1 was observed in the LYTIC-MILD-DEGEN model (Fx: 7.2° to 12.4°; Ex: 7.0° to 9.5°). The greatest increase in sagittal-plane intervertebral translatory motions at L5-S1 was also observed in the LYTIC-MILD-DEGEN model (Fx: 3.5 mm to 5.4 mm; Ex: 1.9 mm to 2.7 mm). Compared with the baseline, average compressive stress in the L5-S1 disc recorded the greatest increase in the LYTIC-DEGEN-SEVERE-COLLAPSED model (Fx: 0.11 MPa to 0.56 MPa; Ex: 0.15 MPa to 0.69 MPa), whereas the average anteroposterior shear stress recorded the greatest increase in the LYTIC-MILD-DEGEN model (Fx: 0.11 MPa to 0.56 MPa; Ex: -0.15 MPa to -0.69 MPa).

**DISCUSSIONS:** An increased prevalence of disc degeneration at the level below spondylolytic defect has been observed in adults over 25 years of age when compared with an age-and-sex matched control group [1]. Our results suggest that mild (and not severe) disc degeneration is implicated in the progression of L5 spondylolysis to spondylolisthesis. Disc height collapse, with mild or severe degenerative changes in material properties, could be one of the mechanisms available to lumbosacral spine to minimise or arrest the progression of a L5 lytic defect to spondylolisthesis.



**Figure 1.** Schematic representation of five different finite element models of the lumbosacral spine showing different states of degeneration in the L5-S1 disc

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## Fulcrum backward bending as a basis for surgical planning in adult spinal deformity

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**Introduction :** In surgical treatment for adult spinal deformity (ASD), indication of 3-column osteotomy (3CO) should be carefully decided because it is highly invasive. In our practice, we evaluate the preoperative flexibility of lumbar spine by fulcrum backward bending (FBB) to determine the necessity of 3CO. If sufficient lumbar lordosis (LL) is obtained in lateral view of radiograph with FBB, 3CO will not be indicated. The aim of this study was to assess the validity of surgical decision making by predicting the post-operative LL obtained without 3CO on the basis of FBB. We predict the post-operative lumbar lordosis (LL) obtained without 3-column osteotomy by this way, and decide surgical procedure whether target correction angle is obtained or not.

**Methods :** This study included ASD patients who underwent corrective surgeries without 3CO at our institution between October 2014 and September 2017. We reviewed the clinical data including preoperative radiographic parameters as follows: pelvic incidence (PI), LL, LL in extension (eLL), LL obtained by FBB (fLL), and postoperative LL (pLL). The radiographs for LL, eLL, pLL were taken in standing position, while fLL was obtained in supine position with a pillow beneath the lumbar spine. We calculated the correction angle (preoperative LL-pLL), PI-LL, pLL-eLL, pLL-fLL, and correlation of each parameter was statistically analyzed.

**Results :** Results are shown as mean±SD. Twenty eight patients (male, 4; female, 24) were eligible, with their mean age, 73.1 (range, 59-83). Most of the UIV were T10, whereas most of the LIV were ilium. The correction angle was 23.8±16.1°, preoperative PI-LL, 34.6±19.2°; postoperative PI-LL, 10.9± 9.6°; pLL-eLL, 12.5±9.7°; pLL-fLL, -2.3±5.5°. In correlation analysis, correlation coefficients for pLL vs eLL were r=0.59 (P=0.002), and pLL vs fLL, r=0.73 (P = 0.00001).

**Discussion :** We aimed to achieve postoperative PI-LL<10° in corrective surgery of ASD. In this study, postoperative PI-LL was 10.9 ± 9.6 °, which was almost satisfactory. Secondly, fLL was more near to postoperative LL as compared to eLL (pLL-eLL, 12.5 °±9.7 °; pLL-fLL, -2.3 °±5.5 °). In addition, although both eLL and fLL correlated with pLL, the latter showed a stronger correlation than the former (r, 0.59 vs 0.73). These indicate that preoperative LL with FBB serve as a good predictor for postoperative LL after corrective surgery without 3CO. In conclusion, FBB is useful in decision making for the necessity of 3CO in corrective surgery for ASD.

## The prevalence and impact of frailty in patients with symptomatic lumbar spinal stenosis

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### INTRODUCTION

Both frailty and lumbar spinal stenosis (LSS) are related with decreased physical functioning and inactivity in elder people. However, there has been no study examining the association between frailty and LSS. Therefore, the purpose of this study was to investigate the prevalence of frailty in patients with LSS and a propensity score-matched control group, and to analyze the association between LSS and frailty.

### METHODS

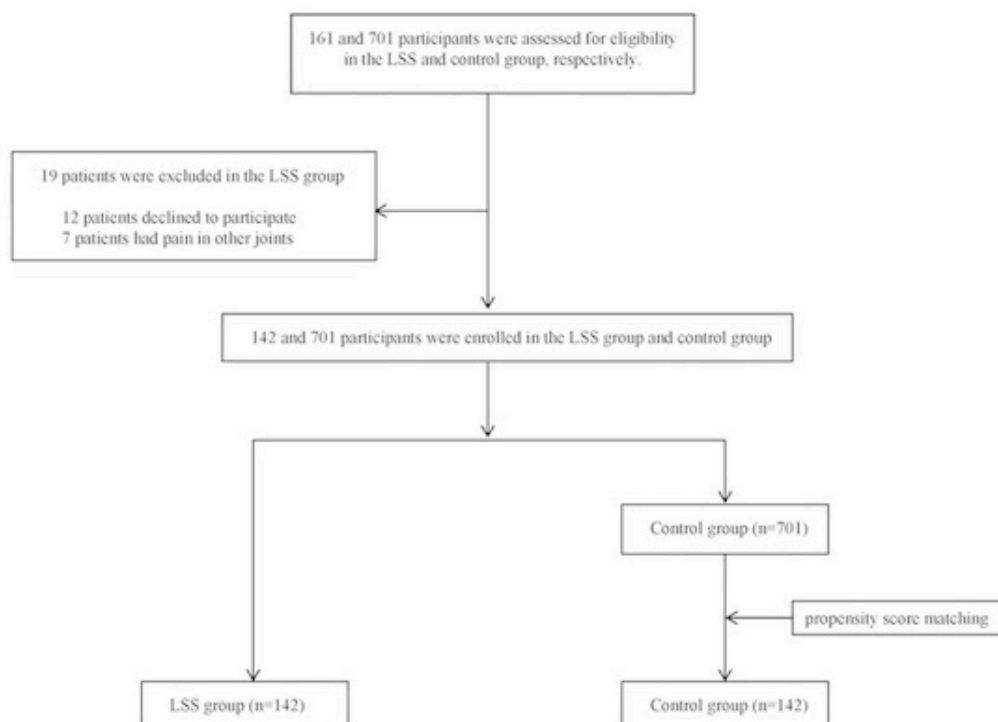
The present study was designed as Propensity matching case-control study, which included 2 groups: 1 consisting of patients with LSS (LSS group) and the other including healthy elderly subjects without degenerative spinal disease (control group). Baseline sociodemographic data, variables regarding frailty assessment, and clinical outcomes were collected. The frailty was assessed with Fried criteria, and the participants were categorized into robust, pre-frail, and frail. Using propensity score matching, 142 well-matched pairs in the LSS and control groups were produced. Among all participants, risk factors for frailty were identified using multivariate logistic regression.

### RESULTS

Totally, 843 subjects participated (142 in LSS group and 701 in control group) in this study. After the propensity score matching (142 in each group), the LSS group had significantly higher prevalence of frail than the control group ( $P < 0.001$ ): 59 (41.5%) participants in the LSS group were frail, whereas 10 (7.0%) participants in the control group were frail. Within LSS group analysis showed that participants with frailty had significantly higher disability and lower quality of life compared to those in a robust state. Among all participants, the multivariate analysis revealed that only age ( $P = 0.003$ ; Odds ratio [OR], 1.085; 95% confidence interval [CI], 1.029 – 1.145) and LSS ( $P < 0.001$ ; OR, 14.348; 95% CI, 7.768 – 25.250) were significantly associated with a higher odds of frailty

### DISCUSSION

The present study highlights a strong association between symptomatic LSS and frailty. Furthermore, symptom severity and disability caused by LSS are significantly related with frailty. Therefore, appropriate treatment of LSS may be a preventive and therapeutic strategy for frailty in patients with LSS and frailty. Likewise, early detection and appropriate treatment for frailty in patients with LSS is important.



## Back endurance test -application for elderly population with spinal deformity-

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**Introduction** A deficiency in isometric lower back muscle endurance is supposed to be a major risk factor for nonspecific low back pain. The Ito test is a simple and valuable test for lumbar trunk muscle endurance and is frequently used to evaluate trunk endurance in clinical practice. Previous research indicated that the Ito test might present a valuable test for back muscle endurance in LBP patients. However, it is assumed that it is difficult to perform the Ito test for a person with hyperkyphotic deformity or decreased physical function due to extra stress to lumbar spine or paraspinals; therefore, we created a new test for trunk muscle endurance. The aim of this study is to identify the characteristics and appropriateness of a new test and the Ito test.

**Methods** Thirteen healthy subjects (8 male, 5 female average age 21 years) without low back pain for past twelve months were recruited to this study. They received full explanation and all agreed to participate in this study. Spinal mouse was used to measure spinal alignment and ultrasound sonography was used to measure lumbar paraspinal muscle thickness. All measurements were obtained during resting and performing the new test and Ito test.

Protocol of the new test is semi-quadruped position; trunk on the bed with 15 degree wedge under the body and LE is off the bed with knees on the floor. The wedge is pulled out once the test is started and hold the trunk at 15 degree from the bed during the test. Protocol of the Ito test is following the original procedure. Endurance time was set from once the sternum loses contact with the bed to when it touches the bed again. All participants received education and practice time for both tests in order to be able to perform them properly prior to assessment. Considering their fatigue, measurements of endurance time were obtained on different dates.

**Results** There were significant differences of spinal alignment during testing in lumbar lordosis ( $p<0.001$ ) and sacrum tilt angle ( $p=0.001$ ) between the new test and the Ito test. There was also a significant difference of spinal curvature changes in lumbar lordosis ( $p=0.005$ ) from resting position to testing position between the new test and the Ito test. Significant differences could also be seen in muscle thickness of multifidus ( $p<0.001$ ) and longissimus ( $p=0.013$ ) between the new test and the Ito test. There was also a significant difference in trunk endurance time ( $p<0.001$ ) between the new test and the Ito test.

**Discussion** The results of this study indicate that the new test is easier to perform with less lumbar lordosis or muscle contraction; therefore, it might be more beneficial to use this test for a person that has spinal deformity or decreased physical function. And the Ito test is more appropriate for people with minimum deformity, young population, or athlete. Yet, these findings have to be verified in consecutive studies in people with spinal deformity or decreased physical function in clinical practice.

### Intermittent claudication due to low back pain in the community: the Minami Aizu Study

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**INTRODUCTION:** One of the important symptoms of adult spinal deformities is intermittent claudication due to low back pain (IC-LBP). We have previously reported that muscular ischemia with increased intramuscular pressure of the paraspinal muscles and muscle fatigue caused by the persistent muscle electric discharge appear to characterize the clinical condition of IC-LBP. However, the actual situation in IC-LBP has not been sufficiently clarified.

**OBJECTIVE:** The purpose of this study was to clarify the factors affecting IC-LBP from the results of a general population examination.

**METHODS:** This was a cross-sectional study. The subjects were 187 community-dwelling people (age range 47-91 years; mean age, 74.1 years) who participated in annual health check-ups in 2014. The presence or absence of IC-LBP, a lifestyle medical history (hypertension, diabetes, dyslipidemia), and a smoking history were assessed using an interview sheet. IC-LBP was defined as lumbago that improved with extension with the anteflexion posture of walking. Trunk muscular strength (flexion, extension, abdominal cavity external pressure), body mass index (BMI), and the ankle-brachial pressure index (ABI) were also evaluated by physical examination. Furthermore, the presence of fatty degeneration of the paraspinal muscles was analyzed by the method of Kjaer, and muscular dystrophy (lumbar indentation) of the paraspinal muscles (multifidus and erector spinae muscles) at the L4/5 level was evaluated on MRI findings. Multivariate logistic regression analysis was performed to examine associations of age, sex, lifestyle medical history, smoking history, trunk muscular strength, BMI, ABI, and paraspinal muscle degeneration with IC-LBP.

**RESULTS:** IC-LBP was seen in 53 cases (28.8%). The odds ratios [95% CIs] of the factors associated with IC-LBP were 1.12 [1.03-1.22] for paraspinal muscular dystrophy, 4.80 [1.19-19.30] for diabetes, 3.97 [0.99-15.98] for dyslipidemia, and 1.28 [0.49-3.36] for the ABI. Age, sex, smoking history, trunk muscular strength, and BMI were not associated with IC-LBP.

**CONCLUSION:** Lifestyle-related diseases, such as diabetes and dyslipidemia, and paraspinal muscular dystrophy are important factors related to IC-LBP.

## The fate of notochordal cell in intervertebral disc degeneration induced by dynamic compressive load through integrin $\alpha 5/\beta 1$ mechanotransduction.

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### Introduction

Intervertebral disc (IVD) degeneration is considered to be induced by daily mechanical loading through mechanoreceptors. We previously reported the role of integrin  $\alpha 5\beta 1$  on IVD degeneration using an ex-vivo culture system in which IVDs were exposed to dynamic mechanical loading. The purpose of this study is to investigate the relationship between integrin  $\alpha 5\beta 1$  and notochordal cell (NC) disappearance, which is considered a key alteration in the early IVD degeneration.

### Methods

Thirty 12-week-old male Sprague–Dawley rats were used. IVD tissues between the 7th and 8th caudal vertebrae were subjected to dynamic compressive stimuli (1.3MPa, 1Hz) in a dynamic organ culture system for 6 days under the following conditions; unloaded condition (Group C, control group), axial mechanical loaded condition with 1.3MPa, 1Hz (Group L) and loaded with an inhibitor of integrin  $\alpha 5\beta 1$  (Group TL). Regarding the assessment, (1) Cell viability analysis was examined using dead/alive staining in the nucleus pulposus (NP). (2) Histological assessment was performed by Masuda's grade. (3) Multi-color immunofluorescence staining for brachyury, sox9, and DAPI was performed. Furthermore, immunopositivity of brachyury and sox9 were calculated by the percentage of each positive cells/all DAPI-positive cells, respectively. Multi-way ANOVA with the Tukey-Kramer post-hoc test was used with significance of  $P < 0.05$ .

### Results

(1) %Cell viability of Group L (69.7%) and Group TL (79.4%) was significantly decreased than Group C (91.6%,  $p < 0.05$ ). And there was also significant difference between Group L and Group TL ( $p < 0.05$ ). (2) Histological grades of Group L (7.6) and TL (6.3) were increased than Group C (4.0), but Group TL was significantly lower than Group L. (3) The immunostaining revealed brachyury and sox9 of Group C were widely observed (82.8%, 93.3%), whereas immunopositivity of brachyury and sox9 were significantly decreased in Group L (3.6%, 51.0%) and TL (17.5%, 62.1%), respectively. The inhibitor of integrin  $\alpha 5\beta 1$  had significantly opposed this trend. These results showed the reduction of immunopositivity of brachyury and sox9 between Group L and Group TL has significant difference, namely the rate of immunopositivity of sox9 / brachyury of Group L (14.1=51.0%/3.6%) was significantly higher than Group TL (3.55=62.1%/17.5%).

### Discussion

In this study, the dynamic compressive loading led to decreased cell viability. In addition, this mechanostress led significant discrepancy of immunopositivity of brachyury and sox9 in NP cells. This cellular response was also inhibited by the presence of the inhibitor of integrin  $\alpha 5\beta 1$ . These findings suggested that integrin  $\alpha 5\beta 1$  may play the role in the pathomechanism of mechanically initiated IVD degeneration.

The current study had suggested that the fate of NC would result in not only cell death but the change of the phenotype in the process of the early IVD degeneration induced by mechanical loading.

## Regional bone mineral density differences measured by QCT: is the clinically used L1/L2 average representative of the entire lumbosacral spine?

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### INTRODUCTION

Quantitative Computed Tomography (QCT) of the lumbar spine is used as an alternative to DXA in assessing bone mineral density (BMD). Clinically, a BMD average of L1/L2 is commonly used as a surrogate marker for overall bone health. Since significant regional BMD differences within the spine have been described, it is unclear if the L1/L2 average is an accurate bone quantity measure of the entire lumbosacral spine. The aim of this study was to assess the agreement between the clinically used L1/L2 BMD average and the other lumbosacral vertebral levels.

### METHODS

Patients that underwent posterior lumbar spinal fusion from 2014 to 2017 at a single, academic institution were included in this study. Subjects with missing preoperative lumbar spine CT imaging were excluded. Standard quantitative computed tomography (QCT) measurements at the L1 and L2 vertebra and additional experimental measurements of L3, L4, L5 and S1 were performed. The correlations between L1-L2 average and the other vertebral bodies of the lumbosacral spine (L3, L4, L5, S1) were evaluated.

### RESULTS

296 patients (women, 55.4%) met inclusion criteria. The patient population was 88.5% Caucasian with a mean age of 63.1 years and mean BMI of 28.0 kg/m<sup>2</sup>. The vertebral BMD values showed a gradual decrease from L1 to L3 and subsequently increased from L4 to S1 (L1 = 118.8 mg/cm<sup>3</sup>, L2 = 116.6 mg/cm<sup>3</sup>, L3 = 112.5 mg/cm<sup>3</sup>, L4 = 122.4 mg/cm<sup>3</sup>, L5 = 135.3 mg/cm<sup>3</sup>, S1 = 157.4 mg/cm<sup>3</sup>) (Figure 1). Our data showed strong correlation between the L1/L2 average and the average of the other lumbosacral vertebrae (L3-S1) with a Pearson's correlation coefficient,  $r=0.85$ . We also analyzed the correlation between the L1/L2 average and each individual lumbosacral vertebra. Similar relationships were observed ( $r$  value, 0.67 - 0.87) with the strongest correlation between the L1/L2 average and L3 (Table 1).

### DISCUSSION

Our data demonstrates considerable regional BMD throughout the lumbosacral spine. Nevertheless, there is high concordance between the clinically-used L1/L2 BMD average and the BMD values in the other lumbosacral vertebrae. As the closest vertebra to the standard measurement site, L3 showed the strongest individual correlation to the L1/L2 average. Although still strongly correlated, the Pearson's correlation coefficients were smaller for the L4, L5 and S1 vertebra. This might be of importance, since the majority of patients in our cohort underwent fusion procedures at L4-5 (71.3%) and/or L5-S1 (44.9%). In summary, the L1/L2 BMD average is a useful bone quantity measure of the entire lumbosacral spine in patients undergoing posterior lumbar spinal fusion.

Figure 1 BMD measured by QCT from L1-S1

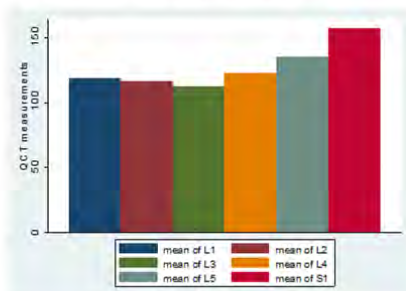


Table 1 Correlations between L1-L2 average and the other vertebral bodies of the lumbosacral spine (L3, L4, L5, S1)

	L1-L2 Average	p-value
L3	0.869	<0.001
L4	0.672	<0.001
L5	0.713	<0.001
S1	0.723	<0.001
L3-S1 Average	0.854	<0.001

## Prevalence of low bone mineral density measured by quantitative computed tomography (QCT) in 296 consecutive lumbar fusion patients

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### INTRODUCTION

Metabolic bone disease is a growing public health concern affecting approximately 200 million people worldwide. Using 2010 census data, the US prevalence of low bone mineral density (BMD) was reported as 43.9% in adults 50yrs or older. Diagnosing low BMD in patients with spinal disorders is an important component of successful treatment. Patients with osteopenia or osteoporosis may require intervention prior to elective spinal fusion procedures. BMD can be assessed radiographically using dual-energy x-ray absorptiometry (DXA) or quantitative computed tomography (QCT). QCT may have advantages over DXA for diagnosing low BMD in the lumbar spine. The American College of Radiology (ACR) defines the diagnostic criteria for the average QCT measurements at L1/L2 as follows:  $BMD > 120 \text{mg/cm}^3 = \text{Normal}$ ,  $80 \text{mg/cm}^3 \leq BMD \leq 120 \text{mg/cm}^3 = \text{Osteopenia}$  and  $BMD < 80 \text{mg/cm}^3 = \text{Osteoporosis}$ . To our knowledge, there is no study reporting the prevalence of low BMD (osteopenia or osteoporosis) based on lumbar spine QCT measurements in subjects undergoing spinal fusion procedures.

### METHODS

A review of prospectively collected clinical data from a single, academic institution was performed. Clinical records were reviewed for previous history of metabolic bone disease. All patients treated surgically for lumbar spine pathology that underwent thin section CT scans preoperatively were eligible for inclusion. QCT measurements were performed at L1 and L2 and the L1/L2 average was calculated. Using the ACR criteria, patients were diagnosed as normal, osteopenia, or osteoporosis. Disease prevalence for the entire cohort was calculated. Subgroup analyses based on Age and Gender were also performed.

### RESULTS

296 consecutive patients (55.4% female) undergoing primary lumbar fusion procedures were enrolled from 2014 to 2017. Mean age was 63yrs (range 21-89yrs). All patients had preoperative thin section lumbar CT scans including L1 and L2. Mean (SD) L1/L2 measurement was  $118 \text{mg/cm}^3$  (37.8). Using ACR criteria for BMD diagnosis groups, 123 (41.5%) were normal, 129 (43.6%) osteopenia, and 44 (14.9%) osteoporosis. Subgroup analysis based on gender demonstrated 132 males (40.2% osteopenia, 15.9% osteoporosis) and 164 females (46.3% osteopenia, 14% osteoporosis). When stratifying by age, 48 patients (16.2%) were <50yrs and 248 (83.8%) were ≥50yrs. Diagnoses within these subgroups were: <50yrs (16.7% osteopenia, 0% osteoporosis) and ≥50yrs (48.8% osteopenia, 17.7% osteoporosis). There were 212 patients with no prior history of osteopenia or osteoporosis. Within this subgroup, 83 (39.2%) had osteopenia and 22 (10.4%) had osteoporosis.

### DISCUSSION

This study reports the prevalence of low BMD measured by QCT in patients undergoing lumbar spinal fusion procedures. Overall, 58.5% had pathologic bone density by ACR criteria. Osteopenia and osteoporosis rates were similar between genders. More patients ≥50yrs had low BMD compared to younger patients. Among patients with no history of low BMD, 49.6% met criteria for osteopenia or osteoporosis. Spine surgeons should be aware of the high prevalence of abnormal BMD in lumbar spine patients and the possibility that patients without a previous diagnosis may have osteopenia or osteoporosis. The clinical impact of these findings and whether patients should have intervention prior to fusion procedures should be elucidated in future studies.



## Does lumbar spine pathology affect bone mineral density measurement by quantitative computed tomography (QCT)?

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### INTRODUCTION

Quantitative computed tomography (QCT) is increasingly used for clinically diagnosing osteopenia and osteoporosis. In contrast to dual x-ray absorptiometry (DXA) which uses a two-dimensional projection, QCT provides a true volumetric bone mineral density (BMD) measurement. Certain conditions like spinal degeneration, abdominal aortic calcification, and other sclerotic lesions can lead to an overestimation of BMD by DXA. Similarly, QCT measurements can be affected by degenerative/sclerotic vertebral body changes if inadvertently included in the field during the measurement process. It remains unclear if excluding pathologic bone regions in the selected field allows for accurate BMD measurements. The aim of this study was to assess whether BMD measured from pathologic levels is different than BMD derived from non-pathologic levels in paired, matched controls.

### METHODS

Patients undergoing posterior lumbar spinal fusion from 2014 to 2017 at a single, academic institution with available preoperative lumbar spine CT imaging were included. QCT measurements of all lumbar and the first sacral vertebra were performed on all patients. Pathologic levels were defined by referencing surgical procedures from clinical records. Degenerative or sclerotic bone regions at pathologic levels were avoided during the measurement process to minimize overestimation of bone density in the vertebral body (Figure 1). Due to known differences in BMD at different levels in the lumbosacral spine, comparisons between pathologic and normal levels within the same patient are not possible. To overcome this limitation, matched normal-pathologic measurements at the same lumbosacral level were identified in matched patient-pairs. Patients were matched 1:1 based on gender, age ( $\pm 5$  yrs), BMI ( $\pm 5$ ), and race. One or more normal-pathologic matched levels were identified from each patient pair. Differences between normal and pathologic levels were assessed using two-tailed paired *t*-tests with significance set at  $P < 0.05$ .

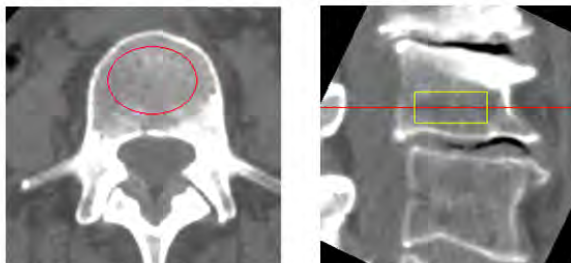
### RESULTS

Seventy-seven matched patient pairs (154 patients) were isolated from a cohort of 296 patients treated surgically for lumbar spine pathology. Patients not matched were excluded due to inability to match on all four matching criteria. From the 77 patient pairs, 152 matched normal-pathologic levels were identified for analysis. The mean (SD) for normal and pathologic levels was 140.4 mg/cm<sup>3</sup> (54.13) and 143.0 mg/cm<sup>3</sup> (49.04), respectively. Paired statistical analyses revealed no significant difference between groups ( $P = 0.563$ ).

### DISCUSSION

Our data demonstrates no difference in BMD measured at pathologic and non-pathologic vertebra at the same lumbar/sacral levels in paired patients matched based on age, gender, BMI and race. When using the recommended methodology for QCT measurements including the avoidance of degenerative and/or sclerotic regions, BMD can be accurately measured at pathologic levels. Lumbar degenerative changes are known to adversely impact the sensitivity and specificity of DXA for diagnosing osteopenia and osteoporosis. Our findings suggest that lumbar QCT measurements may not be affected by degenerative changes and may more accurately represent volumetric bone density in the lumbar spine.

Figure 1 QCT measurement avoiding degenerative or sclerotic bone regions



## Pre-operative education and rehabilitation prior to surgery for lumbar spinal stenosis: patient and physical therapist perspectives

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### Introduction

Lumbar spinal stenosis (LSS) is the most common reason for spine surgery in the Medicare population. However, there is great variation in the outcomes of LSS surgery. Some of this post-operative variation may be attributed to variations in pre-operative care. Currently there are no standardized guidelines for pre-operative care before LSS surgery.

The purpose of this study was to gain the perspectives and opinions of patients who have undergone LSS surgery, and the physical therapists (PTs) who treat such patients. This was achieved via collection of qualitative data from focus groups, in order to find common themes that would be useful in developing a standardized pre-operative protocol.

### Methods

Four focus groups were conducted: two with post-operative patients (N= 16) and two with PTs (N=12) who commonly treat patients before or after LSS surgery. Patients who had undergone LSS surgery within the prior two years were recruited via letters sent directly from their surgeons' offices. PTs who commonly treat such patients were identified and recruited by management personnel within a large PT practice.

A trained facilitator used standard focus group methods including asking open-ended questions and encouraging all group participants to share their opinions. In general, patients were asked about their experiences leading up to surgery, including whether any formal education or "pre-habilitation" was recommended or provided. PTs were asked questions regarding the main goals of pre-operative PT care for this group of patients, and the challenges experienced when treating this population.

After focus groups were transcribed, they were coded and analyzed by two separate research staff members using Atlas.ti qualitative data analysis software. Emerging themes were identified.

### Results

Salient themes identified via qualitative analysis include:

- *Educational Information.* Many patients described their experience as having received very little or inadequate educational information prior to surgery.
- *Patient Perceptions of Preoperative PT:* Several patients had participated in PT prior to their surgery, but felt that it was not beneficial because the focus was on strength training rather than functional activities.
- *Physical Therapists Perceptions of Preoperative PT:* Many PTs felt that the focus of preoperative PT was to try to improve strength and physical activity, but admitted that this was mostly an unrealistic goal.
- *Lack of Coordinated Care.* Participating PTs indicated that there was a lack of coordination and communication between surgeons and PTs regarding the preoperative protocols and goals.

### Discussion

These results suggest that there is a large room for improvement with respect to developing more patient-centered preoperative protocols and goals. Information from this qualitative study has identified specific barriers and facilitators that need to be considered when developing and standardizing new models of pre-operative care before LSS surgery.

## Prevalence of frailty in patients with osteoporotic vertebral compression fracture and its association with fracture severity

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### INTRODUCTION

Previous studies have shown that osteoporotic fractures were associated with frailty, and frailty is worsened; further, deficit accumulation is greater after osteoporotic fractures. Given that osteoporotic vertebral compression fracture (OVCF) is the most common osteoporotic fragility fracture in elderly populations, there might be a possible association between OVCF and frailty. Nonetheless, frailty in patients with vertebral fragility fractures has not been robustly studied yet. The purpose of this study was to assess the association between frailty and OVCF and to evaluate the relationship between fracture severity and frailty.

### METHODS

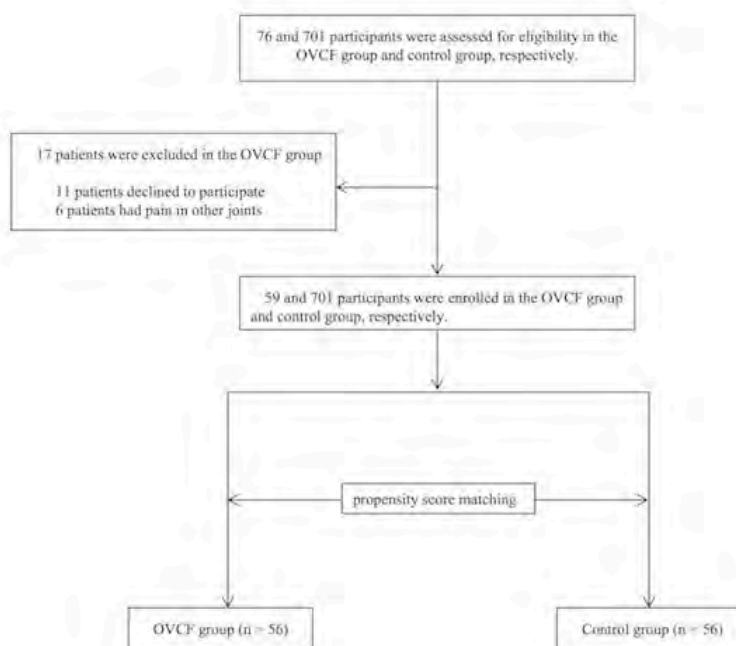
We enrolled 760 subjects, including 59 patients (with healed OVCF) and 701 controls (without OVCF). Successful matching comprised 56 patient-control pairs. We analyzed the principal clinical and demographic information, which included sex, age, height, weight, body mass index (BMI), variable frailty phenotypes as well as the Oswestry Disability Index (ODI) and the EuroQol 5-dimension questionnaire (EQ-5D). Frailty was defined in accordance with the following five phenotypes as reported by Fried et al.: weight loss, exhaustion, physical inactivity, slowness, and handgrip strength. The association between frailty and OVCF was ascertained. In addition, the degrees of disability and quality of life attributable to frailty were determined.

### RESULTS

The prevalence of frailty was significantly higher in the OVCF group than in the control group ( $P < 0.001$ ). Twenty-four (42.9%) and 22 (39.3%) participants in the OVCF group and two (3.6%) and 24 (42.9%) participants in the control group were considered frail and pre-frail, respectively. Most of the frailty phenotypes, such as exhaustion, physical inactivity, slowness, and handgrip strength, were also significantly observed in the OVCF group. Within the OVCF group, the participants with frailty had significantly higher disability and lower quality of life than those in a robust state ( $P < 0.001$  for ODI and EQ-5D). In addition, the multivariate logistic regression analysis demonstrated the patients with low BMI (multivariate odds ratio [OR] = 0.732, 95% confidence interval [CI], 0.566–0.946) and  $\geq 3$  fractures (OR = 10.391, 95% CI, 1.706–63.292) within the OVCF group were associated with higher odds of frailty.

### DISCUSSION

The present study showed significant relationships between frailty and OVCF, severity of symptoms, and disability induced by OVCF. Furthermore, frailty could be a causal and/or resulting factor of OVCFs. Over 50% of the patients in the OVCF group were classified as "frail" using the Fried frailty criteria, and in the OVCF group, the patients with frailty had higher disability and lower health-related quality of life. The numbers of OVCF were significantly related to frailty.



## What motivates engagement in work and other valued social roles despite persistent back pain?

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**Introduction:** The prognosis of persistent back pain is variable, with some individuals adjusting poorly to their condition, while others continue to fully engage in their social roles (i.e., participation, as included in the World Health Organization's International Classification of Functioning, Disability and Health framework). A paradigm focusing on those "participating" at a high level despite substantial persistent pain, instead of those with high levels of disability, may provide valuable insight into the factors most influential to continued participation (e.g., regular employment). The aim of this study was to better understand why some individuals, despite moderate to severe persistent back pain, maintain engagement in their valued social roles.

**Methods:** Individuals with persistent back pain who were participating in their regular duties as a full-time employee, homemaker, student or any combination of these were recruited from a multidisciplinary pain centre and orthopedic physical therapy clinics in Alberta, Canada. A qualitative study was conducted using semi-structured interviews of 15 participants and an inductive thematic analysis to analyze the data.

**Results:** Collectively, the interviews revealed two motivators for participating in the work role: 1) participating in the work role because it formed part of the participant's self-schema (a cognitive framework that includes one's experiences and beliefs about oneself) and 2) participating in the work role because it made it possible to achieve a valued outcome.

**Discussion:** The identification of important motivators for maintaining engagement in valued social roles, such as employment, despite moderate to severe persistent back pain can help inform the development of more successful disability and pain management programs and related treatment strategies. Two motivators worthy of further exploration with patients are: how engaging in a desirable social role fits into their self-schema and what valued outcomes they receive from such engagement. Further back pain research on the characteristics and strategies of individuals experiencing persistent back pain who participate in their social roles (e.g., maintain a job) at a high level is needed.

## Validation of a coding algorithm based on version 10 of the international classification of disease for classifying spinal surgery patient diagnosis

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**Introduction.** Administrative data are frequently used to report procedure rates, surgical safety outcomes, and costs in the management of spinal surgery. This approach often relies on codes from the *International Classification of Diseases (ICD)* to group patients into clinically meaningful diagnosis groups. In 2015, version 10 of the ICD was adopted by hospitals in the United States. However, the accuracy of ICD-10 based coding algorithms to classify spine patients by diagnoses has not been reported.

**Methods.** We performed a retrospective analysis of spine surgery patient's medical chart review linked to hospital administrative claims data at a single institution. We examined the validity of an ICD-10 based coding algorithm for classifying patients by diagnosis. We report the sensitivity and specificity of the cross-classification of diagnoses ascertained from the ICD-10 coding algorithm with those abstracted by five surgeons from the medical chart, considered to be the "gold standard". We examined the accuracy of the coding algorithm to classify lumbar disc degeneration, disc herniation, spinal stenosis, spondylolisthesis or scoliosis. Discordance between coding algorithm and chart reviews were examined in an effort to improve the algorithm.

**Results.** We randomly selected 147 out of 724 spine surgery cases performed at a single institution in 2016. Each case was assigned to one of five participating surgeons who performed a medical chart abstraction. Chart abstraction was performed to capture patient diagnosis, as well as level-by-level procedures, approach and instrumentation. We excluded 30 cases whose procedure did not involve the lumbar region. By diagnosis, the specificity of the ICD-10 based coding algorithm was excellent: 81.2% for disc degeneration, 74.4% for disc herniation, 93.9% for stenosis, 95.9% for spondylolisthesis, and 96.5% for scoliosis. However, with the exception of disc herniation, the sensitivity of the algorithm was low: 36.7% for disc degeneration, 96.2% for disc herniation, 27.7% for stenosis, 38.1% for spondylolisthesis, and 45.2% for scoliosis. Misclassifications were generally due to the coding algorithm attributing a more specific complex pathology to the case.

**Discussion.** An ICD-10 claims-based algorithm for grouping lumbar spine surgery patients by diagnosis has high specificity, but low sensitivity. Research efforts should seek to improve upon the false negative classification of diagnosis and account for this potential misclassification.

## **Transosseous intradiscal screw fixation in lumbar reconstruction; clinical experience with an alternative in osteoporosis fixation**

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**Introduction;** This is a retrospective review of a prospective clinical case series undertaken to review the clinical and imaging results of transosseous screw fixation in lumbar reconstruction performed on clinically osteoporotic patients. Biomechanical data support a number of alternatives in augmenting pedicle screw fixation in osteopenic patients including cement augmentation, expansile or surface-coated screws, and transcortical or cortical-bone trajectory. All these bring incremental cost and/or potential risk to the surgery. Transosseous multicortical fixation purposefully targeting pedicle screws through the next upper end-plate to sit within the disc space shows biomechanical advantage comparable to the alternatives but to date is not reported clinically.

**Methods;** This is a retrospective review of a prospectively accumulated case series where the technique was used in cases of pedicle-screw fixation (PSIF) without interbody implants when clinical osteopenia was encountered at surgery.

**Results;** In seventy-four cases reviewed at an average of five years after surgery there was no screw lucency or accelerated disc degeneration observed and clinical results were good with no undue reports of pain that might have related to the presence of screws protruding into the disc spaces within the confines of the constructs.

**Discussion;** In adult reconstructive practice this technique proved effective in providing stable and secure fixation at the five-years point. There was no screw lucency noted, no acceleration of disc degeneration in the instrumented discs and no incremental pain complaints in the instrumented population. Transosseous intradiscal screw fixation is a potentially viable alternative in osteoporosis lumbar stabilization.

## Comparing the incidence of lumbar spondylolysis between a general population and patients with lumbar degenerative disease who underwent lumbar spine surgery

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**Introduction:** In adolescent patients with acute lumbar spondylolysis, bony union can be expected with adequate conservative treatment. However, bony union is not always achieved. Understandably, acute spondylolysis patients (or their parents) may have justified anxiety about their future. In some cases, especially those involving high-level athletes, patients resist accepting long-term conservative treatment because they do not want to stop playing sports. These patients have to make a difficult decision. Although it is known that spondylolysis patients have higher future incidence of disc degeneration and spondylolisthesis, it is not known whether the risk of developing severe lumbar degenerative disease requiring surgery increases in these patients. Last year, we presented the results of our investigation of the incidence of spondylolysis in a general population (6.4%; 37/580 cases). We hypothesized that the incidence of spondylolysis in patients who underwent surgery for lumbar degenerative diseases would be higher than that in the general population. Thus, we retrospectively examined the incidence of spondylolysis in patients with lumbar degenerative disease who underwent lumbar spine surgery, and compared these results with the incidence of spondylolysis in the previously-reported general population.

**Methods:** Of 366 patients with lumbar degenerative disease who underwent lumbar spine surgery in our institution, 354 patients had preoperative computed tomography of the lumbar spine and were included. Patient age, sex, and spinal disease state (disc herniation, spinal stenosis, spondylolisthesis, and others) were reviewed and whether or not they had spondylolysis was determined. The incidence of spondylolysis was calculated and compared with that of the previously-reported general population.

**Results:** Mean age (63.2 years-old) and men/women ratio (199 men/155 women) of the 354 patients did not differ significantly from the data of the previous study of a general population (64.4 years-old; 336 men/244 women). The 354 patients showed incidence of lumbar spondylolysis (6.5%) similar to that of the general population (6.4%). The incidence of spondylolysis in each disease state was as follows; lumbar disc herniation (8.9%, 10/112 patients); spondylolisthesis (6.8%, 9/133 patients); spinal stenosis (2.0%, 2/101 patients); and others (25 %, 2/8 patients). Patients with disc herniation ( $p=0.058$ ) and spondylolisthesis ( $p=0.087$ ) showed a non-significant tendency toward higher incidence of spondylolysis compared to patients with spinal stenosis.

**Discussion:** The incidence of spondylolysis varies among ethnic groups (3.5-54%). A limitation of this study was that the incidence was compared between two different populations. The present data were compared with data from our previous study, which did examine the incidence of spondylolysis within the same medical care zone. Our results indicate that the rate of patients who develop lumbar degenerative diseases requiring future surgery may not increase, when bony union is not achieved in acute spondylolysis patients. Our results also suggest that spondylolysis patients have a tendency to require surgery for disc herniation or spondylolisthesis more frequently than for spinal stenosis. When we treat patients with acute spondylolysis, the first aim of treatment is fracture healing. However, when patients choose not to stop sports activity or conservative treatment fails, sufficient information about prognosis should be provided to avoid anxiety.

## **A comparative study of early fusion status after PLIF with cortical bone trajectory screw fixation between carbon peek cages and titanium-coated peek cages**

**Hironobu Sakaura, Atsunori Ohnishi, Akira Yamagishi, Tetsuo Ohwada**

**INTRODUCTION:** We recently reported that PLIF using cortical bone trajectory screw fixation (CBT-PLIF) provided better postoperative improvement of clinical symptoms and reduced the incidence of symptomatic adjacent segment disease compared with PLIF using traditional pedicle screw fixation (PS-PLIF) [1]. However, the fusion rate was relatively lower after CBT-PLIF than after PS-PLIF, although no significant difference was found [1]. Since we expected that the titanium-coated PEEK (TP) cage could improve the successful fusion rate after CBT-PLIF, we changed from carbon PEEK (CP) cages to TP cages in January 2016. We thus compared early fusion status, including the incidence of vertebral endplate cysts (cyst signs), between CBT-PLIF using TP cages and that using CP cages.

**METHODS:** The subjects were 36 consecutive patients who underwent single-level CBT-PLIF with TP cages for degenerative lumbar spondylolisthesis (TP group). As a historical control group, 92 consecutive patients who underwent single-level CBT-PLIF with CP cages for the same pathological condition were enrolled (CP group). Clinical symptoms were assessed using the Japanese Orthopaedic Association (JOA) score before surgery and at 1-year follow-up. None of age at the time of surgery, gender and preoperative JOA score showed significant differences between the 2 groups. On MPR-CT at 6months after surgery, cyst signs were evaluated and classified into diffuse or local cysts. Early fusion status was assessed by dynamic plain radiographs and MPR-CT at 1-year postoperatively.

**RESULTS:** The mean JOA score improved significantly from 13.0 points before surgery to 22.8 points at 1 year after surgery (Mean recovery rate, 62.8%) in the TP group, and from 13.9 points preoperatively to 23.7 points at 1-year follow-up (Mean recovery rate, 65.6%) in the CP group ( $P>0.05$ ). The incidence of cyst signs was 38.9% in the TP group and 66.3% in the CP group ( $P<0.01$ ). The rate of a positive diffuse cyst was 16.7% in the TP group and 32.6% in the CP group ( $P=0.072$ ). The early fusion rate was 83.3% in the TP group and 79.3% in the CP group ( $P>0.05$ ). Combining the 2 groups, 22 of the 36 patients (61.1%) with diffuse cysts had non-union at 1 year after surgery, whereas non-union at 1 year after surgery was found in only 2 of the 39 patients (5.1%) with local cysts and in only 1 of the 53 patients (1.9%) without cyst signs ( $P<0.01$ ).

**DISCUSSION:** The early fusion rate at 1 year after surgery was not significantly different between the 2 groups. However, in the TP group, the incidence of a diffuse cyst, which is a significant predictor of non-union at 1-year postoperatively, decreased to about half that of the CP group. These results indicate that TP cages, which provide greater early postoperative fixation strength than CP cages and have osteoconductive activity, may improve the fusion rate at follow-up longer than 1 year after surgery.



## Is bone non-union, vertebral deformity, or spino-pelvic malalignment the best therapeutic target for amelioration of low back pain after osteoporotic vertebral fracture?

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**Study Design.** Prospective observational study.

**Objective.** To identify independent risk factors for residual low back pain (LBP) following osteoporotic vertebral fracture (OVF).

**Summary of Background Data.** Fracture non-union has been proposed as the primary cause of residual LBP following OVF. However, LBP can occur even when union is maintained. Other reported causes of LBP after OVF include vertebral deformities and spino-pelvic malalignment.

**Methods.** Fifty-nine patients with new single-level thoracolumbar OVF who had not received previous osteoporotic treatment were enrolled. Conservative treatment was conducted using soft lumbosacral orthosis plus osteoporosis drugs, either weekly alendronate (BP) or daily teriparatide (TPD). Oswestry Disability Index (ODI) and other pain scores, kyphosis of fractured vertebra, and multiple spino-pelvic parameters were assessed at admission and periodically during treatment. Radiographic union was evaluated independently by three specialists at 24 weeks post-admission. Residual LBP was defined as ODI>40% at 24 weeks, and patients were divided accordingly into LBP (n=14) and Cured (n=45) groups. Temporal changes and statistical associations among variables were examined and multivariable analysis conducted to identify independent risk factors for residual LBP.

**Results.** Union rate was significantly higher in the Cured group compared to the LBP group (82% vs. 50%; P=0.031). Alternatively, kyphosis was higher in the LBP group ( $26.3^{\circ}\pm 2.3^{\circ}$  vs.  $19.4^{\circ}\pm 1.3^{\circ}$ ; P=0.012), as was age ( $77.1\pm 2.0$  vs.  $72.4\pm 1.1$  years, P=0.046) and malalignment (*pelvic incidence minus lumbar lordosis*,  $27.1^{\circ}\pm 3.9^{\circ}$  vs.  $19.2^{\circ}\pm 2.2^{\circ}$ ; P=0.084). Past vertebral fracture incidence was lower in the LBP group (11% vs. 36%, P=0.187). Multivariable analysis identified kyphosis (OR=8.07) and past vertebral fracture (OR=6.9) as independent risk factors for residual LBP. Non-union correlated with kyphosis progression (AUC = 0.908).

**Conclusions.** Kyphosis is the predominant factor leading to residual LBP after OVF, while non-union is the main driver of kyphosis progression. Spino-pelvic malalignment is not an independent risk factor for LBP after OVF.

## Debridement and indwelling irrigation with diluted gentamicin solution for postoperative spinal infection

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**Introduction:** Surgical site infection (SSI) after spinal surgery is a severe complication. It places significant burden to the patients and health care system. SSI significantly increased the morbidity, mortality and health care cost. Thus, the appropriate treatment of SSI is of vital importance.

The standard management of SSI is completely debridement of the necrosis tissue, irrigation with large amount of normal saline, and then intravenous usage of sensitive antibiotics for six weeks, if the causative pathogen is drug resistant, the intravenous antibiotics should be vancomycin persisted for eight weeks. After intravenous antibiotic therapy, the patients were given oral antibiotics. However, long-term antibiotic use will increase the possibility of antibiotic resistant organisms.

In this study we present a new method for the eradication of surgical site infection after instrumented spinal surgery. We aimed to evaluate the therapeutic efficacy of surgical debridement and continuous indwelling irrigation with diluted Gentamicin in the treatment of deep SSIs after instrumented spinal surgery.

**Methods:** 22 patients were retrospectively enrolled in this study. All the patients were underwent debridement and continuous indwelling irrigation with diluted gentamicin solution. Clinical outcomes were assessed by careful physical examination, Macnab criteria, periodic serologic testing to determine whether the infection was successfully cleared.

**Results:** Causative bacterias were identified in 95.5% (21) of 22 patients. The mean duration of indwelling irrigation were 17.9 days. Intravenous antibiotics after debridement continued for an average of 27.8 days. The average number of debridement were 1.3. Erythrocyte sedimentation rate took an average of 21 days to become normal. The average time of elevated C-reactive protein return to normal were 30 days. The mean time of white blood cell (WBC) return to normal were 25.7 days. The mean time to normal body temperature were 17 days. Implants in 72.7% (16) of the 22 patients were retained. 86.4% (19) of the 22 patients were satisfied with their relief of back pain. 3 of the 22 patients who suffered from resistant bacterias or multiple infections had residual low back pain. No surgery related major complications were found.

**Discussion:** Debridement and continuous indwelling irrigation with diluted gentamicin solution were effective in the treatment of deep SSIs after instrumented spinal surgery. This method can effectively shorten the intravenous antibiotic use. However, it may not be amenable for multiple infections and infections caused by drug-resistant bacterias.

## Disruption of erector spinae aponeurosis and facet injury do not alter the passive mechanics of spine muscles after four weeks of recovery in a rat

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**Introduction:** Spine muscles are critical for generating movement of the spine while maintaining spine stability. In full trunk flexion, these muscles develop substantial passive forces. Muscles are highly adaptive to changes in their mechanical environment including increased or decreased use, injury, and denervation. Specifically, the passive mechanical properties of spine muscles are known to respond to intervertebral disc degeneration<sup>1</sup> and spinal ligament mineralization<sup>2</sup>. The purposes of this study were to determine if the passive mechanical properties of spine muscles were altered by (1) mechanical disruption of the thoracolumbar fascia and erector spinae aponeurosis and (2) facet joint injury. It was hypothesized that damaging the thoracolumbar fascia and the erector spinae aponeurosis would initiate fibrotic changes and increase the passive mechanical properties of multifidus and erector spinae muscles. Facet injury was hypothesized to further increase the passive mechanical properties of multifidus in order to stabilize the injured joint.

**Methods:** Male Sprague Dawley rats were randomly assigned to three groups (Control n = 6, Incision n = 8, and Injury n = 8). The thoracolumbar fascia and erector spinae aponeurosis were cut in the Incision and Injury groups to expose the left L5/L6 facet joint. In the Injury group, this facet was additionally compressed for three minutes to induce facet injury and cartilage degeneration. Twenty-eight days after surgery, rats were sacrificed and muscle samples were harvested from multifidus as well as lumbar and thoracic erector spinae for mechanical testing. The passive elastic modulus and passive muscle stress of single muscle fibres and bundles of ~6-10 fibres were tested throughout the physiological range of sarcomere lengths (1.8–3.7  $\mu\text{m}$ ). Facet injury and cartilage degeneration were evaluated using safranin-O/fast green stained sections through the L5/L6 facet joints.

**Results:** Histological staining revealed mild cartilage degeneration and bony remodelling in the Injury group. However, the hypotheses that either (1) disruption of the thoracolumbar fascia and erector spinae aponeurosis (Incision group) or (2) the addition of facet compression (Injury group) would increase the passive elastic modulus and stress of surrounding muscles were rejected. There was no effect of surgery (Incision or Injury) on the passive elastic modulus ( $p = 0.6597$ ; Figure 1A). Passive muscle stresses were also not different between surgical groups at any sarcomere length ( $p > 0.7043$ ; Figure 1B-D).

**Discussion:** Disruption of the thoracolumbar fascia and erector spinae aponeurosis and mild facet injury do not lead to measurable changes in passive muscle mechanical properties within 28 days. This has positive consequences for posteriorly approached spine surgeries, where damage to the thoracolumbar fascia and erector spinae aponeurosis is necessary. These findings contribute to our understanding of how spine muscles are acutely affected by injury and by fundamental aspects of the initial stages of spine surgery.

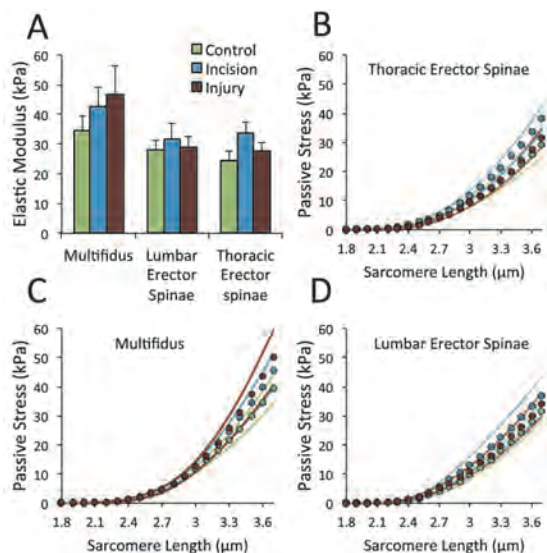


Figure 1: (A) Mean (+ SEM) passive elastic moduli evaluated at a sarcomere length of 3.2  $\mu\text{m}$ . (B-D) Passive stress within spine muscles at physiological sarcomere lengths. Depicted results are from bundles of ~6-10 muscle fibres encased in extracellular matrix.

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## **Intraoperative navigation decreases the risk of reoperation for implant-related complication following spinal fusion surgery**

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**INTRODUCTION:** Although spinal fusion surgery with intraoperative navigation is thought to have advantages on the accuracy for placement of spinal instruments, few large-scale study regarding the impact of intraoperative navigation on clinical outcomes following spinal fusion surgery has been reported. The purpose of this study was to elucidate impact of navigation on reoperation for implant-related complication or surgical site infection (SSI).

**METHODS:** The data of patients who underwent elective spinal fusion surgery from July 2010 to March 2013 were abstracted from the Diagnosis Procedure Combination database, a nationwide administrative inpatient database in Japan. The authors examined patient age, sex, body mass index (BMI), smoking status, Charlson Comorbidity Index (CCI), renal dialysis, blood transfusion, duration of anesthesia, hospital type, hospital volume, surgical site and use of intraoperative navigation. Multivariate analysis was performed to calculate the odds ratio (OR) for the occurrence of reoperation for implant-related complication and SSI, with adjustment for patient background characteristics.

**RESULTS:** A total of 42,878 eligible patients were identified. The mean age was 65.1 years (SD 13.2 years). Among all patients, 21,370 patients (49.8%) were male and 3,263 patients (7.6%) underwent spinal fusion surgery with intraoperative navigation. Overall, reoperation for implant-related complication occurred in 292 patients (0.68%), while reoperation for SSI in 383 patients (0.9%). Multivariate analysis showed reoperation for implant-related complication was associated with BMI, blood transfusion, duration of anesthesia, surgical site, and use of intraoperative navigation. Also, it revealed that reoperation for SSI was associated with age, sex, BMI, blood transfusion, duration of anesthesia, surgical site, hospital type and CCI. The risk of reoperation for implant-related complication was significantly lower in patients with intraoperative navigation compared to those without navigation (OR 0.613, 95% confidence interval 0.387-0.971), while use of navigation was not significant risk factor of the risk of reoperation for SSI.

**DISCUSSION:** In this nationwide database analysis, intraoperative navigation decreased the risk of reoperation for implant-related complication following spinal fusion surgery.

## A novel quantitative computed tomography bone mineral density assessment of the sacrum does not predict sacral fractures following instrumented spinal fusion

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### INTRODUCTION

Postoperative sacral fractures are a rare but potentially devastating complication. Long-fusion constructs including the sacrum that do not extend to the pelvis may result in sacral fractures. Osteoporosis has been proposed as an important risk factor, however, data supporting this is primarily anecdotal. The objective of this study was to evaluate the association between preoperative bone mineral density (BMD) of the sacrum and the occurrence of sacral fractures following lumbar instrumented spinal fusion.

### METHODS

Patients with sacral fractures following posterior instrumented spinal fusion including the sacrum were retrospectively identified and matched 2:1 with nonfracture controls based on sex, age and number of levels fused. Patients with concurrent spinopelvic fixation or missing preoperative CT imaging were excluded. Standard quantitative computed tomography (QCT) measurements at the L1 and L2 vertebra and additional experimental measurements of the sacrum, including the S1 body and the sacral ala, were performed.

### RESULTS

Twenty-one sacral fracture patients had preoperative CT imaging and were matched to nonfracture controls. The groups were well matched with respect to sex, age and number of levels fused. Standard measurements at L1/L2 showed no significant difference between the fracture and the control group (109.9 mg/cm<sup>3</sup> vs. 116.4 mg/cm<sup>3</sup>, p=0.414). Similarly, there was no significant BMD differences between the fracture and control group using the experimental measurements of the S1 body (183.6 mg/cm<sup>3</sup> vs. 176.2 mg/cm<sup>3</sup>, p=0.567) and the sacral ala (8.9 mg/cm<sup>3</sup> vs. 4.8 mg/cm<sup>3</sup>, p=0.616) (Table 1). Univariate conditional logistic regression analysis revealed that BMD of the L1-L2 body, the left and right sacral ala and the S1 body were not associated with the odds of experiencing sacral fractures. However, the odds of experiencing a sacral fracture was approximately 6 times higher for obese patients compared to normal or underweight patients. After controlling for BMI in multivariate conditional logistic regression models, BMD of the L1-L2 body, the left and right sacral ala and the S1 body was still not significantly associated with the odds of experiencing sacral fractures.

### DISCUSSION

To our knowledge this is the first study to assess the association of preoperative BMD measured by QCT with sacral fractures after spinal fusion. Our data does not show any significant difference in BMD utilizing both standard and experimental measures between the study groups. Obesity, however, was associated with higher odds of experiencing postoperative sacral fractures. These results are in line with previous case series reporting only a few patients with osteoporosis who sustained sacral fractures. BMD as a measure of bone quantity, rather than bone quality, may not be as important in these fractures as previously thought. Besides BMD contributing to bone strength and fracture risk, qualitative markers including micro- and macro-architecture, material properties, and bone turnover might play a role in this specific fracture type. In conclusion, factors beyond preoperative BMD might be responsible for the development of sacral fractures following instrumented spinal fusion. An additional study to closer define these factors is currently being performed.

Table 1 Description of the study population

Characteristics	Cases N=21	Controls N=42	P-value
Gender, N(%)			
Females	16 (76.2)	32 (76.2)	
Males	5 (23.8)	10 (23.8)	*
Age, yr., Mean(SD)	66.4 (8.5)	65.3 (7.9)	0.601
# of levels fused, mean (SD)	5.6 (2.0)	5.1 (2.4)	0.517
BMI, mean (SD)	30.0 (7.4)	26.4 (5.0)	0.027
BMI, %			
Underweight/Normal	6 (28.6)	14 (33.3)	
Overweight	4 (19.0)	25 (59.8)	
Obese	11 (52.4)	5 (11.9)	0.002
PI-L1, mean(SD)	34.1 (18.4)	35.8 (15.4)	0.693
PT, mean(SD)	26.3 (9.3)	26.2 (9.9)	0.981
L1, mean(SD)	109.9 (22.5)	116.9 (27.5)	0.170
L2, mean(SD)	109.9 (21.6)	115.9 (27.6)	0.491
Average L1-L2, mean(SD)	109.9 (25.7)	116.4 (26.6)	0.414
Ala Right, mean(SD)	8.8 (37.6)	7.6 (28.8)	0.657
Ala Left, mean(SD)	8.9 (33.4)	1.9 (28.5)	0.191
Average Ala, mean(SD)	8.9 (35.0)	4.8 (27.8)	0.616
S1, mean(SD)	183.6 (44.0)	176.2 (50.8)	0.567

\* Matched on gender

## Evaluation of physical activity before and after lumbar surgery using wearable activity trackers

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**INTRODUCTION:** In evaluating the therapeutic effects of lumbar surgery, most frequent methods of patient-based outcome scores are sometimes insufficient as they lack in objective evaluation of the transition of quality of life (QOL) before and after surgery. Recently the evaluation of physical activity using various devices is attracting attention as a new QOL evaluation method for analysis of daytime activity and sleeping style. A wearable accelerometer (actigraph; Ambulatory Monitoring, Inc.) is a device that captures daily physical activity mentioned above. The purposes of this study were to investigate physical activity measured with an actigraph in patients and to objectively evaluate the amount of activity changes before and after surgery.

**METHODS:** The subjects were 50 patients who received a lumbar spine surgery. All the participants wore a wrist actigraph before and 1, 3, and 6 months after surgery. For analysis of accumulated data, Cole and Kripke's sleep/wake prediction algorithm was used. The daytime average body movement frequency (d movement) in each period was measured and compared with each period. The relationship between the d movement and the lower limb muscle mass, the Japanese Orthopedic Association Back Pain Evaluation Questionnaire (JOABPEQ) score, Oswestry Disability Index (ODI), Roland-Morris Disability Questionnaire (RDQ) score, and visual analog scale (VAS) score were also investigated before and 6 months after surgery.

**RESULTS:** Before surgery, the d movement correlated with the lower limb muscle mass ( $p < 0.05$ ) but not to patient-based outcome and low back pain VAS. The d movement was 0.77 ( $p < 0.01$ ) in 1 month, 0.91 in 3 months, and 1.28 ( $p < 0.05$ ) in 6 months after surgery compared with before surgery. Although it decreased in 1 month, improvement was found 3 months after surgery. Changes in d movement during 1 month, 1 month after, and 3 months after surgery showed very strong correlations of  $R = 0.81$  and  $R = 0.95$ , respectively. On the other hand, no correlation was found between changes in d movement, lower limb muscle mass, and patient-based outcome changes.

**DISCUSSION:** In the present study, the amount of physical activity in lumbar surgery decreased in comparison with that before surgery at 1 month after surgery, and improvement was observed 3 months after surgery. Although the pain improved from the early stage of surgery, it is suggested that it takes time to improve ADL because the amount of physical activity immediately after surgery accidentally decreases from surgical invasion and physical strength reduction due to resting. In addition, we found no association in patient-based outcome and amount of activities. This amount of activity evaluation by actigraph in the QOL analysis of before and after lumbar spine surgery can provide us supplemental data regarding the real QOL/ADL status of the patients which are not available using the traditional questionnaire, suggesting that it can be one of the future new QOL/ADL evaluation methods.

**GP104**

**The prevalence of diffuse idiopathic skeletal hyperostosis (DISH) of the whole spinal computed tomography for the 1189 subjects**

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**INTRODUCTION:** Diffuse idiopathic skeletal hyperostosis (DISH) is a degenerative disease in which spinal longitudinal ligaments and entheses gradually become ossified, proposed by Resnick et al in 1975. Recent a few analysis of CT has reported that the prevalence of Japanese is 8.7% -27.1%. However, these data are also analysis using chest-abdominal CT, there is no report evaluated by whole spinal CT. Therefore, the aim of this study was to investigate the prevalence and characteristic of DISH by whole spinal CT of trauma patients examined in emergency critical care.

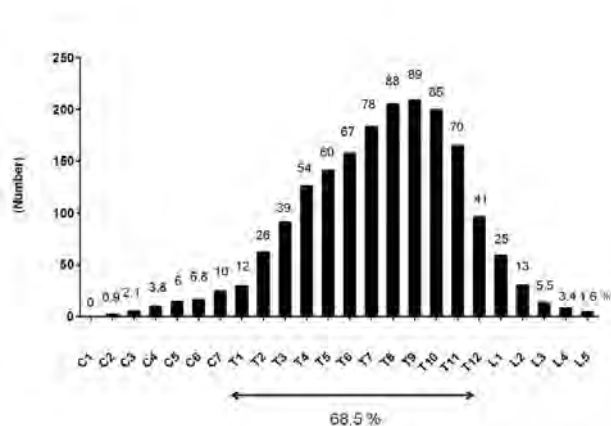
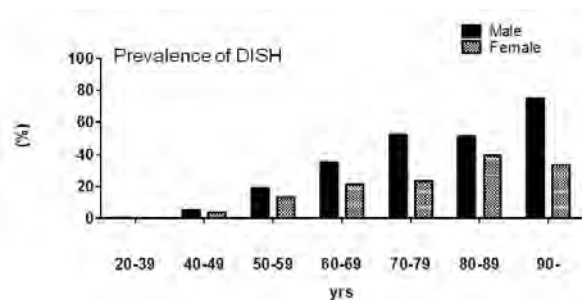
**METHODS:** The subjects of this study were the traumatic patients who have undergone whole spinal CT based on the initial clinical practice guidelines for trauma in our institute from April 2015 to August 2017. The age of subjects to be investigated was 20 years old or over. Total 1189 subjects were recruited for the analysis. The numbers of patients in each age decade 20–39, 40–49, 50–59, 60–69, 70–79, 80–89, and ≥90 years were 319, 190, 172, 195, 197, 103, and 13, respectively. The numbers of male and female grouped by decade were 243, 138, 134, 133, 128, 49, and 4, and 76, 52, 38, 62, 69, 54, and 9, respectively.

The presence and distribution of DISH as well as clinical parameters such as age were retrospectively reviewed by distribution of DISH.

**RESULTS:** Of 1189 subjects, prevalence of DISH was 19.8% (235 subjects). The subjects with DISH were significantly older than those without: 70.7 and 49.5 years, respectively ( $P < 0.001$ ). The prevalence of DISH according to the age groups 20–39, 40–49, 50–59, 60–69, 70–79, 80–89, and ≥90 years were 0.3%, 4.7%, 17.4%, 30.8%, 42.1%, 44.7%, and 46.2%, respectively. The prevalence of DISH in subjects aged ≥70 years was 43.1% (135/313), and one in two people had DISH. The prevalence of DISH increased with age in both male and female. The prevalence rates classified by age and sex groups 20–39, 40–49, 50–59, 60–69, 70–79, 80–89, and ≥90 years were 0.4%, 5.1%, 18.7%, 35.3%, 52.3%, 51.0%, and 75.0% in male and 0%, 3.8%, 13.2%, 21.0%, 23.2%, 38.9%, and 33.3% in female, respectively. Furthermore, DISH was located in the thoracic spine in 68.5% and thoracolumbar spine in 20.4% of patients; the prevalence of involvement of the cervical spine and lumbar spine was low. More than 80% of ligamentous ossifications in DISH were located from T8 (n= 206, 88%), T9 (n= 210, 89%) and T10 (n= 199, 85%).

Interestingly, most of the ossification occurred to the right front of the vertebral body, and there were few ossifications in the area in contact with the artery and vein. As the age increased, ossification in the left anterior area appeared.

**DISCUSSION:** The prevalence of DISH based on whole spinal CT was 19.8%. Ossification was noted more often at T8, T9, and T10, and to the right anterior of the vertebral body.



## **Inhibitory effect of anti-human RANKL antibody on pro-inflammatory responses by human intervertebral disc cells**

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**INTRODUCTION:** The receptor activator of nuclear factor kappa B (NF- $\kappa$ B) ligand (RANKL) is well known to regulate the differentiation of osteoclast and bone metabolism. We have shown that the RANK/RANKL/osteoprotegerin (OPG) system is expressed in the human intervertebral disc (IVD) and that the expression of RANKL by human IVD cells was upregulated by interleukin-1 $\beta$  (IL-1 $\beta$ ) stimulation. Furthermore, RANKL enhanced the expression of a pro-inflammatory cytokine and matrix-degrading enzymes in the presence of IL-1 $\beta$  stimulation. From these results, we hypothesized that blocking the effect of RANKL signaling would reduce the expression of the pro-inflammatory cytokine and matrix-degrading enzymes by human IVD cells. The purpose of this study was to evaluate the effects of an anti-human RANKL antibody on the expression of the pro-inflammatory cytokine and matrix-degrading enzymes, as well as NF- $\kappa$ B activation, in the presence or absence of IL-1 $\beta$  stimulation by human IVD cells.

**METHODS:** Human IVD tissues (n=10, average age: 65.5 years-old) obtained from spine surgeries were used in this study. Annulus fibrosus (AF) and nucleus pulposus (NP) cells were separately isolated by sequential enzyme digestion, and cultured in monolayer. To evaluate the effect of anti-human RANKL antibody on the expression of the pro-inflammatory cytokine and matrix-degrading enzymes, the cells were cultured with or without anti-human RANKL monoclonal antibody (Oriental Yeast Co., LTD., Japan) at 0.1 or 1.0  $\mu$ g/ml in the presence or absence of 1.0 ng/ml recombinant human interleukin-1 $\beta$  for an additional 48 hours. The mRNA expression of the pro-inflammatory cytokine IL-1 $\beta$  and matrix-degrading enzymes [matrix metalloproteinase (MMP)-3, -13, and a disintegrin and metalloproteinase with thrombospondin motifs-5 (ADAMTS-5)] were examined using real-time polymerase chain reaction. The concentration of MMP-3 in the medium and the concentration of NF- $\kappa$ B p65 in the nuclear extract of IVD cells were evaluated using an enzyme-linked immunosorbent assay. Differences in quantitative outcome measures were established using one-way analysis of variance with Fisher PLSD post hoc test.

**RESULTS:** IL-1 $\beta$  significantly stimulated the expressions of MMP-3, -13, ADAMTS-5 and IL-1 $\beta$  compared to those of the control group by both AF and NP cells. However, anti-human RANKL antibody significantly downregulated the mRNA expression of IL-1 $\beta$ , MMP-3, -13 and ADAMTS-5 stimulated by IL-1 $\beta$ . In NP cells, anti-RANKL antibody treatment significantly decreased the MMP-3 released into the medium that was stimulated by IL-1 $\beta$ . Similar, but not significant trends were also identified for AF cells. There was a tendency to reduce the activation of NF- $\kappa$ B with IL-1 $\beta$  stimulation by anti-RANKL antibody treatment in both NP and AF cells.

**DISCUSSION:** This study demonstrated that the anti-human RANKL antibody significantly reduced the expression of a pro-inflammatory cytokine and matrix-degrading enzymes in the presence of IL-1 $\beta$  stimulation by human IVD cells. The results of this study suggest that anti-human RANKL antibody has the potential to suppress the catabolic responses induced by pro-inflammatory cytokines, which are considered to be upregulated in degenerated IVDs. Therefore, this study also suggests the potential use of monoclonal anti-human RANKL antibody to suppress the progression of IVD degeneration.



## Protective effects of “locomotion training” exercise against the sagittal malalignment of the spine-pelvis-lower extremity axis in patients with the locomotive syndrome

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**INTRODUCTION:** Locomotive syndrome is a degenerative condition of reduced mobility due to the impairment of musculoskeletal systems. Exercise intervention is effective in improving motor function. Thus, the concept and measures of the locomotive syndrome are spreading throughout Japan as a national health policy target. However, effects of exercise are difficult to assess objectively. It is unknown whether exercise can improve the sagittal spinal alignment that affects the quality of life (QOL). Therefore, a cohort study was designed.

**METHODS:** Eighty-five patients (age, 76.0±6.0 years; male:female=10:75) who fulfilling the Japanese Orthopaedic Association (JOA) criteria for the locomotive syndrome were enrolled in our outpatient clinic and prospectively followed for >6 months. While 44 patients agreed with participating in our rehabilitation program based on the JOA-recommended “locomotion training” (20-min stretching and evaluation of self-exercise achievement once per week for 6 months), 41 patients denied the participation and received medicinal treatment only (NSAIDs, pregabalin, duloxetine, and/or tramadol). Standing whole-spine radiographs to measure the spine-pelvis-lower extremity axis and questionnaires of the ODI and SF-36 to assess the QOL were taken at baseline and >6 months. Postural stability were similarly measured by using a piezoelectric force plate.

**RESULTS:** [Exercise intervention analysis] There were no significant differences in baseline sagittal vertical axis (SVA): 45.8±41.4 mm in the exercise group versus 31.2±37.8 mm in the control group (p=0.09). However, 6-month SVA changes had significant differences: -5.5±20.0 mm in the exercise group versus +5.2±22.6 mm in the control group (p=0.02). These SVA changes during >6 months primarily depend on the lumbar lordosis (LL): +1.5±8.1° in the exercise group versus -1.3±9.1° in the control group (p=0.14). No obvious differences in the ODI and SF-36 were observed. However, force-plate examination exhibited the center-of-pressure area (-0.4±1.8 versus +0.2±1.6 cm<sup>2</sup>, p=0.07), speed (-0.1±0.4 versus +0.1±0.4 cm/s, p=0.03), and distance (-5.1±24.3 versus +6.5±23.3 cm, p=0.03) all decreased in the exercise group after >6-month intervention, indicating improved standing balance. The control group did not show any postural stability improvement.

[SVA analysis] Of 40 patients with baseline SVA ≥40 mm, 12 (30.0%) improved their SVAs to <40 mm, consisting of 10 (25.0%) in the exercise and 2 (5.0%) in the control groups (p=0.16). Baseline SVA was 51.6±10.2 and 79.5±34.0 mm in patients with and without endpoint SVA <40 mm, respectively (p<0.01). Similarly, baseline C2–7 angle was 10.9±6.0° and 19.6±13.0° (p=0.03). Baseline hip-flexion angle was 8.1±2.4° and 11.2±4.0° (p=0.02). Then, 6-month LL changes were +4.6±9.0° and -0.6±8.1° (p=0.08), supporting that increased LL results in SVA improvement. Furthermore, in force-plate examination, 6-month area changes were -1.6±5.3 and +0.2±1.7 cm<sup>2</sup> (p<0.01), suggesting decreased imbalance in patients with SVA improvement.

**DISCUSSION:** This is the first study to demonstrate that JOA-recommended “locomotion training” exercise intervention is protective against the locomotive syndrome-associated radiographic SVA forward shift, which primarily results from the LL increase. Furthermore, exercise facilitated clinical improvement of the standing balance, which also corresponded to SVA improvement. Noteworthy, this study found limited exercise-induced SVA improvement in patients with marked forward SVA shift, hyperlordosis of C2–7, and hip contracture at baseline.

### 30-day emergency department visits after primary lumbar fusion: incidence, reasons, risk factors, and costs

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#### INTRODUCTION

Emergency department (ED) visits are associated with long wait times, high costs, low patient satisfaction, and are the source of almost half of all hospital readmissions.<sup>1-4</sup> ED visits after elective surgery constitute an important determinant of quality and cost of care. No study has previously analyzed 30-day ED visits after lumbar fusion from an etiological and cost perspective. Our objective was to describe the incidence, reasons, risk factors, and costs associated with 30-day ED visits after primary lumbar fusion (PLF) for degenerative pathology in a large national patient cohort.

#### METHODS

A national insurance database was used to study patients with PLFs performed for degenerative pathology of the spine between 2007 and Q3-2015. The incidence of all-cause, cause-specific 30-day ED visits, and ED to inpatient transfer were recorded. Risk factors for ED visits, and ED to hospital transfer were studied using multiple-variable logistic regression analysis. Total and average reimbursements for management of complications in ED, and hospital have been reported.

#### RESULTS

Our cohort included 37,559 patients with a mean age of 66.0± 10.0 years. From the overall cohort, 4,806 (12.8 %) patients had 10,281 ED visits within 30-days after surgery. Of all patients visiting the ED, 945 (19.9%) had multiple (≥3) visits, and 1,466 (30.5%) were admitted to the hospital for management. Common reasons for presentation in the ED were cardio-respiratory complaints (49.4%, n=2,377), and back and/or leg pain (47.7%, n=2,294). Several risk factors for all-cause ED visits (**Fig 1**), multiple ED visits (**Fig 2**), and hospital admission from the ED (**Fig 3**) were identified. Additionally, patients visiting the ED once were far more likely to get transferred to inpatient care than patients with two or more ED visits (OR 44.1, 95% CI: 38.8 – 50.2). Based on our analysis, we propose two subsets of patients utilizing acute-care within 30-days after lumbar fusion (**Fig 4**). The overall ED cost burden was nearly two-thirds as much as hospital readmissions within 30-days (\$6,994,260 vs. \$10,880,999).

#### DISCUSSION

There is a sizable subset of patients that present to the ED for acute care but do not require hospitalization. The reasons and risk factors for presentation in these patients are somewhat different from those of patients requiring readmission. Specifically, poor control of pain and cardio-respiratory symptoms are common reasons for multiple ED visits after lumbar fusion, and reducing these visits will require interventions targeted differently than those for reducing hospital readmission. The overall cost burden of ED encounters was 64% that of hospital readmission, so reducing ED visits has the potential to meaningfully decrease healthcare spending. Additionally, ED visits within 30 days have been associated with lower Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS) scores after lumbar spine surgery.<sup>3</sup> Early return to the ED also reflects poor care transition and fragmented coordination, both at and after discharge.<sup>2,3,5,6</sup> Therefore, focus should not only be directed on reducing hospital readmission but also on decreasing the frequency of ED visits after lumbar fusion to help improve quality and cost of care.

Fig 1. Risk factors for all-cause 30-day emergency department (ED) visits after primary lumbar fusion for degenerative pathology. Humana Ortho database (2007 – Q3 2015).

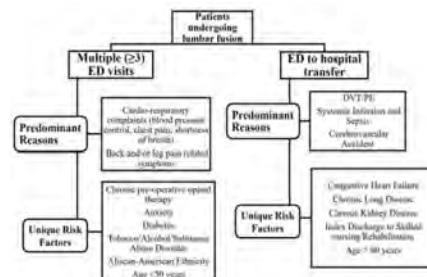
Risk Factor	Adjusted Odds Ratio (OR)	95 % Confidence Interval (CI)	P-value
Pre-operative chronic opioid therapy	1.11	1.04 – 1.18	<0.001
Anxiety disorder	1.16	1.06 – 1.26	<0.001
Depression	1.19	1.10 – 1.30	<0.001
Diabetes	1.09	1.01 – 1.17	0.02
Hypertension	1.15	1.08 – 1.22	<0.001
Congestive Heart Failure	1.22	1.08 – 1.38	<0.001
Ischemic Heart Disease	1.11	1.03 – 1.20	0.004
Chronic Lung Disease	1.16	1.07 – 1.26	<0.001
Chronic Liver Disease	1.18	1.02 – 1.36	0.01
Obesity	1.11	1.02 – 1.21	0.01
Anemia	1.14	1.07 – 1.24	<0.001
Tobacco Use Disorder	1.16	1.08 – 1.28	<0.001
Drug Abuse Dependence	1.23	1.05 – 1.42	0.003
Age <50 years	1.14	1.10 – 1.17	<0.001
African-American Ethnicity	1.20	1.09 – 1.36	0.004
Medicare Advantage Insurance	1.06	1.00 – 1.07	<0.001
>3 Level Fusion	1.32	1.20 – 1.42	<0.001
Anterior Lumbar Fusion	1.42	1.28 – 1.57	<0.001
Front-Back Fusion	1.29	1.12 – 1.45	<0.001
Insurance of Intertbody Cage	1.10	1.03 – 1.18	0.004

Fig 2. Risk factors for 30-day multiple (≥3) emergency department (ED) visits after primary lumbar fusion for degenerative pathology. Humana Ortho database (2007 – Q3 2015).

Risk Factor	Adjusted Odds Ratio (OR)	95 % Confidence Interval (CI)	P-value
Pre-operative chronic opioid therapy	1.21	1.05 – 1.38	0.001
Anxiety disorder	1.36	1.15 – 1.61	<0.001
Diabetes	1.21	1.05 – 1.39	0.01
Anemia	1.30	1.10 – 1.53	0.002
Tobacco Use Disorder	1.44	1.21 – 1.70	0.002
Drug Abuse Dependence	1.53	1.18 – 1.97	0.001
Age <50 years	1.34	1.07 – 1.66	<0.02
Alcohol abuse/dependence	1.45	1.01 – 2.04	0.04
African-American Ethnicity	1.32	1.03 – 1.67	0.04
Medicare Advantage Insurance	1.31	1.06 – 1.63	0.01
>3 Level Fusion	1.32	1.09 – 1.60	0.004
Anterior Lumbar Fusion	1.48	1.21 – 1.79	<0.001
Fusion	1.48	1.21 – 1.79	<0.001
Front-Back Fusion	1.78	1.44 – 2.19	<0.001

Fig 3. Risk factors for 30-day ED to hospital transfer after primary lumbar fusion. Humana Ortho database (2007 – Q3 2015).

Risk Factor	Odds Ratio (OR)	95 % Confidence Interval (CI)	P-value
Hypertension	1.34	1.17 – 1.54	<0.001
Congestive Heart Failure	1.62	1.37 – 1.92	<0.001
Chronic Lung Disease	1.29	1.14 – 1.46	<0.001
Chronic Kidney Disease	1.26	1.10 – 1.45	0.001
Anemia	1.31	1.15 – 1.49	<0.001
Medicare Advantage Insurance	1.39	1.17 – 1.68	<0.001
>3 Level Fusion	1.35	1.17 – 1.57	<0.001
Anterior Lumbar Fusion	1.32	1.12 – 1.57	0.001
Front-Back Fusion	1.39	1.15 – 1.67	<0.001
Index discharge to Skilled Nursing Care/Inpatient Rehabilitation	1.17	1.04 – 1.33	0.01
Age <50 years	1.29	1.08 – 1.54	<0.004



## Association between epidural fat accumulation and metabolic conditions

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**Introduction:** Epidural fat (EF), which surrounds the dura mater, is commonly found along the thoracic, lumbar, and sacral regions. Excess lumbar EF sometimes leads to the compression of cauda equina or nerve root. This condition is usually defined as spinal epidural lipomatosis (SEL). We previously reported that SEL is associated with obesity and hyperlipidemia (1, 2). However, these studies included mainly patients with lumbar canal stenosis. At our facility, individuals undergoing regular medical screening examinations are given the option of a musculoskeletal examination, including magnetic resonance imaging (MRI) of the lumbar spine. This has provided us with clinical data on both metabolic- and lumbar spine-related disorders from a relatively large pool of active adults presenting for routine medical screening. Using these datasets, we aimed to clarify the potential associations between EF accumulation and metabolic conditions.

**Methods:** Clinical data of consecutive subjects undergoing a musculoskeletal examination in addition to regular medical screening between July 2012 and November 2016 were retrospectively reviewed. A total of 329 subjects, comprising 177 men and 152 women, were assessed. Examinations included blood tests, lumbar MRI, abdominal computed tomography (CT), and dual-energy X-ray absorptiometry (DXA). Blood tests included metabolic-related parameters such as high- and low-density lipoprotein, triglycerides, adiponectin, and HOMA-IR. The cross-sectional areas and antero-posterior diameters of EF and of the spinal canal (SC) at each level were measured in axial views of lumbar MRIs, and occupancy and length ratio (EF/SC) were calculated for each level. Metabolic syndrome was defined as previously reported. SEL was defined as  $0.6 \leq$  maximum length ratio (EF/SC).

**Results:** EF/SC occupancy was higher in men than in women at every level and was the highest at L3/4, followed by L2/3, L4/5, L1/2, and L5/S1. EF/SC occupancy was significantly correlated with BMI ( $r = 0.37$ ,  $p < 0.0001$ ), abdominal circumference ( $r = 0.33$ ,  $p < 0.0001$ ), and visceral fat area on CT ( $r = 0.33$ ,  $p < 0.0001$ ), but not with age ( $r = 0.09$ ) or body fat percentage on DXA ( $r = 0.14$ ). Blood tests revealed no association of any parameter with EF/SC occupancy. Finally, subjects were divided into two groups: metabolic ( $n = 59$ , 17.6%) and non-metabolic ( $n = 271$ , 82.4%). EF/SC occupancy was significantly higher in the metabolic group than in the non-metabolic group ( $p < 0.0001$ ). In addition, the prevalence of SEL was significantly higher in the metabolic group (19.0%) than in the non-metabolic group (7.0%) ( $p < 0.005$ ).

**Discussion:** Our results are consistent with those of the previous reports indicating that SEL is more common in men and is associated with obesity. In this study, EF accumulation was also associated with abdominal circumference and visceral fat area, indicating that EF has a similar pathological character to visceral fat. Furthermore, we found a considerable association between SEL and metabolic syndrome. These findings may indicate a novel approach to develop a conservative therapy for SEL.

1. Reference 1. Fujita N, et al. Potential involvement of obesity-associated chronic inflammation in the pathogenesis of idiopathic spinal epidural lipomatosis. *Spine* 2016;41:E1402-7. 2. Ishihara S, et al. Idiopathic Spinal Epidural Fat Accumulation is Associated With Hyperlipidemia. *Spine* 2017; DOI: 10.1097/BRS.0000000000002392.

## Prophylactic muscle flap reconstruction in complex degenerative spine surgery

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### INTRODUCTION

Wound dehiscence following complex multilevel spinal surgery occurs in up to 19% patients and has disastrous consequences. The hardware is exposed, and at-risk for infection - but since it is obligate it cannot be easily removed. Tissues are scarred, attenuated and slow to heal, making secondary reconstruction challenging. Patient-morbidity sky-rockets, as do the costs from prolonged care and secondary surgeries. To avoid these problems we used prophylactic muscle flap (bilateral paraspinous, trapezius or combination) coverage only in 'at-risk' patients with either significant co-morbidities and/or those undergoing complex re-do multilevel spinal fusion with higher propensity for wound complications.

### METHODS

An institutional review board (IRB) approved retrospective analysis of patients who underwent multi-level posterior spinal fusion for degenerative disease or adult spinal deformity, and had prophylactic muscle flap coverage of their wound. Adult (18-85 years) patients who were operated at a single academic institution between August 2016 and February 2017 with regular follow-up of at least six-months were included. Primary and revision procedures of the cervical, thoracic, and/or lumbo-pelvic spine were studied. Patients who had flap coverage after oncological resection, or primary management of previous wound dehiscence/infection were excluded. Spinal fusions were done by orthopaedic surgery board-certified spine surgeons (SNK, EY) and flap coverage was done by a single board-certified plastic surgeon (RC) in all cases.

### RESULTS

A total of 26 consecutive patients with a mean age of 59.7 ±13 years, and 19 (73.1%) females were included. The mean body mass index (BMI) of patients was 31 ±8.6 kg/m<sup>2</sup> (Fig 1). Eighteen (69.2%) patients underwent a revision spinal fusion. The average number of levels operated was 10.2. Paraspinous muscle flap (61.5%), trapezius (3.8%), or a combination of both (34.6%) were procedures used for wound coverage (Fig 2). All wounds healed completely with no complications at an average of 8.4 months follow-up. Only one patient developed a seroma for which IR-drainage was sufficient.

### DISCUSSION

There is a higher risk of complications with increasing number of levels of surgery. Wound dehiscence and surgical-site infections are common, and have been reported in up to 19 % of patients undergoing complex spinal surgery. These complications often require prolonged antibiotics, additional surgery, and prolonged hospital stay for management, all which result in increased morbidity and healthcare costs. As a result, identifying viable ways to reduce complications is of utmost importance. In our experience, prophylactic flap coverage reduces the risk of wound dehiscence in 'at-risk' patients - especially those undergoing re-do multi-level spinal fusion with attenuated/scarred tissues from previous surgery or patients with significant co-morbidities that affect wound healing.

Fig 1. Demographic and clinical profile of included patients

	N(%)		N (%)
<b>Total Patients</b>	<b>26 (100)</b>	<b>Comorbidities</b>	
<b>Age (Mean ± SD)</b>	<b>59.7 ± 13</b>	Hypertension	15 (57.7)
<b>Sex</b>		Hyperlipidemia	10 (38.5)
Female	19 (73.1)	Mental Health	7 (26.9)
Male	7 (26.9)	Diabetes Mellitus	5 (19.2)
<b>Race</b>		Anemia	4 (15.4)
White	22 (84.6)	Chronic Kidney Disease	3 (11.5)
Black	5 (15.4)	Ischemic Heart Disease	2 (7.7)
<b>Insurance</b>		Heart Failure	2 (7.7)
Private	7 (26.9)	History of Malignancy	2 (7.7)
Medicare	18 (69.2)	Obstructive Sleep Apnea	2 (7.7)
Medicaid	1 (3.8)	Chronic Lung Disease	1 (3.8)
<b>BMI (Mean ± SD)</b>	<b>31 ± 8.6</b>	<b>Smoking</b>	
		Never smoked	9 (34.6)
		Quit in last 6 months	5 (19.2)
		Quit longer than 6 months ago	11 (42.3)
		Current smoker	1 (3.8)
		<b>Albumin* (Mean ± SD)</b>	<b>3.2 ± 0.3 **</b>
		<b>Pre-op Hgb (Mean ± SD)</b>	<b>10.1 ± 1.5</b>
		<b>ASA</b>	
		Grade 2	7 (26.9)
		Grade 3	18 (69.2)
		Grade 4	1 (3.8)
		** n=8	

Fig 2. Procedure related profile of included patients

	N(%)
<b>History of previous spine surgery</b>	
Yes	18 (69.2)
No	8 (30.8)
<b>Levels of Surgery</b>	
Thoracopelvic	12 (46.2)
Cervicothoracic	4 (15.4)
Thoracosacral	3 (11.5)
Thoracolumbar	3 (11.5)
Lumbopelvic	2 (7.7)
Lumbar	2 (7.7)
<b>Vertebrae involved (Mean ± SD)</b>	<b>10.2 ± 4.5</b>
<b>Flap type</b>	
Paraspinous	16 (61.5)
Trapezius	1 (3.8)
Paraspinous and Trapezius	9 (34.6)
<b>Flap Coverage</b>	
Bilateral	25 (96.2)
Unilateral	1 (3.8)
<b>Area of Closure (cm<sup>2</sup>) (mean ± SD)</b>	<b>250.3 ± 177.3</b>
<b>Antibiotic powder used</b>	
Yes	8 (30.8)
No	18 (69.2)
<b>Wound Vac used</b>	
Yes	2 (7.7)
No	24 (92.3)
<b>Hospital Stay (days) (Mean ± SD)</b>	<b>9.1 ± 4.6</b>
<b>Discharge</b>	
Home	15 (57.7)
In patient-rehab	4 (15.4)
Skilled Nursing Home	7 (26.9)

## **Efficacy of balloon kyphoplasty for fresh osteoporotic vertebral fractures with poor prognostic factors - a propensity-score-matched analysis using data from the multicenter prospective study**

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**【Introduction】** We previously reported that characteristic magnetic resonance (MR) imaging findings (high-intensity or diffuse low-intensity area in the fractured vertebrae on T2-weighted MR images) predicted an increased risk of delayed union. The purpose of this study was to investigate the efficacy of balloon kyphoplasty (BKP) for treatment of fresh OVF in patients with poor prognostic factors.

**【Methods】** We evaluated 53 patients with fresh OVFs (average age, 79.3 years; 44 female and 9 male) who had a high-intensity or diffuse low-intensity area in the fractured vertebrae on T2-weighted MR images and underwent BKP within 2 months after injury. As controls, 53 patients with fresh OVFs who were matched according to calculated propensity scores in a logistic regression model adjusted for age, sex, and fracture level; had the same poor prognostic factors; and had undergone conservative treatment were selected from the previous prospective study database. The primary outcome was a reduction in ADL by at least a single grade at 6 months after fracture, and the secondary outcomes were improvement in quality of life (physical and mental component summary scores on the Short Form 36), back pain (visual analog scale score), and vertebral body deformity (vertebral body wedging angle and percent vertebral body height).

**【Results】** A decrease in ADL occurred in 5.7% of patients in the BKP group and 32.1% of patients in the conservative treatment (control) group ( $P < 0.05$ ). Improvement in physical component summary score was 17.3 points in the BKP group and 19.3 points in the control group (no significant difference). Improvement in mental component summary score was 13.3 points in the BKP group and 6.3 points in the control group ( $P < 0.05$ ). Improvement in back pain was shown by a visual analog scale score of 48.4 in the BKP group and 44.4 in the control group (no significant difference). Improvement in vertebral body wedging angle in the BKP group was 5.9 degrees, and that in the control group was -6.5 degrees ( $P < 0.01$ ). Improvement in %vertebral body height in the BKP group was 18.3%, and that in the control group was -19.9% ( $P < 0.01$ ).

**【Discussion】** BKP intervention for fresh OVF with poor prognostic factors was more effective than conservative treatment in terms of ADL, QOL, and vertebral deformity 6 months after injury. Our treatment strategy for fresh OVF is to decide BKP intervention depending on the presence or absence of a poor prognostic factor, which can provide the improvement of treatment results for fresh OVFs.

## **Cranio-caudal biostructural asymmetries of vertebral bodies - why vertebral fractures usually involve the superior end plate?**

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**Purpose:** The aim of this study was to determine the structural differences between the superior and inferior halves of the thoracolumbar vertebrae by analyzing the trabecular structures with micro-computed tomography ( $\mu$ -CT) and measuring the bone mineral density with dual-energy X-ray absorptiometry (DEXA).

**Materials and methods:** Forty vertebral bodies (T10 through L2) from 8 cadavers were studied. After dividing the vertebral bodies into superior and inferior halves  $\mu$ -CT images were obtained for analyzing the trabecular structures and bone mineral density was measured by using DEXA scans. During the period from July 2016 to December 2016, the BMD of 20 female subjects aged  $\geq 55$  years were studied and analyzed the differences between superior and inferior halves of the thoracolumbar vertebrae.

**Results:** In the cadaver studies, the trabecular bone volume fraction was  $18.40\% \pm 0.22\%$  in the superior and  $21.35\% \pm 1.24\%$  in the inferior half ( $p = 0.025$ ), the separation between the trabeculae was  $0.81 \pm 0.02$  mm and  $0.76 \pm 0.02$  mm ( $p = 0.046$ ) and the structure model index was  $1.64 \pm 0.02$  and  $1.57 \pm 0.01$  showing a plate structure in the inferior half ( $p = 0.004$ ). The BMD was  $3.20 \pm 0.48$  g/cm<sup>2</sup> and  $3.59 \pm 0.92$  g/cm<sup>2</sup> ( $p = 0.019$ ). The BMD of 20 female subjects was  $0.74 \pm 0.03$  g/cm<sup>2</sup> and  $0.72 \pm 0.03$ g/cm<sup>2</sup> without significant difference.

**Conclusion:** The differences of trabecular structures and BMD between superior and inferior halves of thoracolumbar vertebrae could explain that vertebral fractures usually involve the superior end plate.

### In vivo 3D characterization of the lumbar transverse process orientation and symmetry in healthy and low back pain subjects

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**INTRODUCTION:** Thorough description of the lumbar transverse process (TP) anatomy is limited in the literature; specifically when it comes to length and orientation with respect to anatomical planes. These parameters can vary with pathology and spinal degeneration, particularly TP apophysitis [1], Bertolotti's syndrome [2], fractures [3], facet joint osteoarthritis, low back pain (LBP), etc. Physiologically, the TPs also play an important role as spinal musculature attachment sites, and changes in their orientation may affect spinal biomechanical balance. The objective of this study was to determine the spatial anatomical variations of the lumbar transverse processes and their correlation, if any, with the presence of symptoms of low back pain.

**METHODS:** This IRB-approved study recruited n=88 individuals (mean age 37.6 y.o.; range: 22–59 y.o.) with both healthy and symptomatic LBP volunteers, who underwent lumbar CT scans. The resulting DICOM data was used to create subject-specific lumbar spine models from L1-S1. A custom-written Visual C++ routine detected the tip of the transverse process and also took advantage of the mostly 'tubular' structure of the TP in order to obtain its centroid [4]. These two points defined a vector that was later referred to the three anatomical planes using a coordinate system set on the centroid of the lumbar vertebra posterior wall (Fig. 1). With these references, three angles were computed with reference to each anatomical plane between the projection of the vector ( $R_{TP}$  or  $L_{TP}$ , as appropriate) on the reference plane and an axis that was coplanar with the projected vector on the corresponding anatomical plane. The pairs were (Fig. 2):  $\alpha$ : angle between the projected vector on the transverse plane and the Y axis;  $\beta$ : angle between the projected vector on the sagittal plane and the Z axis;  $\gamma$ : angle between the projected vector on the transverse plane and the X axis. Lastly, the angle in space between both vectors was also calculated. Data is presented in degrees (mean  $\pm$ SD). Level, gender and symptoms effects were sought with ANOVA, and an unpaired Student's t-test was used to evaluate the symmetry on the transverse plane both between transverse plane projection vectors and the angles in space.

**RESULTS:** The angle between both vectors in space was mostly constant by level and showed level dependency, increasing by level. The sagittal angle peaked at L3, and the Coronal angle decayed sharply from L1 to L3 (Left) and to L4 (Right) with a plateau at L4-L5. The remaining factors were also shown to influence the angles.

**DISCUSSION:** To the best of the authors' knowledge, this is the first study describing the inclination and asymmetry of the lumbar TPs in a cohort that includes both normal and symptomatic subjects. The hypothesized influence of LBP symptoms on the TP morphology was shown not to be as acute as initially thought, however our sample size may be a limitation. Beyond spinal degeneration, the biomechanical unbalance possibly linked to asymmetric musculature, may be relevant to scoliosis studies. Larger studies with these specific cohorts are thus warranted.

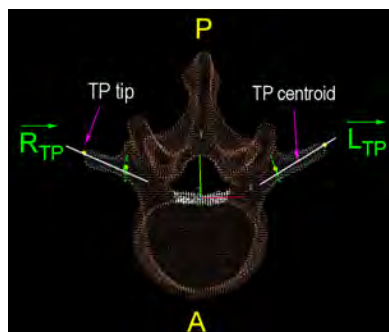


Figure 1. Parameters used to define both TP vectors ( $L_{TP}$  and  $R_{TP}$ , respectively).

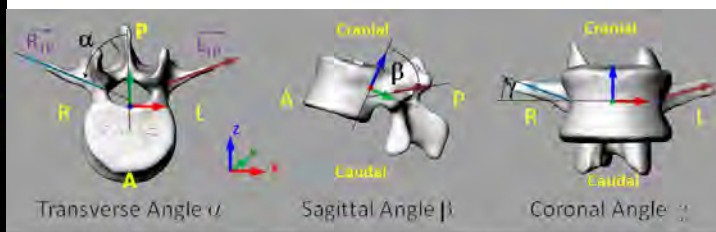


Figure 2. Definition of the angles between the anatomical planes based on the coordinate system set at the posterior wall centroid and the projections of the TP vectors with each of them.

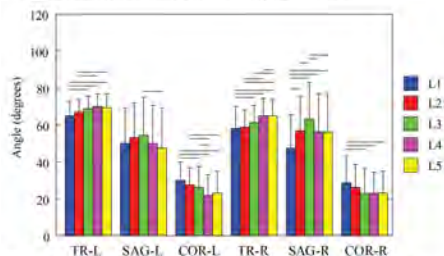


Figure 3. Angles on each anatomical plane and their level-dependency. Error bars span one SD. The bars above the charts show statistically significant differences between groups at  $P < 0.05$ . TR: transverse; SAG: sagittal; COR: coronal. L: left and R: right.

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## Which are the risk factors for implant failures in long-level fixation for thoracolumbar fracture?

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### Introduction

The levels of fixation for thoracolumbar fracture still remain controversial. Load sharing classification was developed to predict the implant failure in short-level fixation. Although long-level pedicle screw fixation and fusion are known to be more stable than short-level fixation, the implant failures and the progression of kyphosis can occur. The aim of this study is to investigate the risk factors of the implant failure risk after long-level fixation for thoracolumbar fracture.

### Methods

We retrospectively reviewed consecutive 126 one-level unstable thoracic or lumbar fractures (T1-L5) that were treated with posterior only, long-level (two-level above and below) instrumentation and fusion. Baseline demographic data was obtained from medical records. Using radiograph, computed tomography and magnetic resonance image, AO type, load sharing score, baseline and post-operative bi-segmental Cobb's angle of fractured vertebra were measured. At the final follow up (Mean 50.5±32.5 months), the presence and type of instrumentation failure, bi-segmental Cobb's angle of fractured vertebra were measured.

### Results

The incidence of instrumentation failure was 6 cases (4.8%), in which the number of screw breakage, rod breakage and de-capping were 3, 2, and 1, respectively. Two rod breakages occurred at fracture level. All screw breakages occurred at mid shaft. There was only 1 case (0.8%) with progressive kyphosis and treated with re-operation with anterior support. Twelve cases were combined with kyphosis (> 20° of bi-segmental Cobb's angle of fractured vertebra at the final follow-up). All cases with instrumental failure had 6 or more load sharing score. The fracture level was L3 in 5 patients and L2 in 1 patient. Among fracture at L3 (n=10), five cases (50%) were combined with instrumentation failure. Another two patients were old (> 60 years) and combined with screw loosening.

### Discussion

Instrumentation failures were quite rarely in long-level instrumentation for thoracolumbar fracture, even with 7 or more load sharing score. With the results of this study, fracture level at L3 with severe comminuted fracture was a risk factor for instrumentation failure and anterior support will be needed with 7 or more load sharing score.



## Inter-rater and intra-rater repeatability and reliability of EOS 3-dimensional imaging analysis in comparison with manual methods

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Sagittal alignment of spine and pelvis is closely related with overall posture of a person and evaluation and treatment of spine disease. So far sagittal curvature was generally evaluated by whole spine standing lateral radiographs for various reasons. However, radiographic system causes distortion from the center to the edges of the radiograph, leading to increasing errors in scale for structures far from the central region. In the last few years, EOS (EOS Imaging, Paris, France) imaging system, a new radiation dose X-ray device, became available for orthopedic applications. EOS gets images in the standing position of patients and limits the distortion of the patient's image occurs at the distance between source and detector.

The patients were selected from a EOS imaging system records. In total, 46 patients (17 females, 29 males; mean age, 34.6 years) were selected in retrospective study who were examined at our hospital between November 2016 and April 2017. The exclusion criteria of subjects were as follows: (1) congenital spinal anomaly or deformity, (2) previous spine, pelvis operation history. Each subject was examined as a part of routine clinical protocol. Full-body standing orthogonal AP and Lat images were obtained using an EOS imaging system, using a standardized arm positioning optimized for sagittal visualization of cervical and thoracic spine regions

Sagittal parameters of spine and pelvis were measured by three examiners (two orthopaedic surgeons, one radiologist) using both manual and EOS method. Manual and EOS measurements were performed three times by each examiner. Means comparison t test, Pearson bivariate correlation analysis, reliability analysis by intraclass correlation coefficients for intrarater and interrater reliability were performed using R package 'irr.'

We found excellent intra-rater reliability and inter-rater reliability for EOS measurements. For intra-rater reliability, ICC ranged from 0.898 to 0.982. For inter-rater reliability, ICC ranged from 0.794 to 0.837. We used paired t-test to compare the values measured by Manual and EOS. There was no statistically significant difference between the two groups of Manual and EOS. Correlation analysis also showed a statistically significant positive correlation for each measurer.

We used the EOS software system to measure the sagittal alignment of the spine and pelvis and want to know the reliability of these measurements. The EOS system showed a higher correlation when compared to the manual method for each researcher, and the EOS system showed excellent reliability in measuring sagittal alignment of spine and pelvis.

## Relationship between sagittal spino-pelvic alignment and the acetabular anteversion angle on computed tomography in patients with hip osteoarthritis

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### INTRODUCTION

The importance of evaluating the sagittal spino-pelvic alignment (SSPA) has been recognized in treatment planning. Lazennec et al. advocated a concept of spine users and hip users: spine users have a high pelvic incidence (PI) and lumbar lordosis (LL) in order to mainly move their spine, which results in low anatomic acetabular anteversion (AAA); hip users have low PI and LL values in order to mainly move their hips, which results in high AAA. The purpose of the present study is to investigate relationship between SSPA and AAA in patients with hip osteoarthritis.

### METHODS

A retrospective comparative cohort study of 427 women who underwent primary total hip arthroplasty (THA) for the treatment of primary hip osteoarthritis was performed. The patients were classified into the following age groups (in years) <60 (n=92), 60–69 (n=148), 70–79 (n=114), ≥80 (n=73). The PI, pelvic tilt (PT), sacral slope (SS), LL, and AAA were measured. Malalignment (PI-LL>20° and PT>30°) was investigated. The patients were classified according to the PI as follows: <40 (n=105), 40–60 (n=256), and PI>60 (n=66) and investigated the relationship between the PI and AAA.

### RESULTS

Elderly patients tended to have a high PT (r=0.66), a low SS (r=-0.94), low LL (r=-0.94), and high AAA (r=0.79) values. The values did not differ to a statistically significant extent according to age or PI (P=0.17). The frequency of PI-LL>20° and PT>30° was 15.7% and 8.0%, respectively, in all patients, 9.8% and 2.2% in the patients of <60 years of age, 10.1% and 6.1% in the patients of 60–69 years of age, 17.5% and 7.9% in the patients of 70–79 years of age, and 31.5% and 19.2% in the patients of ≥80 years of age. Aging increased the degree of malalignment (P<0.05). The AAA was 13.5° in PI<40, 14.1° in PI 40–60, and 18.2° PI>60. The PT was -1.1° in PI<40, 13.9° in PI 40–60, and 26.7° in PI>60. There were positive correlations between the PI and AAA (r=0.92), and also between the PI and PT (r=0.94).

### DISCUSSION

It is necessary to evaluate the SSPA in the elderly. We reaffirmed the importance of taking the SSPA into consideration when planning an operation. It was revealed that patients who have a high PI also tend to have a high AAA. Roussouly et al. reported that patients who have a high PI tend to have a high PT. A high PT result in the onset of pelvic retroversion. Pelvic retroversion causes the AAA to increase because the ventral horn runs less caudally than the dorsal horn. A high AAA is a risk factor for anterior impingement and dislocation of the acetabular component in THA; thus a high PI is a risk factor for anterior impingement and dislocation of the acetabular component in THA.

## Use of MRI muscle cross-sectional area to determine whether lumbar muscle atrophy occurs after long-term brace therapy in early-stage spondylolysis patients

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### Introduction

In patients with early-stage spondylolysis, which is thought to be a stress fracture of the pars interarticularis, bony union can be obtained by using a rigid corset and refraining from sports activity for a long period of time. However, refraining from sports activity with long-term bracing therapy may lead to decreased physical fitness. The aim of this study was to investigate, using MRI, whether lumbar muscle atrophy occurs during rigid corset treatment.

### Methods

Patients (n=9, <19 years-old; 9 males/1 females) diagnosed with unilateral early-stage spondylolysis by MRI and CT were included. Diagnosis of early-stage spondylolysis was made when the lumbar spine pedicle showed bone marrow edema on MRI. Patients who showed bilateral spondylolysis, progressive or terminal stage spondylolysis on CT, and patients who did not refrain from sports activity were excluded. The levels of spondylolysis were L4 in 4 cases and L5 in 5 cases. All patients were treated with a rigid brace for 2-3 months. Before and after bracing treatment, the cross-sectional area of bilateral lower back muscles (multifidus, longissimus, and iliocostalis muscles) and the iliopsoas muscle on MRI was assessed using imaging software (mm<sup>2</sup>: Image J). Each muscle was evaluated at the central portion of the vertebral body and one slice above and below (slice thickness: 4 mm; interslice gap: 0.4 mm; 3 slices in total). The mean time interval between initial and second MRI examinations and the mean cross-sectional area before and after bracing treatment were examined.

### Results

The mean time interval between initial and second MRI examinations was 71.8±14.9 days. Before and after bracing treatment, the mean cross-sectional area of the lower back muscles was 1657.8 and 1691.9 mm<sup>2</sup> and that of the iliopsoas was 1375.6 and 1399.2 mm<sup>2</sup>. The cross-sectional areas of lower back muscles and iliopsoas showed no significant differences between before and after bracing treatment (p>0.05).

### Discussion

Muscle atrophy was not evident after long-term brace therapy in this study. This information is useful for patients because most with early-stage spondylolysis are athletes. Further investigation is needed to clarify whether selective strength training of lower back muscles and the iliopsoas can increase the cross-sectional area of each muscle during brace treatment for early-stage spondylolysis.

## The need to improve prediction of responders and non-responders in elective spine, hip, and knee surgery: a health-economic argument

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### Purpose

Surgeries for joint/spine disorders are among the most frequently performed elective procedures, with growing global annual volumes. Over 1.6 million joint replacement and spinal fusion surgeries were performed in the US in 2012 and 120,000 were performed in Canada in 2014, with corresponding hospital costs of US\$32 billion and CAN\$1 billion respectively. Despite these substantial costs, 20-25% of these procedures result in poor patient outcomes. This suggests that approximately US\$6.4 billion and CAN\$200 million are spent each year on elective joint/spine procedures for people who do not benefit from them. The purpose of this study was to evaluate the one year cost-utility of elective joint replacement and spinal decompression with or without fusion with respect to patient-reported surgical outcome.

### Method

Incremental cost-utility analysis from the hospital perspective, based on a single-centre prospective longitudinal cohort study. Hospital case cost data were obtained for a cohort of 403 elective surgical cases in 2011-2012, comprising inpatient spine (n=48), outpatient spine (n=39), inpatient hip (n=150), and inpatient knee (n=166) procedures. Costs were adjusted to 2016 Canadian dollars. Patients completed the SF-12/36 health status survey before and one year after surgery.

Clinically important improvement was defined as a 4.6-point improvement in SF-12/36 Physical Component Summary score one-year post surgery. This criterion was used to categorize patients as "responders" and "non-responders".

One year incremental cost-utility ratios (ICURs) were calculated for each group as cost per Quality Adjusted Life Year (QALY) gained following surgery. QALYs were determined using SF-6D utility scores before and one year after surgery.

### Results

The cohort was 47% female and had mean age 64 years. Overall, 71% of cases were categorized as responders one year after surgery: 62% of spine cases, 85% of hip cases, and 63% of knee cases.

In the combined group, mean per procedure hospital cost was \$10,937 (SD=\$6,657) and patients gained 0.12 QALY (SD=0.14) in the year after surgery, corresponding to \$89,464 per QALY gained in the year after surgery.

Patients categorized as non-responders had higher mean case cost: \$12,447 versus \$10,319 for responders (p=0.02). Non-responders also had substantially smaller QALY gains at one year, gaining 0.03 QALY versus 0.13 QALY in responders (p<0.01). The resulting one year ICURs varied greatly with responder status: \$64,015/QALY for responder cases compared to \$460,399/QALY for non-responder cases.

Estimates also varied by operative site: responder / non-responder ICURs were \$115,694 / \$1,574,451 for inpatient spine cases; \$23,599 / \$139,362 for outpatient spine cases; \$57,975 / \$118,068 for hip cases; and \$77,761 / \$1,121,714 for knee cases.

### Discussion

Considering the ICUR for all patients, elective joint replacement and spine surgery meet an acceptable threshold for cost-effectiveness. However, the cost-utility estimate for the 29% of patients who do not achieve clinically important change in physical status demonstrates that surgery in this subset of patients is grossly cost-ineffective. This is particularly the case for knee replacement and spinal fusion. These findings provide a strong economic argument for further research in surgical prognostication, and development of real-world predictive analytics tools for joint replacement and spinal surgery.

## Does lumbar spinal stenosis induce fall? A prospective one-year follow-up

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**Introduction:** In the aging society, it is well known that lumbar spinal stenosis (LSS) influences various health problem. The purpose of this study was to clarify the relationship between the presence of LSS and the occurrence of fall within a year.

**Participants and Method:** 1124 participants (389 male, 735 female, most frequent generation: 70 years old level) aged 40 years or over agreed to participate this study. All participants were self-sufficient (living in their own houses without the need for supplemental care and walking independently with or without support such as a cane or a walker). LSS was determined by a validated LSS diagnostic support tool, which is a self-administered, self-reported history questionnaire (LSS-SSHQ) (Konno S. 2007). In 2004, LSS, comorbidities (respiratory disease, diabetes, cardiovascular disorder, cerebrovascular disorder, hypertension), knee and hip OA, and body mass index (BMI) were evaluated. One year later, fall for the past one year was assessed. Related factors of fall for one year were analyzed using the data collected in 2004, in a multiple logistic regression analysis. A p-value of less than 0.05 was considered statistically significant.

**Results:** Only the presence of LSS affected the occurrence of fall for past one-year (odds ratio 1.498, 95% CI = 1.063-2.110).

**Discussion and Conclusion:** We have already reported that LSS was associated with impairment of balance-function evaluated by stabilometer and the occurrence of fall. But that study was a cross-sectional study. From the result of the prospective one-year follow-up study, LSS shows the independent factor for the cause of the fall occurrence. In the aging society, LSS is very important to prevent fall and fracture.

## **Bipolar and anxiety disorders increased the incidence of infection and wound complications after posterior lumbar spine surgery**

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**Introduction:** Several studies have demonstrated poor treatment outcomes and higher medical expenses in various medical fields including spine for patients with psychiatric disorder. To the best of our knowledge, there is no study focusing on the effect of psychiatric disorder on post-operative infection and wound complications following major posterior lumbar spine surgery.

**Methods:** This was a retrospective study using Humana database within PearlDiver from 2007-2016. The presence of post-operative infection and surgical wound complication at one and three month after posterior lumbar spine surgery was recorded. Existence of psychiatric disorders (Major Depressive Disorder, Bipolar, Anxiety, and Schizophrenia) prior to surgery was used in this study. The Chi-Square test was used to calculate p-value, Odd-ratio (OR), and 95% Confidence Interval (95%CI).

**Results:** A total of 64,004 patients (28,995 patients with psychiatric disorder) were included in this study. Patient with no psychiatric disorder developed post-operative infection rate of 1.32% and 1.84% at one and three months respectively. On the other hand, patients with psychiatric disorder developed post-operative infection rate of 2.42% and 3.57% at one and three months respectively with significantly higher risk of post-operative infection (1month: OR 1.85, p-value < 0.001; 3months, OR 1.97, p-value < 0.001). Patients with psychiatric disorder were significantly at a higher risk of developing post-op wound complication than the patients without mental disorders (1month: OR 1.79, p-value < 0.001; 3months: OR 1.92, p-value < 0.001). Patients with Bipolar and Anxiety disorder had up to 5 and 7 time higher odds of developing post-op infection and wound complications compared to the patients without mental disorders.

**Discussion:** Patients with psychiatric disorders, especially bipolar and anxiety disorder, undergoing posterior fusion had a significantly higher rate of post-operative infection and surgical wound complication both at one and three months.

## Population-based study of medical resource usage by patients with lumbar spinal stenosis

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### Introduction

The super-aging society in Japan requires cost-effective use of medical resources. Although more patients are presenting with lumbar spinal stenosis (LSS), the actual cost effectiveness of its treatment is unclear because high-quality evidence is not available. The influence of LSS on medical resource usage should be evaluated in the entire population for a better understanding of usage trends, but this has not yet been investigated. The present study aimed to determine the nationwide usage of medical resources by randomly extracted patients with LSS.

### Methods

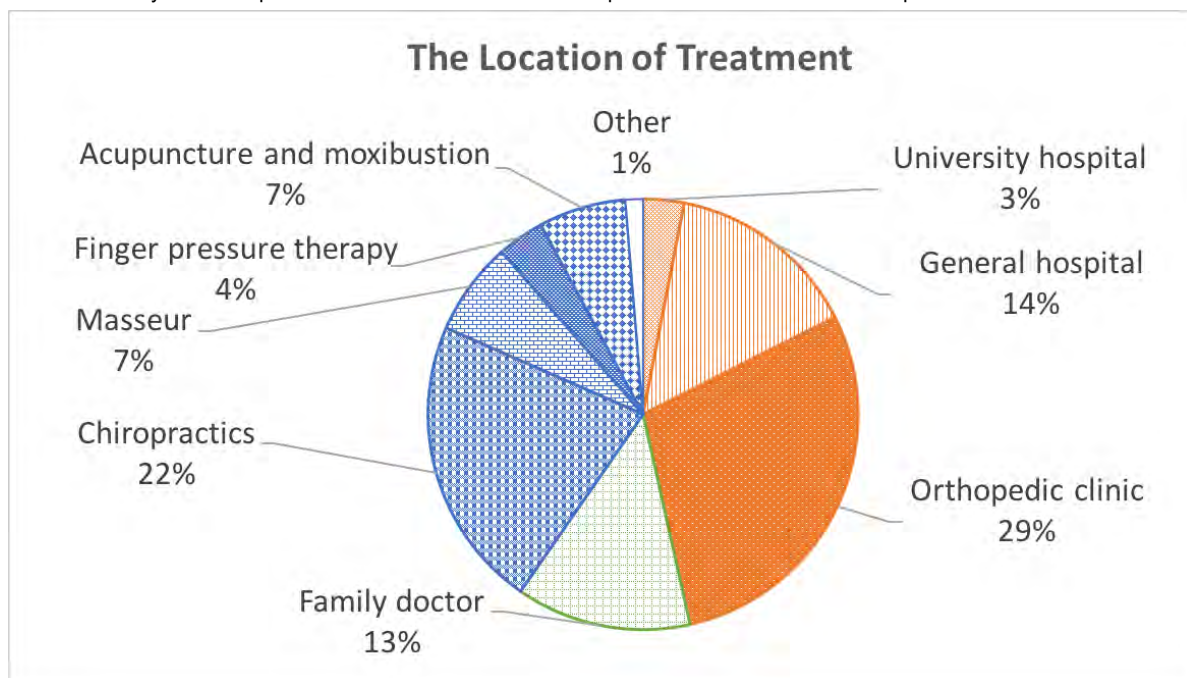
We applied a two-stage stratified random sampling method to select 4,400 Japanese individuals (age 40 to 79 years) to participate in this cross-sectional analysis with a questionnaire. Data were obtained from 2,666 individuals with LSS (male, 47.4%; mean age, 60.0 ± 10.9 years; valid collection rate, 60.6%) defined using the self-administered, self-reported history questionnaire: SSHQ (Konno et al., BMC Musculoskelet Disord, 2007). We investigated the prevalence of LSS, whether or not it had been treated, the location of treatment, rates for outpatients and inpatients, and the number of patients who left or changed jobs due to LSS symptoms.

### Results

The prevalence of presumed LSS was 153 (5.7%) of 2,666 individuals. The numbers of patients who were treated, untreated, and did not respond to the question were 115 (75.2%), 35 (22.9%), and 3 (2.0%), respectively. The rates of treatment venues were 46%, 59%, and 40% for orthopedics, all types of medical institutions, and alternative medicine clinics, respectively. The numbers of treated outpatients and hospitalized patients were 102 (66.7%) and 18 (11.8%), respectively, and the mean numbers of outpatient visits and hospital days were 40.5 ± 55.7 and 46.2 ± 82.3, respectively.

### Discussion

This first population-based study for LSS in Japan found a 5.7% prevalence of LSS in the general population. Among them, 20% did not seek medical help and 40% chose alternative medicine. These findings might imply that patients with LSS are dissatisfied with the treatment received at medical institutions. In addition, 10% of patients left or changed jobs because of LSS symptoms. Intervention for workers with LSS could improve absenteeism and screening for LSS might be helpful. Further investigation is needed to clarify how to improve cost-effective medical care for patients with LSS who seek help elsewhere.



## What is an appropriate rehabilitation program for the symptomatic patients with adult spinal deformity before and after surgery?

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**INTRODUCTION:** Surgical treatment is performed to the symptomatic patients with adult spinal deformity (ASD) unless conservative treatment is successful. Rehabilitation such as stretching and muscle strengthening is undergone as an adjunct therapy before and after the surgery. However, it remains how it can be effective to improve the surgical results. The purposes of the current study were to evaluate the influence of spinopelvic alignment and physical function on the quality of life (QOL) after the surgery and to consider what rehabilitation program should be recommended for the surgical candidates with ASD.

**Design:** Retrospective Cohort Study

**SUBJECTS AND METHODS:** There were 106 patients with symptomatic ASD treated surgically from 2011 through 2015, based on SRS-Schwab ASD classification. Forty-six patients with a minimum of 2-year follow-up were investigated. There were 5 males and 41 females with a mean age of 67 year. All patients were fixed to ilium using S2Al screws. Radiographic measures included sagittal vertical axis (SVA), pelvic incidence (PI), lumbar lordosis (LL), and pelvic tilt (PT). Physical function was represented to measure trunk range of motion (ROM), thoracic and lumbar spinal ROM, trunk muscle strength, hip and knee extension ROM, hip and knee extension muscle strength. Spinal Mouse and hand-held dynamometer were utilized for the measurement. Roland-Morris Disability Questionnaire (RDQ) was measured before and two year after the surgery. For statistical analysis, Wilcoxon signed-rank test was used to compare postoperative data with preoperative ones. Multivariate logistic regression analysis was used to investigate the factors related to postoperative RDQ improvement. The relationship between the spinopelvic alignment and physical function was analyzed using a general linear model. Significance was defined as a *p*-value of less than 0.05.

**RESULTS:** RDQ significantly improved 2 years after the surgery. SVA, PI-LL and PT were also significantly improved. Factors related to improvement of RDQ were preoperative SVA. In other words, the greater the SVA was, the less the RDQ scores were. Based on the preoperative spinopelvic alignment, the subjects were divided into two groups using sagittal modifiers of the SRS-Schwab classification; SVA+ group (n=12) vs. SVA++ group (n=34). The extension ROM of the hip joint was significantly lower in the SVA ++ group (Rt. 5.6 and Lt. 5.3 degrees) than in the SVA + group (Rt. 13.2 and Lt. 12.6 degrees). The extensor muscle strength of the hip joint was also lower in the SVA ++ group (Rt. 9.2 and Lt. 9.6 kg.) than in the SVA + group (Rt. 14.1 and Lt. 13.8 kg.).

**DISCUSSION:** The current study demonstrated that the QOL in the ASD patients was influenced by the sagittal spinopelvic malalignment in both before and after the surgery. The physical function such as ROM and muscle strength in the hip joints was strongly correlated to the sagittal spinopelvic alignment. Hip joint function plays an important role in ADL on standing and walking. A rehabilitation program should be focused on the hip joint function before and after the surgery.



## Analysis of surgical site infection surveillance in spinal surgery

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### Introduction:

Surgical site infection (SSI) after spinal surgery inflict significant morbidity and associated expenses increase socially and economically. In this study, we prospectively investigated SSI surveillance specialized in spinal surgery. The purpose of this study is to investigate this SSI surveillance in spinal surgery to identify risk factors of SSI and evaluation of prophylactic treatments.

### Methods:

A total of 810 patients underwent spinal surgery were registered to this surveillance before the surgery. There were 318 female and 492 male patients. Mean age at the initial surgery was 64.9 years. Surveillance items included age, gender, preoperative nasal cavity cultivation, comorbidities, smoking, surgical procedural characteristics, duration of operation, amount of blood loss. About the prophylactic treatment, the diabetic that HbA1c was more than 8% was hospitalized for one week to manage the blood sugar level. Smokers were forced to quit smoking one month before the surgery. Meticilin resistant staphyrococcus aureus (MRSA) carrier was applied mupirocin calcium hydrate into nasal cavity. In addition, the MRSA carrier was obliged to carry out a preoperative shower with hydrochloric acid chlorhexidine and was given Vancomycin hydrochloride intravenously 30 minutes before an operation. If infection extends to the deep spinal constructions beyond fasciae within one month after an operation, it is defined as early deep part SSI. Statistical analysis for association between survey items and EDSSI was performed.

□

**Results:** Out of 810 patients, 17 patients (2.2%) were diagnosed as EDSSI. The increase in EDSSI showed that age and a man were statistically significant. It was revealed that 29 MRSA carriers were (3.5%) in nasal cavity culture. However, the incidence of their EDSSI was not considerably higher than the patient who was not an MRSA carrier. There were 165 patients of diabetes, 41 patients of hemodialysis and 68 patients of the steroid use. The incidence of EDSSI of the hemodialysis patient was high than the incidence of EDSSI of the patient without comorbidities. However, the incidence of EDSSI of a diabetes and steroid used patient was not significantly high in comparison with the patient without comorbidities. Incidence of EDSSI of smokers was not significantly higher than that of non-smokers. As for surgical procedural characteristics, incidence of EDSSI of fusion surgery with instrumentation, decompression surgery and endoscopic surgery was 3.4%, 0.8% and 0.0%, respectively. Incidence of EDSSI of fusion surgery with instrumentation was significantly higher than those of the others. Increasing duration of operation, amount of blood loss and number of personnel in the operating room showed a statistically insignificant trend toward increasing rates of infection.

### Conclusions:

In this surveillance, gender, hemodialysis and fusion surgery with instrumentation were identified as risk factors of EDSSI. Incidences of EDSSI of MRSA carrier, diabetes patients and smokers were not significantly higher than those of patients without MRSA, diabetes and smoking. Our prophylactic treatments for MRSA carrier, diabetes patients and smokers may be effective for the prevention of EDSSI.

## Analgesic efficacy of Tramadol/Acetaminophen combination tablets in postoperative patients following spinal surgery

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**INTRODUCTION:** Non-steroidal anti-inflammatory drugs (NSAIDs) have generally been used in the treatment of postoperative acute pain after orthopedic surgeries. However, it is difficult to use NSAIDs for orthopedic patients with chronic kidney disease (CKD) because of drug side effects. Tramadol/acetaminophen combination tablets (TACs) have been used for patients with chronic pain and it has recently been reported that TACs have analgesic effects for patients after arthroplasty surgery. The purpose of this study was to evaluate the analgesic effect of TACs on acute postoperative pain following spinal surgery.

**METHODS:** This non-randomized control study included 127 patients (70 male, 57 female, average age: 67.2 years-old) who underwent spinal surgeries between April 2015 and January 2017. The patients were divided into two groups by day of surgery; 92 patients received Tramadol/acetaminophen combination tablets (TACs) (3 tablets/day) from one to 14 days following surgery between April 2015 and June 2016; 35 patients received Celecoxib (200 mg/day) from one to 14 days following surgery between July 2016 and January 2017. The patients, whose estimated glomerular filtration rate (eGFR) <60 ml/min/1.73 m<sup>2</sup>, were regarded as having CKD, were assigned to the TAC group. Visual analog scale (VAS), number of rescue uses, days until ambulation, and drug side effects of both groups were evaluated during the 14 postoperative days. Significant differences between groups were statistically analyzed.

**RESULTS:** There were no significant differences in age, gender and spinal level of surgery between TAC and NSAIDs groups. 34 patients (27% of total) identified as having CKD were included in the TAC group. The VAS of both groups showed a significant decrease over time following surgery; however, no significant difference in VAS was identified between groups (Day 1: TAC 47.3±26.5, NSAIDs 45.9±31.5; Day 14: TAC 12.7±19.7, NSAIDs 14.5±24.5, P=0.6, 2-way repeated measures ANOVA). No significant differences in number of rescue uses and days until ambulation were found between groups. However, the TAC group showed more drug side effects than the NSAIDs group (TAC: 22 cases [24%]; NSAIDs: 4 cases [11%]), and the incidence of constipation was higher in the TAC group than in the NSAIDs group.

**DISCUSSION:** The results of this study showed that TAC has the same degree of analgesic effect as NSAIDs in postoperative patients following spinal surgery. Those patients (34) who could not use NSAIDs because of CKD also obtained adequate analgesia by using TAC. However, the incidence of drug side effects of TAC was higher than that of NSAIDs.

## Early postoperative magnetic resonance imaging after surgery for lumbar disc herniation

Tadao Tsujio, Masatoshi Hoshino, Hiroaki Nakamura

**Introduction:** Lumbar disc herniation (LDH) affecting a spinal nerve root is the most common cause of radiating pain to the lower extremity. When conservative treatment fails, surgery is the preferred treatment for symptomatic LDH. However, symptoms occasionally remain. Magnetic resonance imaging (MRI) of the lumbar spine is performed in the postoperative period. The relationship of residual symptoms with a residual mass after herniotomy is not known. Few prior studies have assessed how a residual mass after herniotomy affects residual symptoms by comparing the preoperative and postoperative MRI findings.

**Objective:** To assess early (1-week) postoperative MRI after surgery for LDH. **Patients and Methods:** Twenty-seven patients (19 men, 8 women) underwent herniotomy and 1-week postoperative MRI from August 2015 to February 2017. The median patient age was 48.8 years (range, 18–83 years). The median follow-up period was 8 months (range, 4–19 months). The occupation rate of LDH in the spinal canal was calculated on preoperative axial MRI. Similarly, the occupation rate of the residual mass in the spinal canal after herniotomy was calculated on 1-week postoperative axial MRI. The occupation rate of the residual mass was compared with that of LDH in the spinal canal. The predominant signal intensity of LDH on preoperative T2-weighted MRI was compared with that of the residual mass after herniotomy. Nine patients who were followed up for >1 year and underwent MRI were assessed with respect to the occupation rate of the residual mass, residual rate, and signal intensity. The clinical outcome was assessed preoperatively and postoperatively using the Japanese Orthopaedic Association (JOA) score.

**Results:** The mean JOA score improved from 11.2 points preoperatively to 27.2 points postoperatively. The mean preoperative occupation rate of LDH in the spinal canal was 45.1%. However, at 1 week postoperatively, the mean occupation rate of a residual mass in the spinal canal decreased to 37.1%. The residual rate compared with LDH in the spinal canal was 79.1%. The size of the LDH decreased by half or more in only three patients (11.1%). Thirteen patients (48.1%) had a residual mass >90% as large as the LDH in the spinal canal. The signal intensity of the preoperative LDH was low in 21 patients and isointense in 6 patients. The signal intensity of the residual mass on MRI at 1 week postoperatively decreased in 3 patients with low intensity and increased in 18 patients with isointensity; the signal intensity became high in the remaining 6 patients. At 1 year postoperatively, the occupation rate of the residual mass in the spinal canal decreased to a mean of 20.9%. The residual rate compared with the LDH in the spinal canal decreased to 46.5%.

**Conclusion:** At 1 week postoperatively, the residual mass after herniotomy was almost the same as the preoperative LDH in half of the patients. The mass had low intensity preoperatively, and the residual mass after herniotomy showed isointensity or high intensity. Therefore, the residual mass after herniotomy was considered to be residual nucleus pulposus or a hematoma.

## The mechanism of adhesion in human dura mater cells: the roles of increased affinity to collagen through integrin $\alpha_2\beta_1$ and matrix metalloproteinase

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### INTRODUCTION

Dural traction by peridural adhesion and direct neural compression by excessive fibrosis might be one of major factors causing axial and radicular pain after spine surgery. This study was designed to explore the molecular mechanism of dural adhesion by using primary culture of human dura mater cells (hDMCs).

### METHODS

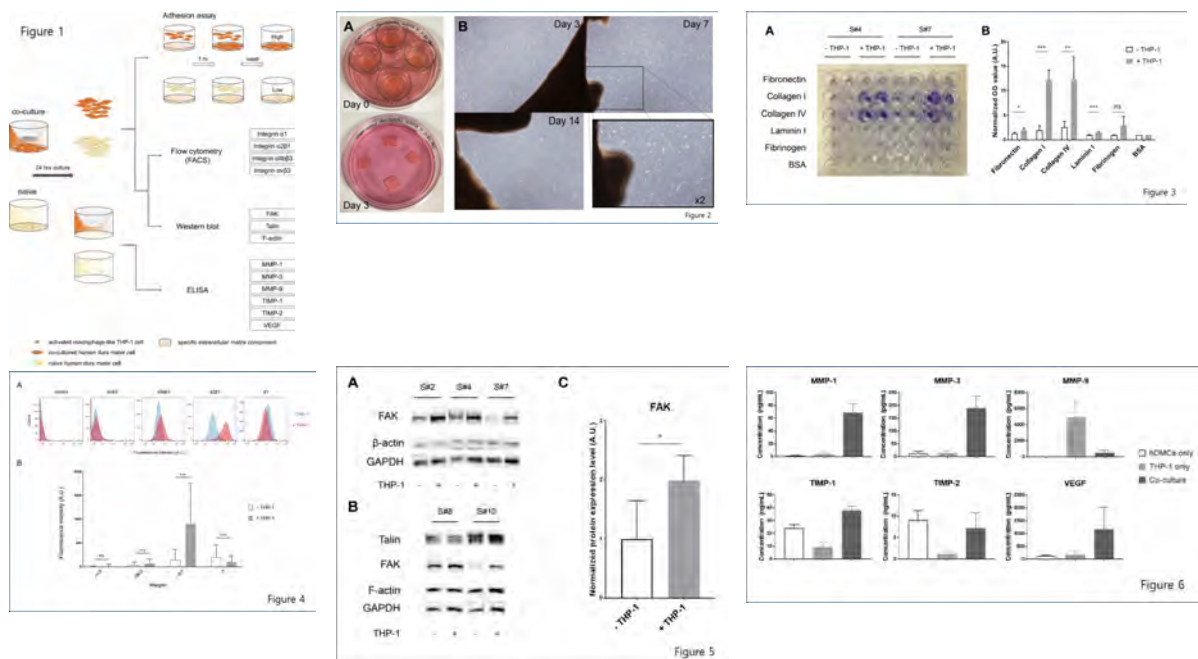
hDMCs were cultured on the collagen I coated plate from human dura mater tissue (8 men and 2 women, mean age  $55.4 \pm 17.86$ ) obtained during duroplasty following decompressive craniectomy. The comparison between naïve hDMCs and co-culturing hDMC with macrophage like THP-1 cells (M $\Phi$ ) is performed in various assays to reflect inflammatory circumstances of post-operation. Adhesion assay was performed for investigating major adhesive substrates to human dura mater cells (hDMCs). Flow cytometry about integrins and western blot about intracellular proteins related with adhesion (focal adhesion kinase (FAK), talin 1, and F-actin) was performed for investigating the alteration on adhesion-related molecules in hDMCs. ELISA about secreted matrix metalloproteinases (MMPs) was performed for investigating ECM remodeling factors for adhesion (Figure 1).

### RESULTS

The human dura mater tissue was sufficiently well adhered to the collagen I coated-dishes and plates within 3 days of gentle compression. After 3 days, the hDMCs which had similar compatible morphology of fibroblasts were appeared from the edge of the explanted tissues. The cells had elongated or multiple protruding pseudopods in shape initially, and gradually migrated away from the tissue (Figure 2). The adhesion profiles of hDMCs with collagen I, IV, fibrinogen and fibronectin after co-culture was significantly increased 6.4, 5.0, 3.0 and 1.6 times comparing to those of control group respectively ( $P < .001$ ) (Figure 3). There were significant increase in expression of the integrin subtype  $\alpha_2\beta_1$  about 6.3 times ( $142.7 \pm 222.8$  for control and  $898.8 \pm 859.1$  for co-culture,  $P < .001$ ) and  $\alpha_{11b}\beta_3$  about 2.0 times ( $32.7 \pm 64.7$  and  $65.8 \pm 94.8$ ,  $P < .001$ ).  $\alpha_1$ , which had highly expressed in naïve hDMCs, showed significant decrease after co-culture ( $196.9 \pm 261.8$  and  $100.2 \pm 135.1$ ,  $P < .001$ ) (Figure 4). FAK showed significant increase 1.99-fold in co-culture ( $P < .001$ ). There was no significant alteration between control and co-culture group in talin and F-actin (Figure 5). Co-culturing of the hDMCs with the M $\Phi$  induced significant increment of MMP-1, MMP-3, and VEGF concentrations compared to the sum of naïve hDMCs and M $\Phi$  (MMP-1:  $p < 0.01$ , 13.9 fold change; MMP-3:  $p < 0.01$ , 7.6 fold change; VEGF:  $p < 0.01$ , 3.8 fold change). MMP-9 secretion at co-culture ( $481.9 \pm 357.2$  pg/mL) was significantly suppressed into 9.7% comparing to that of activated THP-1 cells only. TIMP-1 and TIMP-2 showed no specific alteration between the conditions (Figure 6).

### Conclusion

hDMCs could be successfully utilized for the study of dural adhesion. Collagen might be a critical substrate of hDMCs in terms of adhesion, mediated by integrin  $\alpha_2\beta_1$  rather than  $\alpha_1$ . The increase of MMP 1, 3 and suppression of MMP 9 from hDMCs after exposure to inflammation might have critical roles in adhesion of hDMCs through ECM remodeling after peridural tissue injury.



## Progression of pathological disc degeneration, innervation, immune cell infiltration and spinal cord plasticity following single lumbar disc puncture in mice: a one year multiple-cohort study

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### INTRODUCTION

Persistent **low back pain (LBP)** results in more global disability than any other condition. Multiple anatomical, cellular and molecular components of the spine are implicated in LBP, and pain-related neuroplasticity is observed throughout the neuroaxis. To improve therapeutic outcome(s) and quality of life for people suffering from chronic back pain, we need to advance our understanding of the underlying (disease) mechanisms. We have developed a mouse model of disc injury-induced LBP that incorporates behavioral signs of axial discomfort and radiating leg pain. In the current study, we investigate whether **intervertebral disc (IVD)** innervation, immune cell infiltration and spinal cord plasticity correlate with the severity of IVD degeneration and the development of chronic LBP in a clinically-relevant mouse LBP model over the course of 12 months.

### METHODS

The L4/5 IVD underwent a single puncture using a 30G needle in 2-month old CD1 female mice. Animals were euthanized 6- and 12-months post-injury. Lumbar spines and spinal cords were sectioned at 16  $\mu$ m. Histological staining was adapted from the FAST (Fast Green, Alcian Blue, Safranin-O and Tartrazine) method for colorimetric histological staining for IVDs. Individual IVDs were graded for the severity of degeneration. IVD innervation was measured by immunohistochemistry using antibodies against PGP9.5 (pan-neuronal marker), calcitonin gene-related peptide (CGRP; peptide-rich nociceptors) and tyrosine hydroxylase (TH; sympathetic fibers). Macrophage infiltration was detected by F4/80 immunoreactivity. **Immunoreactive (ir)** nerve fibers and macrophages in IVDs were quantified. Changes in immunoreactivity of the neuropeptide CGRP and astrocyte marker Glial Fibrillary Acidic Protein (GFAP) were used as measures of spinal cord plasticity. The progression of and relationships between IVD degeneration, innervation, immune cell infiltration and spinal cord neuroplasticity were analyzed.

### RESULTS

FAST staining confirmed that injured IVDs were degenerated compared to sham-operated mice. In addition, degeneration in IVDs adjacent to injured discs was frequently observed at 12 months post-injury. A significant increase in PGP9.5-ir nerve fiber density was observed in outer **annulus fibrosus (AF)** of injured IVDs at 6 and 12 months post-injury compared to both non-injured IVDs of sham animals and adjacent lumbar IVDs of injured animals. Increases in CGRP-ir nerve fibers were also detected at both 6 and 12 months post-injury, but the increase was more prominent at 12 months. Few TH-ir sympathetic nerve fibers were observed and disc puncture had no effect. Significant numbers of F4/80-ir macrophages infiltrated the outer AF of degenerating and herniated IVDs. Increases in expression in CGRP-ir nerve terminals and GFAP-ir astrocytes were observed as a function of both disc injury and aging.

### DISCUSSION

Chronic LBP is a complex disease with multiple underlying pathologies and varying presentations. Possible contributors to this variation may include spinal neuroplasticity changes as well as changes in disc innervation. Here we show a slow, progressive increase in disc degeneration, innervation, macrophage infiltration and signs of spinal cord plasticity following a single lumbar IVD puncture over the course of 12 months. These changes highlight the need to understand the individual roles of the multiple components of LBP to develop more targeted and improved therapeutic strategies.

## Determinants of low bone mineral density in patients undergoing lumbar spinal fusion

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### INTRODUCTION

Posterior spinal lumbar fusions are commonly performed interventions. Many of the patients undergoing these procedures have undiagnosed osteopenia or osteoporosis. Several risk factors contribute to low bone mineral density (BMD), however, previous studies evaluating their association show conflicting results. The aim of this study was to assess which independent risk factors for metabolic bone disease are associated with low bone mineral density (BMD) measured by quantitative computed tomography (QCT) in a large lumbar fusion patient cohort.

### METHODS

Subjects undergoing posterior lumbar spinal fusion from 2014 to 2017 at a single, academic institution with available preoperative lumbar spine CT imaging were included. QCT measurements at L1 and L2 were used for osteopenia and osteoporosis diagnosis according to previously accepted standards. In addition, we performed experimental measurements of L3, L4, L5 and S1. Bivariate and multivariate analyses were performed on age, sex, BMI and bone medication use (teriparatide, bisphosphonates, denosumab) to identify factors associated with QCT BMD measurements at L1-2 and throughout the lumbosacral spine (L1-S1).

### RESULTS

The study population consisted of 132 male and 164 female patients. The mean age was 63.1 years and the mean BMI was 28.0 kg/m<sup>2</sup>. 173 patients (58.5%) had osteopenia or osteoporosis based on L1/L2 QCT measurements. The uni- and multivariate analyses identified age as significant independent risk factor for low L1/L2 BMD. Sex, BMI and the use of bone medications were not significant by multivariate analysis (Table 1). Sensitivity analysis was performed with the addition of the remaining lumbosacral levels (L3-S1) to the L1-L2 measurements. Age remained a significant risk factor for lower BMD after adjusting for sex, BMI and bone medication use (Table 2).

### DISCUSSION

The prevalence of osteopenia/osteoporosis is high in patients undergoing posterior lumbar spinal fusion. Advanced age appears to be a major risk factor for low BMD. Overall, our data suggests a 1.5 mg/cm<sup>3</sup> BMD decrease per year in lumbar fusion patients. Furthermore, our data confirms previous studies which have shown no volumetric density differences based on sex in the lumbar spine. Our data did not support BMI having a significant effect on BMD as measured by QCT. This is in line with recent studies which challenge the belief that high BMI may impart a protective factor against osteoporotic fractures. In summary, our results indicate that bone density declines with age, whereas sex and BMI have no significant effect on BMD measured by QCT in patients undergoing lumbar spinal fusion.

Table 1 Patient factors and BMD measured by QCT at L1-L2

	Bivariate analysis		Multivariate analysis	
	Coeff (95% CI)	P-value	Coeff (95% CI)	P-value
<b>Age</b>	-1.527 (-1.810, -1.244)	<0.001	-1.528 (-1.816, -1.240)	<0.001
<b>Sex</b>				
Female	ref		ref	
Male	3.103 (-5.613, 11.820)	0.484	-2.991 (-10.820, 4.843)	0.453
<b>BMI</b>				
Underweight/normal	ref		ref	
Overweight	4.371 (-6.361, 15.103)	0.429	6.117 (-3.390, 15.624)	0.206
Obese	8.138 (-2.765, 19.095)	0.143	6.871 (-2.820, 16.362)	0.155
<b>Bone treatments</b>	-16.148 (-34.198, 1.902)	0.079	-5.296 (-21.321, 10.730)	0.516

Table 2 Patient factors and BMD measured by QCT at L1-S1

	Bivariate analysis		Multivariate analysis	
	Coeff (95% CI)	P-value	Coeff (95% CI)	P-value
<b>Age</b>	-1.597 (-1.887, -1.307)	<0.001	-1.578 (-1.871, -1.284)	<0.001
<b>Sex</b>				
Female	ref		ref	
Male	3.818 (-5.151, 11.788)	0.401	-2.711 (-10.097, 4.275)	0.505
<b>BMI</b>				
Underweight/normal	ref		ref	
Overweight	2.916 (-8.138, 3.959)	0.604	3.391 (-5.798, 13.584)	0.450
Obese	5.200 (-2.997, 9.437)	0.150	6.071 (-3.602, 15.748)	0.218
<b>Bone treatments</b>	-24.368 (-42.836, -5.900)	0.010	-13.594 (-29.929, 2.742)	0.103

## Disc degeneration and chronic back pain are decreased by chronic toll-like receptor 4 inhibition in an animal model

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**Introduction:** Currently, therapeutic strategies for painful intervertebral disc degeneration are limited and no disease-modifying drugs exist. During degeneration, the extracellular matrix is degraded and fragmented, and inflammatory and pain mediating factors increase. *In vitro* work with human disc cells has found toll-like receptors (TLR) regulate cytokines, neurotrophins and proteases. TLRs are cell-surface pattern recognition receptors are activated by fragmented extracellular matrix proteins, which are termed '**alarmins**'. Many fragmented extracellular matrix proteins found in the disc, such as fibronectin, aggrecan and hyaluronic acid, can activate toll-like receptors. We **hypothesized TLR inhibition would slow the progression of disc degeneration and reduce pain** in a mouse model of disc degeneration and chronic low back pain. The SPARC-null mouse is a well characterized model of age-related disc degeneration and back pain. SPARC-null mice also display several behavioral signs of axial and radiating pain, including decreased grip strength (axial pain) and increased acetone evoked behavior (radiating pain).

**Methods:** Animal experiments were approved and followed the guidelines of the Canadian Council on Animal Care. 7-month old male wild-type (n=6/group) and SPARC-null (n=9/group) mice were injected *i.p.* with TAK-242, a TLR4 specific antagonist, or vehicle. Mice were treated 3 times/week for 8 weeks and behavior was assessed weekly. Lumbar discs were excised and cultured for 48 hours. Conditioned culture medium was assessed using a protein array (Ray Biotech). Data was analyzed using one- or two-way ANOVAs with GraphPad Prism.

**Results:** Chronic TLR4 inhibition with TAK-242 decreases signs of axial and radiating pain following 6 and 8 weeks of treatment in SPARC-null mice compared to vehicle (p<0.05). Mice receiving TAK-242 travelled similar distances, performed similarly on a rotarod test, and maintained similar weights to vehicle treated mice, indicating chronic TAK-242 treatment does not have adverse effects. Compared to wild-type, lumbar discs from SPARC-null mice secrete increased levels of many proinflammatory cytokines including IL-1 $\beta$ , IL-2, LIX and CCL2 (p<0.05). Chronic TLR4 inhibition decreases proinflammatory cytokine secretion to in SPARC-null mice to levels similar to that of wild-type mice.

**Discussion:** Chronic TLR4 inhibition reduces behavioral signs of back pain in SPARC-null mice likely by acting on degenerating intervertebral discs. If the drug effected neuronal or neuro-immune pain transmission, pain behavior would likely improve after a single treatment or at early time points. However, pain behavior only begins to improve after 6 weeks of TLR4 inhibition. This conclusion is supported by decreased secretion of proinflammatory cytokines. Cytokines, can directly act on nerve fibers to cause pain and thus cytokines likely contribute to the pain phenotype in SPARC-null mice. Alarmins that act as TLR ligands, are present in degenerating human discs and *in vitro* cell culture work strongly suggests a roll for TLRs in disc degeneration and pain. However, the current study is the first to explore TLRs as a druggable target in an *in vivo* model of disc degeneration and pain. Taken together, these results indicate TLR4 inhibition slows the progression of disc degeneration and decreases pain as a result, thus TLRs may represent a disease-modifying target.

### Effect of direct vertebral rotation in single thoracic adolescent idiopathic scoliosis

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**INTRODUCTION:** There is a paucity of literature demonstrating the long term surgical outcomes of DVR in patients with thoracic AIS.

**METHODS:** AIS patients with single thoracic curves (n = 110) treated by STF from neutral vertebra (NV) to NV or NV-1 with a minimum 2-year follow-up were retrospectively analyzed. The patients were divided into two groups; non-DVR (n = 63) and DVR groups (n = 47). Patients in non-DVR group underwent STF with bilateral rod derotation maneuver (RD) while patients in DVR group underwent STF with bilateral RD and DVR maneuver.

**RESULTS:** There was significant difference in the number of fused segments between the non-DVR and DVR groups ( $P < 0.000$ ). There was significant difference in the curve magnitude of main thoracic curve postoperatively ( $P = 0.001$ ) and at the last follow-up ( $P = 0.006$ ) between the non-DVR and DVR groups. However, there was no significant difference in proximal thoracic (PT) and lumbar curve postoperatively (PT curve:  $P = 0.186$ , lumbar curve:  $P = 0.155$ ) and at the last follow-up (PT curve:  $P = 0.250$ , lumbar curve:  $P = 0.060$ ) between the two groups. There was significant improvement of LIV tilt and disc angle and relatively well maintained during the follow-up period in both groups. There was no significant difference of rotation of apical vertebra and end vertebra preoperatively ( $P > 0.05$ ). However, there was significant difference postoperatively ( $P < 0.05$ ), and at the last follow-up ( $P < 0.05$ ).

**DISCUSSION:** DVR could effectively achieve better deformity correction, and more rotational correction with reduced number of fusion segments. However, it is important that DVR should be applied in proper direction with adequate force.



## Appropriate use of surgery for adult spine deformity: a multidisciplinary perspective

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### Introduction

Adult spinal deformity is a common disorder that has a significant impact on health-related quality of life and places a large burden on our healthcare economy, measured by direct cost of care and the opportunity cost of the disease. Presently, despite some computer models that predict clinical outcomes, the management of adult spinal deformity is characterized by significant variability. Indications for surgery, preoperative preparations, intraoperative strategies, and postoperative care are variable between physicians who care for patients with spinal disorders.

### Methods

Adult surgical candidates for complex spinal deformity were presented at a multi-disciplinary case conference. Inclusion criteria were adults with spinal deformity defined as scoliosis >30 degrees or sagittal deformity (SVA>6cm, PT>25°, LL-PI>20°). Exclusion criteria were tumors and infection. Providers from multiple disciplines including surgery (orthopaedic and neurosurgical), anesthesia, pain management, ICU, and radiology met in a monthly conference to discuss complex spinal deformity cases. All providers completed questionnaires regarding predicted benefit from surgery (scale from 1-6), predicted risk of medical and surgical complications (scale from 1-6), and appropriateness of surgery (inappropriate, uncertain, or appropriate). The variance and an agreement statistic,  $\kappa$ , were calculated for each category of predictions. The variance measures the degree of variability of responses and the agreement statistic  $\kappa$  ranges from -1.000 (no agreement) to 1.000 (perfect agreement).

### Results

A total of 39 cases were discussed and 204 responses from different providers were included in the analysis. The number of responders per case ranged from 2 to 12 (median = 5). The mean  $\kappa$  for predicted benefit of surgery was 0.052, and the variance of responses was 0.58. The mean  $\kappa$  for predicted major, minor, and surgical complications was 0.036, 0.081, and 0.20, respectively, and with 0.64, 0.95, and 0.57 as the respective variances. Finally, the mean  $\kappa$  for predicted appropriateness of surgery was 0.567, with a variance of 0.09.

### Discussion

Preoperative multi-disciplinary conference has several advantages when assessing the appropriateness of spinal surgery for patients. Interactive discussion at these conferences ensures accurate and detailed analysis of each case encompassing variables and subtleties not adequately represented in computer models. We found slight agreement among a multidisciplinary group of physicians when predicting benefit of surgery and medical and surgical complications, and moderate agreement when predicting appropriateness of surgery. Nevertheless, there exists significant inter-observer variability when deciding a treatment course, necessitating the need to further standardize the perioperative management and evaluation of appropriateness of surgery in patients with spinal disorders.

## Do participants with and without chronic low back pain present different phenotypes illustrated by texture analysis of disc degeneration on MR T<sub>2</sub>-map images?

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**Introduction:** The lumbar intervertebral disc (IVD) is the focus of extensive research, as low back pain (LBP) has been attributed to IVD degeneration and pathology. Defining degenerative spinal phenotypes on imaging is a primary goal of the Degenerative Spinal Phenotypes Focus Group of the ISSLS. Quantitative measures are needed because qualitative disc classification methods are usually unreliable. Texture analysis, which computes statistical patterns of signal intensity variations within a region of interest (ROI), may be useful for differentiating degeneration phenotypes related to pain. The aim of the present study was to determine which texture features extracted from T<sub>2</sub> maps present sensitivity and specificity to identify the lumbar IVDs of participants with LBP.

**Methods:** Fourteen participants with chronic LBP were matched for age, weight, and gender with 14 healthy volunteers. Mid-sagittal T<sub>2</sub> multi-echo images were acquired using a 3T whole-body Philips Intera MRI. Processing was done using Matlab<sup>®</sup> algorithms developed in house. Semi-automatic segmentation based on texture features was done for the lumbar discs and nucleus using the 3<sup>rd</sup> echo image and T<sub>2</sub>-maps were constructed using five echoes. A grey-level co-occurrence (GLCM) matrix with one to four pixels offset and four directions (0°, 45°, 90° and 135°) was constructed to extract texture features: contrast (the local variations in the grey-level co-occurrence matrix), correlation (measures how correlated a pixel is to its neighbor over the whole image), energy (the sum of squared elements in the GLCM), and homogeneity (measures the closeness of the distribution of elements in the GLCM to the GLCM diagonal). Mean, the coefficient of variation and signal intensity range were also extracted for each disc and nucleus ROI. A repeated measure ANCOVA with the group as a between-subjects factor and level as a within-subject factor using Sidak for post-hoc comparisons was employed to compare texture measurements. Age and area of the second lumbar vertebra (adjusts for size differences) were included as covariates. The Cohen's d effect size (ES) was estimated for group differences.

**Results:** A significant difference was observed between controls and LBP participants in whole disc contrast when one offset (a reference pixel and its immediate neighbour) was used (ES: 0.39; P-value=0.04). No statistical difference was observed for the energy, correlation and homogeneity for both disc and nucleus between two groups (ES<0.25). The mean T<sub>2</sub> of the pain group for the disc and nucleus was lower than the controls, but the differences did not reach significance (ES:0.18). Although the coefficient of variation and the range were higher in the pain group for disc and lower for the nucleus than the in the controls, no statistically significant differences were observed between groups.

**Discussion:** This study identified a novel biomarker for detecting different phenotypes of disc degeneration related to pain on MR images. The disc contrast information provided a better ability to detect differences between participants with and without pain than traditional disc signal measurements, including mean T<sub>2</sub>. Discs of the healthy subjects were more uniform than those with LBP. Traditional disc signal measurements did not detect differences between groups.

## Back pain in adolescents with spinal deformities

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### Background

Back pain prevalence ranges from 7 to 58% of subjects aged between 13 and 15, equally distributed in males and females. Back pain prevalence in scoliosis adolescents was found to be around 47%, but no studies investigated the prevalence of back pain in different spinal deformities, despite pain is considered a typical symptoms of spinal pathologies.

To document the prevalence of back pain, in all its forms in a large population of adolescents with spine deformities and to investigate the association of back pain and different spine pathologies.

### Methods

This is a retrospective cross-sectional study from a clinical prospective database. All the patients visited between 2010 and 2015 were asked for pain at first clinical evaluation by a single expert physician. If they referred any kind of pain belonged to the PAINGroup, if not they were assigned to the NOPAINGroup. Pain description was then classified into 4 subtypes (localized or generalized, limiting or occasional).

Inclusion criteria: age between 10 and 18, spine deformity diagnosis, Exclusion criteria: secondary deformities and other associated pathologies.

T-test was used to check for difference in the two groups considered for SRS-22 score, age and BMI. Chi-2 test was applied for checking the association between the presence of pain and diagnosis and pain subtypes; sports activities and previous treatment with brace.

### Results

702 completed the SRS-22, (males n=468), mean age 13.3+-1.92. The included patients have the following diagnosis: adolescent idiopathic scoliosis (n=387;55.1%), sagittal unbalance (which includes hyperkyphosis and junctional kyphosis without Scheuermann disease (n=134; 19.1%) Scheuermann deformities (n=67;9.55%); all other diagnosis including postural collapse, leg length discrepancy and aspecific back pain (n=114; 16.2%). The sample was divided in two groups: PAINGroup (258 subjects 36.8% of the entire sample) and NOPAINGroup. Mean age in PAINGroup 13.6+-1.9 and in NOPAINGroup 13.06+-1.9 p>0.05. Pain score at the SRS-22 was 4.10+-0.57 in PAINGroup and 4.75+-0.71 in NOPAINGroup (p= 0.0000). Among patients with AIS 32% referred pain, in the group of sagittal unbalanced patients 55% and in the group with Scheuermann disease 52%. Pain type was localized for 17.8%, generalized for 2.7%, occasional for 39.9% and limiting for 39.5%. Only Scheuermann disease predispose to pain (chi2= 10.2 Fisher exact test = 0.002), Sagittal unbalance is slightly associated to pain with chi2 = 3.65 Fisher exact test = 0.05. BMI and Age were not significantly associated with SRS SCORE, nor sports activities and previous brace treatment.

### Discussion

This is the first study investigating the epidemiology of different type of back pain in a large population of adolescents with spine deformities, by using a SRS-22 and narrative information on pain subclassified in 4 main types. Thoracolumbar and lumbar occasional pain are more frequent in patients with Scheuermann deformities, scoliosis patients have milder pain symptoms and refer to the specialist for pain in fewer cases. Sports activities and previous brace treatment, as AGE and BMI have no relationship with pain complaints, SRS-22 score or pain localization.

**Role of weekly teriparatide administration in bony union enhancement after posterior or transforaminal lumbar interbody fusion for osteoporosis-associated lumbar degenerative disorders: a multicenter, prospective, randomized study**

**Tomohiko Hasegawa, Hiroataka Haro, Shigeto Ebata, Jun Takahashi, Yukihiro Isogai, Yukihiro Matsuyama**

**Introduction:** Posterior or transforaminal interbody fusion (PLIF or TLIF) are usually performed to treat lumbar degenerative diseases, however some elderly patients show pseudarthrosis postoperatively. The teriparatide has been used recently for osteoporotic patients. Our multicenter, prospective, randomized, study investigated the role of once-weekly teriparatide on patients recovering from a surgery.

**Methods:** Patients were females older than 50 years who had a bone mineral density (BMD) less than 80% of the young adult mean and/or previous spinal or femoral fractures, and suffered from lumbar degenerative disease. Surgery was indicated for single-level PLIF or TLIF. Patients were randomly allocated to receive either weekly teriparatide, administered subcutaneously starting week one, for six months postoperatively in the teriparatide arm, or no teriparatide in the control arm. Blinded radiological evaluations were performed using dynamic x-ray and computed tomography (CT). Clinical and neurological symptoms were evaluated using the Japanese Orthopaedic Association Back Pain Evaluation Questionnaire (JOA-BPEQ) and the Oswestry Disability Index (ODI). Serum concentrations of P1NP and TRACP-5b, and femoral neck BMD were examined.

**Results:** Seventy-five patients were randomized, and sixty-six patients received treatment. Bone fusion was significantly increased in the teriparatide arm compared with the control arm. JOA-BPEQ and ODI results were significantly improved postoperatively in both treatment arms. The femoral neck BMD/YAM% and T-score were not significantly increased postoperatively and there were no significant differences between treatment arms. In the teriparatide arm, P1NP was increased and TRACP-5b was decreased.

**Discussion:** Weekly administration of teriparatide promoted bone formation at surgical site and decreased bone resorption, based on the bone metabolic marker results within the early postoperative period. Based on our study, combining lumbar interbody fusion and teriparatide treatment may be one of the options for managing lumbar degenerative disease in the elderly.

## Relationship between lumbar disc degeneration and back muscle degeneration

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### Introduction

The degenerative cascade of the spine, first described by Kirkaldy-Willis has been accepted as a basic mechanism for spine degeneration. However, muscles of the back are not included in this model. There are studies that reported significant correlation between back muscle degeneration and facet joint arthritis. The Purpose of our study is to evaluate relationships between lumbar disc degeneration and degeneration of back muscles.

### Methods

In this study, 65 patients who had taken lumbar spine MRI in our orthopaedic clinic were recruited. Back muscle degeneration was classified into 3 grades by the degree of fat signal in muscle layer qualitatively including both multifidus and erector spinae. Lumbar disc degeneration was measured based on Pfirrmann grading system. Paraspinal muscle was classified into 3 categories by the degree of fat signal in muscle layer qualitatively including both multifidus and longissimus: grade 1 (mild) fatty infiltration (FI) below 10%, grade 2 (moderate) FI between 10% to 50%, and grade 3 (severe) FI above 50%. Correlations between back muscle degeneration grade and radiological parameters were analyzed.

### Results

Average age of all patients was 61.65(±7.01) years old. Of 65 patients, 34 were male and 31 were female. Average percentage of fat infiltration of multifidus was 34.64(±12.55)%. And that of erector spinae was 25.58(±10.27)%. In analysis of multifidus, 28 patients had fatty infiltration of grade 1, 30 patients grade 2 and 7 patients grade 3. Grade 1 degeneration was most frequent. Fatty degeneration of back muscle was correlated with age(P=0.044). BMI was not significantly correlated with back muscle degeneration. Lumbar lordosis, pelvic incidence, pelvic tilt and sacral slope was not correlated. Disc degeneration of L2-3 segment was significantly correlated with fatty degeneration of back muscle(P=0.020). In analysis of erector spinae, 35 patients had grade 1 fatty infiltration, 27 patients grade 2 and 3 patients grade 3. Grade 1 degeneration was most frequent. Fatty degeneration of back muscle was correlated with age(P=0.034). BMI was not significantly correlated with back muscle degeneration. Lumbar lordosis, pelvic incidence, pelvic tilt and sacral slope showed no correlation. Disc degeneration of L2-3 segment was not significantly correlated with fatty degeneration of back muscle.

### Discussion

Disc degeneration was correlated with degeneration of multifidus, but not with erector spinae. This can be explained by anatomical difference of paraspinal muscle innervations. Multifidus receives direct innervations from a single medial branch of posterior ramus. If there is a pathology in the spinal segment, multifidus can be denervated easily compared to erector spinae which is innervated by multisegment spinal roots. This anatomical feature may contribute to the difference in degeneration of multifidus and erector spinae. There is significant correlation between lumbar disc degeneration and back muscle degeneration. The degenerative cascade of the spine is accompanied by back muscle degeneration.

## Clinical experiences of percutaneous biportal endoscopic spine surgery

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**INTRODUCTION** Traditionally, lumbar spine diseases that require surgical intervention are treated with an open decompressive procedures. Microsurgery is a very effective technique. PELD (Percutaneous Endoscopic Lumbar Discectomy) was introduced and some experienced surgeons had good results. But it may have limited vision and complete decompression may not be successful in some cases. Biportal endoscopic surgery is different from other spinal endoscopic system with one portal. There are two skin portals, one portal for endoscope and the other for working instruments. Thus the endoscopic system is similar to joint arthroscopy. Percutaneous biportal endoscopic operating procedure is the same pattern as open spine surgeries under excellent visualization. The authors present cases of lumbar discectomy, central and foraminal decompression, lumbar interbody fusion, and posterior cervical foraminotomy and discectomy using percutaneous biportal endoscope.

**METHODS** We collected data retrospectively from February 2011 to February 2016.

**RESULTS** A total 534 patients (357 female, 177 male) were operated. 84.5% patients improved clinically and radiographically after percutaneous biportal endoscopic surgery.

**DISCUSSION** Percutaneous biportal endoscopic spinal decompression would be a safe and effective minimally invasive procedure compared to conventional open surgery.

## Relationship between muscle strength after lateral interbody fusion using quantitative evaluation of leg strength and image findings of psoas muscle

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### INTRODUCTION:

Muscle trauma and damage to intermuscular nerves due to dissection of the psoas are recognized perioperative complications of lateral interbody fusion (LIF). Although the decline in leg strength is temporary in many cases, the underlying changes have not been studied in detail. The aim of this study was to investigate the relationship between muscle strength after LIF using quantitative evaluation of leg strength and image findings of psoas muscle.

### METHODS:

The subjects were 38 patients who underwent LIF (9 male, 29 female; mean age: 70). Twenty cases had degenerative lumbar scoliosis and 18 cases had degenerative lumbar spondylolisthesis. Twenty cases that simultaneously underwent the posterior lumbar approach were assigned to the Posterior group. Muscle measurements were taken prior to surgery and 1 week, 2 weeks, 3 weeks, 1 month, 2 months, and 3 months after surgery. Psoas strength was measured using a hand-held dynamometer (HHD) and quadriceps strength was measured using Cybex. Muscle strength decline was defined as muscle strength of less than 80% of the preoperative measurement. Using axial T2-weighted magnetic resonance images, the psoas position (PP%) was calculated as the distance between the posterior margin of the intervertebral disc and posterior border of the psoas major muscle divided by the anteroposterior diameter of the intervertebral disc. Spearman rank correlation analysis was used to compare PP% and degree of psoas and quadriceps muscle strength decline at 1 week after surgery on the approach side.

### RESULTS:

Psoas muscle strength decline at 1 week after surgery was 60.5% (23/38) on the approach side, 39.5% (15/38) on the healthy side, and 30.0% (6/20) in the Posterior group. Quadriceps muscle strength decline at 1 week after surgery was 34.2% (13/38) on the approach side, 39.5% (15/38) on the healthy side, and 25.0% (5/20) in the Posterior group. Our investigation of muscle strength decline on the approach side indicated that all cases showed improvement in muscle strength at the following rates: Psoas at 3 months after surgery and quadriceps at 1 month after surgery. Psoas muscle strength and quadriceps strength at 1 week after surgery were correlated ( $\rho=0.57$ ,  $P<0.001$ ). There was a weak inverse correlation between PP% and quadriceps strength at 1 week ( $\rho = -0.31$ ,  $P<0.001$ ) and no correlation between PP% and psoas muscle strength.

### DISCUSSION:

Although both the psoas and quadriceps muscle groups experienced temporary declines in strength after LIF, we showed that strength improves over time. These results with the healthy side and the Posterior group indicated that the lateral approach caused only a slight muscle strength decline in the psoas. Also, in cases where the position of the psoas muscle is more anterior, there is the potential for increased irritation of the lumbar plexus during the psoas muscle splitting maneuver. Therefore, this might lead to postoperative quadriceps muscle decline related to the psoas muscle strength and position. Quantitative assessment of leg muscle strength is useful as an objective assessment technique.

## Vertebral augmentation can induce early signs of degeneration in the adjacent intervertebral disc: evidence from a rabbit model

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**Introduction:** Vertebral augmentation with polymethylmethacrylate (PMMA) reportedly may predispose the adjacent vertebra to fracture. The influence of PMMA augmentation on the adjacent disc, however, remains unclear. This study established a rabbit model of vertebral augmentation to determine changes of the adjacent disc.

**Methods:** Using a retroperitoneal approach, PMMA augmentation was performed for 23 rabbits. For each animal, at least 1 vertebra was augmented with 0.2-0.3 ml PMMA. The disc adjacent to the augmented vertebra and a proximal control disc were studied using magnetic resonance (MR) imaging and then histological evaluation at 1, 3, and 6 months postoperatively. Marrow contact channels in the endplate were quantified in histological slices and number of invalid channels (those without erythrocytes inside) was rated. *Quantitative* polymerase chain reaction was used to quantify the expression of various cytokines and terminal deoxynucleotidyl transferase-mediated dUTP nick-end labeling (TUNEL) was performed to determine disc cell apoptosis.

**Results:** On MR images, the signal and height of the adjacent disc did not change 6 months after vertebral augmentation. Histological scores of the adjacent disc increased over time, particularly for the nucleus pulposus. The adjacent disc had greater nucleus degeneration score than the control disc at 3 months (5.7 vs. 4.5,  $p < 0.01$ ) and 6 months (6.9 vs. 4.4,  $p < 0.001$ ). There were more invalid marrow contact channels in the endplate of augmented vertebra than the control (43.3% vs 11.1%,  $P < 0.01$ ). mRNA of *ADAMTS-5*, *MMP-13*, *HIF-1  $\alpha$* , and *caspase-3* were significantly upregulated in the adjacent disc at 3 and 6 months ( $P < 0.05$  for all). In addition, there were more TUNEL-positive cells in the adjacent disc than in the control disc (43.4% vs. 24.0%,  $P < 0.05$ ) at 6 months postoperatively.

**Discussion:** PMMA augmentation can induce histological and molecular signs of degeneration in the adjacent disc. The adjacent disc degeneration may be due in part to impaired nutrient supply to the disc. Such disc degeneration, however, was relatively weak and time-dependent, and therefore, related clinical significance remains to be further studied.



## Difference in the fusion rate and bone formation between the grafted materials inside cages in lateral interbody fusion in patients with adult spinal deformity – a comparison between porous hydroxyapatite/type 1 collagen composite and autologous iliac crest bone

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### INTRODUCTION

Lateral interbody fusion (LIF) with cages equipped with large bone grafting space leads to the graft material shortage and the use of artificial bone is getting popular. However, its ability to acquire bony fusion as the graft material within LIF cages compared to autograft is still unclear. A porous hydroxyapatite/collagen composite (HAp/Col) composed of nano-scale HAp and porcine type 1 collagen is newly developed artificial bone<sup>1</sup>. This study was aimed to investigate difference in the effects on bony fusion inside the LIF cages between HAp/Col and autograft in patients with adult spinal deformity (ASD).

### METHODS

Twenty-three ASD patients who treated with LIF (in total 66-disc levels) prior to posterior corrective fusion were retrospectively investigated. In the LIF surgeries, one of bone grafting hole in the LIF cage was filled with HAp/Col and the other hole was filled with iliac crest bone graft (ICBG) (Fig 1). Whether to use HAp/Col on the left or right side of the cage holes was decided at random. From the computed tomography (CT) scans taken one year postoperatively, the trabecular continuity between adjacent vertebrae passing through the cage holes was assessed in each side of the cage holes. Bony fusion in each cage hole was defined by the presence of the trabecular continuity. Bone formation inside each cage hole was quantified with the change in the Hounsfield unit (HU) values of the CT scans between just after surgery and one year after surgery (Fig 2). The difference of fusion rate and HU values between the sides of cage holes were analyzed. The fisher's exact probability test or Wilcoxon signed-ranks test were performed for the statistical analysis. Differences with a p value of <0.05 were considered significant.

### RESULTS

The fusion rate in the cage holes filled with ICBG was significantly higher than those with HAp/Col (71.2% vs. 19.7%,  $p < 0.001$ ). A case presentation is shown in Fig 3). In the cage holes filled with HAp/Col, the fusion rate was significantly higher in the concave side than the convex side (31.3% vs. 8.8%,  $p = 0.02$ ); however, in the holes filled with ICBG, the fusion rate did not differ between the concave and convex sides (73.5% vs. 68.8%,  $p = 0.41$ ). The HU values in the cage holes filled with ICBG significantly increased between just after surgery to postoperative one year ( $228.9 \pm 90.3$  HU to  $286.1 \pm 125.5$  HU,  $p < 0.001$ ). In contrast, those with HAp/Col did not change postoperatively ( $118.6 \pm 74.6$  HU to  $128.9 \pm 71.5$  HU,  $p = 0.89$ ).

### DISCUSSION

This study revealed that the fusion rate in the cage holes filled with HAp/Col was inferior to that with ICBG, which was supported by the difference of postoperative changes in the HU values inside the cage holes between the two graft materials. The single application of HAp/Col for the bone graft in LIF cages is not suitable in ASD surgery. HAp/Col should be used for bone expander concomitant use of autologous bone.



Fig 1. One hole was filled with HAp/Col and the other was filled with ICBG

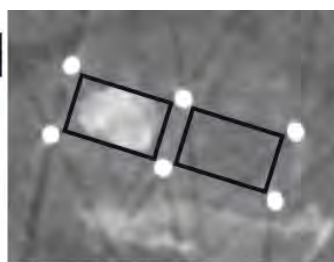


Fig 2. The quadrangle indicated the implanted hole. HU values of implanted hole was measured.

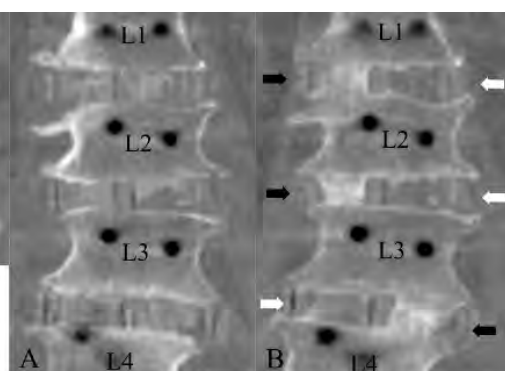


Fig 3. only ICBG implanted cage holes showed bony fusion (black arrows) and all HAp/Col implanted cage holes showed nonfusion (white arrows).  
A, just after surgery. B, one year after surgery

1. Sotome S, Ae K, Okawa A, Ishizuki M, Morioka H, Matsumoto S, Nakamura T, Abe S, Beppu Y, Shinomiya K. Efficacy and safety of porous hydroxyapatite/type 1 collagen composite implantation for bone regeneration: A randomized controlled study. *J Orthop Sci* 2016 May;21(3):373-80.

## Utilization of minimally invasive lateral lumbar interbody fusion for lumbar spinal canal stenosis associated with osteoporotic vertebral collapse

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### INTRODUCTION

Various surgical procedures have been reported for the treatment of lumbar spinal canal stenosis (LSCS) associated with osteoporotic vertebral collapse (OVC), each with its advantages and disadvantages. We have applied minimally invasive lateral interbody fusion (LLIF) since 2014 for LSCS associated with OVC. The purpose of this study is to introduce our less invasive anterior-posterior combined surgery, and to clarify the clinical effectiveness of the method and any issues which should be resolved in the future.

### METHODS

Thirteen patients suffering from LSCS associated with OVC received this surgery and were followed for an average of 19.7 months. The mean age at surgery was 77.7-year-old. All patients were unable to walk without support due to severe low back and leg pain. Mean Japanese Orthopedics Association (JOA) score was 6.6/15 points and mean bone mineral density was 0.621g/cm<sup>2</sup> (young -adult mean; 69%), preoperatively. LLIF were performed and anterior support were reconstructed remaining the collapsed vertebrae. Corpectomy, vertebral osteotomy, even or ligation of segmental vessels was not required for the affected vertebra. Fusion levels were determined according to the deformity of the OVC as follows; When rostral endplate of the affected vertebra was collapsed and the caudal endplate was intact, single level LLIF was performed between a rostral adjacent vertebra and the affected vertebra. When both rostral and caudal endplate were collapsed, two level LLIFs were performed. After LLIF, posterior spinal fusion was performed with placing pedicle screws including the OVC vertebra with as short levels as possible. For pseudoarthrosis case, the cage pressed down the cleft of the vertebra and reconstructed consecutive anterior support. All patients were allowed to ambulate in plastic orthosis 2 days after surgery.

### RESULTS

The mean number of fusion levels were 1.72. All patients were relieved from severe pain favorably. Mean JOA score was improved to 12.8/15 at final follow up and the recovery rate was 73.9%. Donor site pain was not observed at discharge. Significant displacement of cages or implant failures were not observed through the follow-up period. Mean preoperative local lordotic angle was -11.2 degree and was corrected to 8.0 degree postoperatively. It was maintained as 4.3 degree at final follow up.

### DISCUSSION

With the LLIF approach, a large cage can be placed into the intervertebral space and reconstruct anterior support in consecutive segments without performing any destructive manner for the associated vertebra (vertebral osteotomy or corpectomy including segmental vessels ligation), and the wide cage adds stability and prevents subsidence even though the bone mineral density is poor. Pedicle screws insertion into the affective vertebra provides a good anchor and may prevent subsidence of the cage above. Therefore, supplemental posterior instrumentation can be shorter as possible. In fact, five of thirteen cases underwent the surgery with single level fusion. Although an anterior-posterior combined surgery entails the burden of changing operative position, this method achieves neural decompression, reconstruction of anterior support, and correction of alignment in a less invasive manner.

## Factors influencing instrumentation failure after total en bloc spondylectomy of the thoracolumbar junction and lumbar spine

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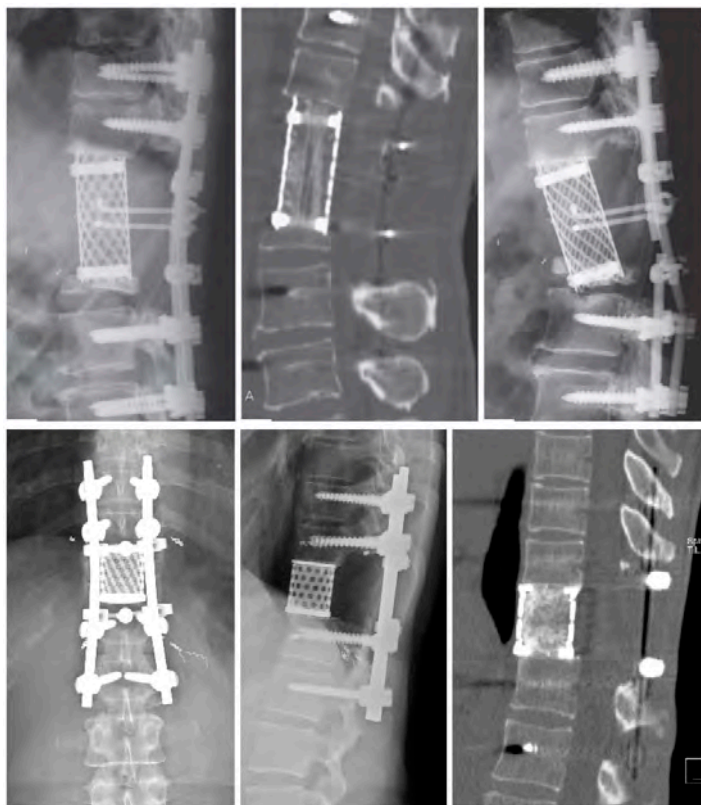
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**Introduction:** Spinal reconstruction in total en bloc spondylectomy (TES) is important for long-term functional prognosis. Especially, the frequency of instrumentation failure is high in TES at the thoracolumbar junction and lumbar spine; however, no data has been reported for spinal reconstruction in this region. Therefore, the purpose of this study is to assess the factors influencing the instrumentation failure after TES below the thoracolumbar spine.

**Methods:** This is a retrospective review of 45 cases (27 men, 18 women) who underwent TES at the thoracolumbar junction and lumbar spine (Th10-L5) between 2010 and 2016. Their mean age at the time of surgery was 49 years (14–73 years) and the mean follow-up period was 49 months (12–89 months). Anterior reconstruction was performed using a titanium mesh cage filled with autograft. Conventional cage was used in 28 cases and more robust cage was used in 17 cases. Cage with the end caps on both ends was used in 14 cases, while no end caps were used in the other. Posterior instrumentation was performed with two-above and two-below segmental fixation using pedicle screws and rods. Titanium alloy rod was used in 31 cases and cobalt chrome rod was used in 14 cases. The incidence of instrumentation failure was evaluated in relation to various factors. Statistical analyses were performed with Spearman correlation analysis and multiple logistic regression analysis. A *p*-value <0.05 was considered statistically significant.

**Results:** Instrumentation failure occurred in 14 cases (31%) including 12 rod breakage, 4 cage breakage, 1 screw breakage, and the mean time to instrumentation failure was 29 months (8–60 months). BMI ( $r = 0.33$ ), length of resected vertebrae ( $r = 0.35$ ) and cage subsidence at 1 month after the surgery ( $r = 0.30$ ) showed significant positive correlation with the incidence of instrumentation failure. In addition, use of cobalt chrome rod ( $r = -0.35$ ), use of more robust cage ( $r = -0.52$ ) and use of cage end caps ( $r = -0.45$ ) had significant negative correlation. On the other hand, preoperative irradiation, preoperative chemotherapy, cutting inside vertebral body showed no significant correlation. Multiple logistic regression analysis demonstrated that BMI (OR = 1.5; 95% CI = 1.1–2.0) and length of resected vertebrae (OR = 1.1; 95% CI = 1.1–1.2) were significant independent risk factor for instrumentation failure, whereas use of cobalt chrome rod was associated with decrease in the risk (OR = 0.02; 95% CI = 0.001–0.58).

**Discussion:** It was shown that enhancing instrument strength leads to reduction of instrumentation failure. In particular, the use of cobalt chrome rod turned out to be effective in preventing instrumentation failure. The reason for this is presumed to be that by increasing the rigidity of the posterior instrument, the load on the anterior column which is a cause of cage subsidence was reduced, which resulted in the reduction of the instrumentation failure. Since BMI and length of resected vertebrae are independent risk factors for instrumentation failure, more robust spinal reconstruction such as use of three or more rods should be considered in high-risk cases.



## Remodeling of the dome deformity in the immature rat lumbar spondylolisthesis model

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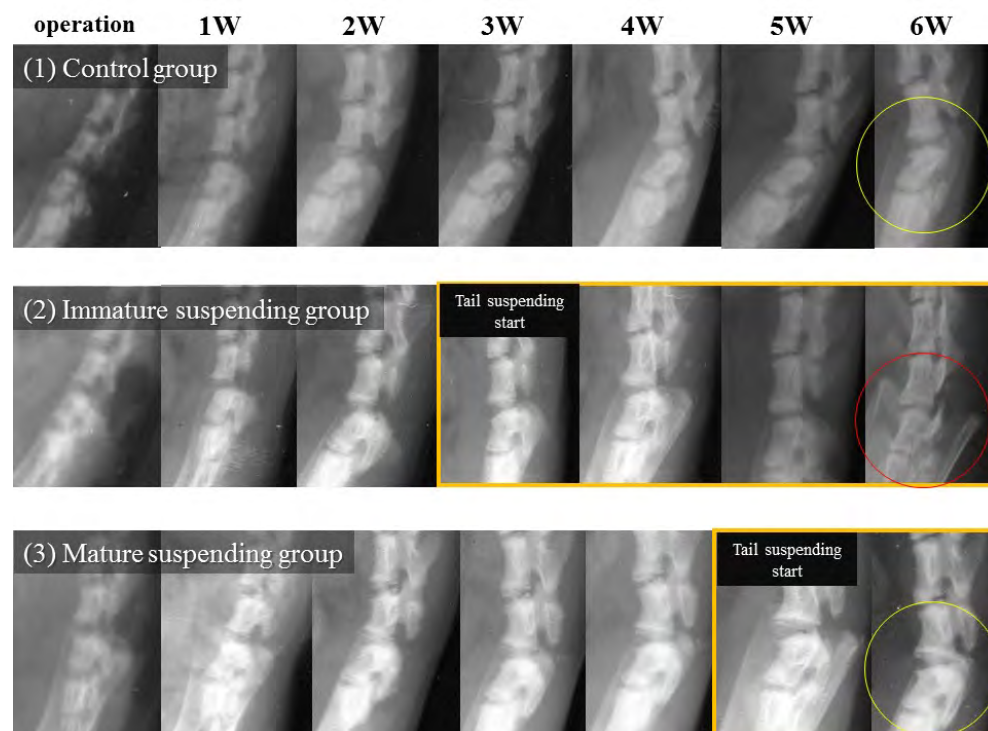
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**INTRODUCTION:** Rounding deformity of the sacral dome are commonly observed in the pediatric patients with isthmic spondylolisthesis. It was reported that repetitive mechanical stress to the anterior upper corner of the endplate may cause rounding deformity of the sacral dome due to growth plate involvement. And the deficient endochondral ossification of the growth plate could be the pathomechanism of the rounding deformity of the sacrum. To prove that by reducing the mechanical stress at the growth plate at the slipped vertebra can make remodeling the rounding deformity.

**METHODS:** Spondylolisthesis rats model (4-week-old, L5/6 bilateral facetectomy and L5 partial laminectomy) were used. The load to anterior part of lower vertebra was reduced using a tail suspending device. The spondylolisthesis model rats were divided into three groups, (1) Control group; observation without tail suspending (6 rats), (2) Immature suspending group; starting tail suspending at 2 weeks after surgery (6 rats), (3) mature suspending group; starting tail suspending at 4 weeks after surgery (6 rats). Radiographs were taken weekly for 6 weeks after the surgery and measured percent slip, rounding index, lumbar index. In addition, each groups of rats were sacrificed at 1, 2, 4, 6 weeks and the lumbar spines were harvested for histology. Hematoxylin and eosin, alcian blue staining were used.

**RESULTS:** In control group, the rounding deformity of the lower vertebra had progressed as time passed. In immature suspending group, remodeling of the upper corner of lower vertebra had seen at 3 weeks after surgery and it had continued improving with time. In mature suspending group, the improvement had not been seen. Regarding the histological findings of the growth plate, the hypertrophic cell at that site had disappeared and proliferating cell had increased in control group and in mature suspending group. In immature group, the hypertrophic cell at the repaired site had re-appeared though the cell arrangement of growth plate had fallen into disorder.

**CONCLUSION:** Reducing mechanical stress at the growth plate during immature bony age can make remodeling of sacral dome.



## DXA and BIA are useful measuring tools for trunk muscle mass

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### (Introduction)

It is said that there are no tools to accurately measure trunk muscle mass. However, it is standard to estimate trunk muscle mass from its cross sectional area (CSA) using MRI or CT. Dual-energy X-ray absorptiometry (DXA) and bioelectrical impedance analysis (BIA), which are the standards for limb muscle mass measurement, may provide tools for trunk mass measurement, although their accuracy is questionable, and few reports have specifically examined their effectiveness. The purpose of this research is to investigate the correlation between measured values obtained by DXA and BIA, with the CSA obtained by MRI and to confirm whether they are useful or not.

### (Methods)

We evaluated 65 patients with low back pain (30 men and 35 women, average age  $64.6 \pm 13.5$  years old), excluding patients with artificial joints/spinal implants for the arms/legs and trunk. Trunk muscle mass (kg) was measured with DXA (HOLOGIC Discovery) and BIA (TANITA MC – 780A). The CSA of the multifidus, spinal erector, and large psoas muscles were measured at the L4/5 level from axial images taken with MRI. The sum of the CSA of these muscles was taken as the CSA of the total trunk musculature ( $\text{mm}^2$ ).

We evaluated the correlation between DXA- and BIA-based measures of trunk muscle mass, and differences between these two measurements. We also evaluated the correlation between the measurements of DXA and BIA, and the CSA of the trunk muscles, both total mass and the mass of each individual muscle. Pairwise differences were examined using the t test, and correlations were evaluated using the Spearman's correlation coefficient.

### (Results)

Both BIA and DXA measures were highly correlated. ( $r = 0.82$ ,  $p < 0.01$ ), and the mean values for trunk mass were:  $19.9 \pm 4.6$  kg for DXA, and  $22.5 \pm 4.9$  kg for BIA. BIA gave a value for trunk muscle mass that was significantly greater than the value measured by DXA ( $p < 0.01$ ). The correlation between mass measurements by DXA and BIA, and the CSA of the total trunk musculature was 0.86 for DXA ( $p < 0.01$ ) and 0.76 for BIA ( $p < 0.01$ ). The correlation between the measurements of DXA and BIA, and the CSA of each muscle (multifidus, spinal erector, large psoas) was 0.45 ( $p < 0.01$ ), 0.55 ( $p < 0.01$ ), and 0.82 ( $p < 0.01$ ) for DXA, and 0.52 ( $p < 0.01$ ), 0.38 ( $p < 0.01$ ), and 0.77 ( $p < 0.01$ ) for BIA. Measurements by DXA and BIA were most highly correlated with the CSA of the large psoas muscle.

### (Discussion)

This research provides additional insight into two clinical issues related to trunk muscle mass. First, the BIA provides values for total trunk muscle mass significantly larger than those given by DXA. Second, measurements of both DXA and BIA can reflect the mass of individual muscles, as both were highly correlated with the CSA of the large psoas muscle. We conclude that both DXA and BIA are useful measuring tools for trunk muscle mass, just as they are for limb muscle mass.

## **Effective graft materials for spinal fusion surgery: Combined use of bone allografts and platelet-rich plasma shortens the time to bone union**

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### Introduction:

In spinal fusion surgery, reliable and early bone fusion is an important factor affecting postoperative outcomes. Their efficacy has led to increasing demand for bone allografts.

Although bone allografts have osteoconductive ability, they have almost no osteogenic potential or osteoinductive ability, and reliable bone union is unlikely after a single grafting attempt. Therefore, this study investigated whether bone union is promoted by use of bone allografts and platelet-rich plasma (PRP).

### Methods:

Patients who underwent lumbar spinal fusion at our hospital between December 2015 and June 2017, and who agreed to participate in this study were included. This was a randomized, open-label, blinded-endpoint study, with random assignment to the control group (use of bone allografts alone) or the PRP group (combined use of bone allografting and PRP).

Evaluation items included the bone union rate at 1 year postoperatively, the time to bone fusion, adverse events, and Visual Analogue Scale (VAS) scores for low back pain and lower extremity pain at 1 year postoperatively. Bone fusion was evaluated by three spinal surgeons using coronal computed tomography.

### Results:

Of 16 patients evaluated, 6 were men and 10 were women, and the average age was 70.5±6.4 years. There were 9 patients in the control group and 7 in the PRP group. The bone union rate at 1 year postoperatively was 88.8% in the control group and 100% in the PRP group. The average time to bone union was 8.5 months in the control group and 6.6 months in the PRP group, showing statistical significance ( $p<0.05$ ).

The average decrease in VAS scores (mm) at 1 year postoperatively showed no significant difference between the control group (13.3, 7.8) and the PRP group (17.1, 10.0) ( $p>0.05$ ). Moreover, there were no significant adverse events in all cases.

### Discussion:

This study results showed that the time to bone union was about 2 months shorter in the combination treatment group, suggesting that PRP promotes bone fusion. In addition, combination treatment with bone allografts and PRP was safe, without adverse events.

In future, combined treatment should be evaluated in additional orthopedic procedures.

## **Variances in opiate use between patients implanted with micron-textured titanium vs peek implants for TLIF procedures**

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**Background:** Little data exists to describe factors affecting opioid use after TLIF procedures. Research suggests variable osteogenic properties between roughened titanium and PEEK implants that may be relevant to outcomes.<sup>1</sup>

**Objective:** To determine if implant surface material properties can influence outcomes and narcotic requirements in patients after TLIF.

**Methods:** Consecutive patients (single surgeon) underwent 1-level TLIF procedures and were followed for 6 months. Demographics and biologics were similarly matched in each group. Pain and function were assessed by Visual Analog Scale (VAS) and Oswestry Disability Index (ODI). Opiate usage was measured in Milligram Morphine Equivalents Per Day (MME/Day) and percentage of subjects not requiring pain medications.

**Results:** 127 consecutive patients: 43 PEEK followed by 84 micron-scale roughened surface titanium implants. There was a statistically significant difference at 6 months with 77% of titanium patients not requiring narcotics compared to 56% of PEEK patients. Back pain VAS reached statistical significance at 6 months with superior outcomes in the titanium group (2.6) compared to the PEEK group (3.7). ODI scores trended towards better improvement (NS) at 6 months in the titanium patients. Patients with titanium implants had statistically significant reductions in MME/day at 3 and 6-month data points. At 6 months, the titanium group had a mean of 3.6 MME/Day while the PEEK group had a mean of 17.8 MME/day.

**Conclusion:** Implant properties can influence clinical outcomes and opiate usage in TLIF cases. Patients fused with micron-scale titanium implants recovered faster and required significantly less opioids than their matched counterparts with PEEK implants.

1. *Spine*; 40 (6) 399-404; 2015

## Does spondylolisthesis develop or progress with microdecompression for stenosis?

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### Introduction

Studies have suggested that up to 20% of patients having normal lumbar pre-op alignment will develop spondylolisthesis following midline laminectomy. In patients having a pre-op degenerate spondylolisthesis, post laminectomy progression of the spondylolisthesis has been noted in up to 68%. Multiple surgical options have been explored for lumbar stenosis with/without associated spondylolisthesis. However, a clearcut "best" approach has yet to be identified.

With the trend towards minimally invasive surgery, questions have arisen whether post decompression spondylolisthesis can be prevented or progression avoided using MISS techniques. MISS such as microscopic lumbar laminotomies and bilateral canal decompression via a unilateral approach (ipsilateral laminotomy/contralateral laminoplasty) largely maintain the major posterior elements/secondary stabilizers. Theoretically, one would expect a lower rate of progressive spondylolisthesis in minimally invasive posterior element sparing procedures. However, there is little actual data in this area. We performed an analysis of 100 consecutive patients having a microsurgical decompression to explore the issue of development or progression of degenerative spondylolisthesis.

### Methods

The purpose was to investigate the relative risk of developing de-novo spondylolisthesis or progression of pre-existing slip following posterior element sparing decompressive procedures (laminotomy, laminoplasty) for spinal stenosis.

The study design was a retrospective, 100 patient consecutive, single surgeon cohort review from a tertiary care private medical center.

All patients had a primary diagnosis of spinal stenosis and underwent microscopic decompression using laminotomies or bilateral decompression via a unilateral approach (ipsilateral laminotomy/contralateral laminoplasty). Charts and imaging studies were reviewed a minimum of 2 years following the index surgery. Spondylolisthesis status was reviewed and compared to pre-op.

The primary outcome measure was the presence of spondylolisthesis on imaging studies (plain film/MRI/CT).

### Results

There were 62 males and 38 females average age 64.7 (range 21 – 95). Forty of the patients had unilateral laminotomies with the average number of levels 1.48 (range 1 – 3). Sixty of the patients had bilateral canal decompression via a unilateral approach (lumbar laminoplasty) at at least one level (average 2.35, range 1 – 5).

Pre-operatively, 22 patients had a Grade I stable degenerate spondylolisthesis (less than 3 mm horizontal translation on flexion/extension x-rays). Two of the 22 had unilateral laminotomies. Neither patient had progression. Twenty of the 22 had bilateral laminoplasties (8 males average age 76.5), 12 females average age 84.2. Average number of levels in the laminoplasty group 2.7 (range 1 – 3). No progression to fusion occurred in the pre-existing spondylo group.

In the 78 patients without a pre-op spondylolisthesis, 4 developed a spondylolisthesis (4/78=5.1%). Three of the four (3/78=3.8%) had a fusion in the follow up period (average 21.3 months after the index procedure, range 11 – 39 months).

### Conclusions

The natural history of spinal degeneration dictates that some patients even without a pre-existing spondylolisthesis will require fusion post decompression. However, this was a small number (3.8%) of all patients in our study group. Our data suggests that minimally invasive microdecompression is a surgical option in stenosis patients having no pre-op spondylolisthesis or a stable, Grade I spondylolisthesis.

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## Initiation of sedative use is associated with development of musculoskeletal pathology: a longitudinal cohort study from the midlife development in the U.S. (MIDUS) Study

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**Introduction:** The study of substance abuse in adults with musculoskeletal disorders is controversial. Some studies show a higher incidence of substance abuse in patients with chronic musculoskeletal pain and others show no association. There is a paucity of literature relating development of musculoskeletal pathology to initiation of sedative usage. We evaluated a longitudinal cohort for the association of development of musculoskeletal pathology to the initiation of sedative use through the MIDUS longitudinal series.

**Methods:** This study used data from the MIDUS national study, a longitudinal study assessing health and well-being that was conducted by random dialing a sample of English-speaking, non-institutionalized adults in the U.S. MIDUS 1 was conducted in 1995-1996, yielding 7108 participants. MIDUS 2 was conducted 9-10 years later through outreach to the original participants, of which 4963 successfully completed the survey. Three outcomes for musculoskeletal pathology were assessed. Patients responded to whether they had: 1) experienced or been treated for arthritis, rheumatism, or other bone or joint disease; 2) experienced or been treated for sciatica, lumbago, or recurrent backache; and 3) in the past 30 days taken prescription medicine for arthritis? To evaluate sedative use, patients were asked to respond to the question: "Did you ever use any of the following substances on your own during the past 12 months? A) Sedatives, including either barbiturates or sleeping pills." Patients who denied both musculoskeletal pathology and sedative usage in the MIDUS 1 survey were included. Evaluation using two-tailed student's t-tests and chi-square tests compared demographic data as appropriate, and McNemar's tests assessed the association between musculoskeletal pathology and use of sedatives.

**Results:** Of the 4963 participants who completed both MIDUS 1 and MIDUS 2 surveys, 3793 participants did not use sedatives in the MIDUS 1 survey and had a valid response in the MIDUS 2 survey. 3033 of 3793 participants answered the question to bone and joint disease; participants with new use of sedatives had a higher incidence of new onset bone and joint (21 of 82, 25.6%, vs. 496 of 2951, 16.8%,  $p < 0.001$ ; relative risk [RR] 1.68). 3046 of 3793 participants answered the question to back pain; participants with new use of sedatives had a higher incidence of newly developed back pain (15 of 78, 19.2% vs. 356 of 2968, 12.0%,  $p < 0.001$ ; RR 1.72). 2835 of 3793 participants answered the question to use of prescription arthritis medication; participants with new use of sedatives had a higher incidence of development of use of arthritis medications (22 of 79, 27.8% vs. 381 of 2756, 13.8%,  $p < 0.001$ ; RR 2.34).

**Discussion:** These results suggest a positive association between initiation of sedative use and the development of musculoskeletal pathology and the use of arthritis medication. The wording of the question for sedative use explicitly assessed usage "either without a doctor's prescription, in larger amounts than prescribed, or for a longer period than prescribed," suggesting an association of abusive patterns of sedative use with musculoskeletal pathology. Our results suggest the importance of detecting comorbid substance abuse in patients with chronic musculoskeletal pathology.

## Factors related to spinal sagittal imbalance among an elderly population in a suburban community : The Shiraniwa study.

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### INTRODUCTION

Spinal sagittal imbalance induces low back pain, gastroesophageal reflux, and poor quality of life among elderly people. Even though corrective surgery has been sophisticated to treat spinal sagittal imbalance, it has not been a complete solution because of complications and medical cost. On the other hand, it seems plausible to argue that trunk muscle strength training may have the potential to improve postural alignment. However, there is still little known about the effect of trunk muscle mass and the strength on spinal sagittal imbalance. Therefore, the purpose of this study was to clarify the factors related to sagittal imbalance among elderly people focusing on trunk muscle.

### METHODS

This study was based on the results obtained from cross-sectional measurements of participants who enrolled in the Shiraniwa study. The Shiraniwa study, which began in a suburban community from 2016, is a population-based prospective cohort study that aims at investigating locomotive syndrome, sarcopenia, frailty, and spinal sagittal imbalance. It was also designed to elucidate risk factors for these conditions.

We enrolled 409 people aged 65 years or older (164 males, 245 females, mean age: 73.5±5.4 years) and investigated body mass index (BMI), trunk muscle mass (using bioimpedance analysis machine: MC780A, TANITA, Japan), back muscle strength (using T.K.K.5402, TAKEI, Japan), C7 sagittal vertebral axis (SVA), and prevalent vertebral fractures from lateral view of whole spine radiograph.

We defined the people whose SVA > 95mm as sagittal imbalance group, and SVA ≤ 95mm as normal group. Each item was compared between two groups using Mann-Whitney U test and chi-squared test. Factors related to sagittal imbalance were assessed using multivariate logistic regression analysis.

### RESULTS

Sagittal imbalance was present in 11.0% (45 people) of the study population. There was no significant difference in sex and BMI between two groups. Age (78.4years vs 72.9years) and the ratio of prevalent vertebral fracture (46.7% vs 10.7%) were significantly higher in sagittal imbalance group. Back muscle strength (male: 45.2kg vs 85.3kg, female: 26.7kg vs 46.5kg) and trunk muscle mass (male: 24.6kg vs 26.0kg, female: 18.1kg vs 19.5kg) was significantly lower in sagittal imbalance group.

Back muscle strength indicated high accuracy in ROC curve analysis about sagittal imbalance (area under the curve: male 0.871, female 0.807) and the cutoff value were 58kg in male, and 34kg in female.

Multivariate logistic regression analysis revealed that age (female: OR: 1.11, 95% CI 1.02-1.21), prevalent vertebral fractures (male: OR 9.19, 95% CI 1.16-72.9, female: OR 2.63, 95% CI 1.04-6.68), and decreased back muscle strength (male: OR 7.04, 95% CI 1.50-32.89, female: OR 4.24, 95% CI 1.55-11.55) were independently related to sagittal imbalance. On the other hand, BMI and trunk muscle mass were not independently related to sagittal imbalance.

### DISCUSSION

Factors related to sagittal imbalance were aging, prevalent vertebral fractures, and decreased back muscle strength. It is not clear the causality due to the cross-sectional nature. However, this study support the possibility that prevention of vertebral fracture and maintenance of back muscle strength (male: >58kg, female: >34kg) are effective for prevention of sagittal imbalance.

## Mini-open anterior lumbar interbody fusion (mini-ALIF) for degenerative spondylolisthesis.

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**INTRODUCTION** Spinal fusion has become a great procedure for instability in degenerative spondylolisthesis patients. Recently, several minimal invasive techniques have been introduced. We have performed mini-open anterior lumbar interbody fusion (mini-ALIF) since 1999. Furthermore, we used anterior interbody fusion cage and screw fixation since 2004 and we could modify this mini-ALIF to less invasive manner. In this study, we reviewed the surgical outcomes of these anterior procedures.

**MATERIALS and METHODS** 143 patients with a minimum 2 years follow-up were enrolled in this study. At the beginning, we needed additional posterior fixation to prevent bone collapse in 54 patients (Group A: anterior and posterior surgery). 89 patients underwent only anterior surgery with the anterior cage (Group B). We further investigated long follow-up outcomes (> 5years) in 29 Group A cases and 51 Group B cases.

We checked bone union with radiographs and CT-MPR. We also evaluated degenerative changes and dynamic factors during follow-up. Clinical results were estimated by Japanese Orthopaedic Surgery Association (JOA) score and low back pain status.

**RESULTS** At first this anterior procedure made mini-ALIF less invasive manner. The average operation time was 211 minutes in Group A and 105 minutes in Group B. The blood loss was 251 ml vs. 97 ml.

Clinical improvement was reliable in both groups. Satisfactory results were achieved in most Group A cases. JOA score showed their favorite conditions (pre-Op: 14.0, post-Op: 22.5, 2years: 24.2/29). In Group B, most patients were free from back pain and returned to daily life. The average JOA score was 17.3/29 at pre-op., 21.2 at post-op. and 25.3 at two years. The minor complaint like dullness at their back was less compared to Group A.

Most cases achieved bony fusion (Group A: 52/54, Group B: 86/89 cases). Correction loss was detected in 2 bone collapse and 3 cage migration cases. During 5 years follow-up (80 cases), degenerative changes were detected in some cases. Disc narrowing at adjacent level was more seen in Group A. Angular instability was more seen in Group B. Though these adjacent lesions were detected, new instability was appeared in only 2 Group A cases. This single anterior procedure, Group B, might possess the possibility to reduce degenerative changes.

**DISCUSSION** Mini-ALIF showed great clinical outcomes. Image analysis also presented good bony fusion in spite of slightly correction loss during follow-up. Mini-ALIF procedure has many advantages. One is to pass through the neural arch. It can prevent any intraoperative complications and unfavorable conditions like postoperative neural adhesion. Moreover the anterior procedure with the cage and screw fixation can skip posterior procedure. It is good for preservation of back muscle and can reduce postoperative symptoms. We expect that this single stage procedure might be useful for reducing further degenerative changes.

**CONCLUSION** We reviewed our surgical outcomes of mini-ALIF for degenerative spondylolisthesis. It was MIS procedure and showed acceptable outcomes. The single anterior technique with anterior cage can skip posterior procedure and preserve posterior elements. It might reduce postoperative symptoms and adjacent degenerative changes.

## Endoscopic transforaminal thoracic discectomy on upper thoracic spine

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### Introduction

Thoracic disc herniation is relatively uncommon. Considering the complexity of neural and vascular structure, surgical treatment of upper thoracic disc herniation (UTDH) is technically challenging. Although endoscopic thoracic discectomy (ETD) has been introduced, technical feasibility and outcomes for UTDH have not been reported. The purpose of this report is to describe percutaneous endoscopic approach to remove disc herniation on upper thoracic spine via transforaminal approach.

### Material and methods

Included patients were those who presented with symptomatic disc herniation on upper thoracic spine not responding to conservative treatments. Calcified disc herniation or concomitant OPLL were excluded. Under the local anesthesia and intravenous sedation, ETD was performed by 4.7mm endoscope (TESSYS, Joimax GmbH, Germany) that introduced via transforaminal approach with foraminoplasty using reamer and bone-drill. Patients' outcome was evaluated using VAS and ODI scores. Patients' satisfaction was measured with Macnab's criteria.

### Result

Eleven consecutive patients (mean 41.3 years old, 9 males) who underwent ETD from 2001 to 2017 were reviewed. Regarding surgical levels, there were 3 for T2-3, 4 for T3-4, and 4 for T5-6. At mean 52 months follow-up, all patients showed significant improvement of pain (6.8 to 2.3 for VAS and 53.5 vs. 16.8 for ODI,  $p < 0.05$  for all). No serious complication has been reported during the follow-up.

### Conclusion

Endoscopic thoracic discectomy for upper thoracic disc herniation is a feasible and effective minimally invasive treatment option with favorable clinical results.

## The prospective cohort study for the predicting factor of symptomatic spinal metastasis

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### Introduction

Spinal metastasis is a growing problem in patients with cancer. The management of symptomatic spinal metastasis (SSM) is very important to achieve the goal of palliative care for cancer patients. The authors reported the role of spine surgery for SSM at the previous meeting. The aim of study was to investigate the predicting factor of SSM.

### Materials and Methods

A prospective cohort study on the predicting factor of SSM was performed. A consecutive cohort of 128 patients, who didn't have the intractable pain or neurologic deficit at first visiting, was enrolled. Regarding the onset of SSM, age, gender, the grade of malignancy, performance status, Barthel index, radiation therapy, bone modifying agent (BMA), chemotherapy, molecular target drugs and spinal instability neoplastic score (SINS) and each component of SINS were studied as the candidate of predicting factor of SSM. The multivariate analysis was performed by the logistic analysis. In addition, the cut-off point of the significant factor was calculated by ROC curve.

### Results

Thirty seven patients (28.9%) represented SSM during the follow up period. The SINS (OR; 1.976,  $p < 0.01$ ), the location of component of SINS (OR; 0.300,  $p < 0.05$ ) and BMA (OR; 0.298,  $p < 0.05$ ) were identified as the significant predicting factor of SSM. Furthermore, the cut-off point of SINS was 9.5. Twenty five of 40 patients (62.5%) with over 10 points of SINS represented the SSM during the follow up period. The day of SSM occurred was the mean  $3.6 \pm 3.5$  months from the first visiting. All patients (5 patients) with more than 13 of SINS represented the SSM at  $1.5 \pm 1.1$  months.

### Discussion

The natural history of spinal metastasis still remains unclear. There was no reports about the natural history. The current study had revealed the natural history of spinal metastasis. If the patient with spinal metastasis represented over 10 points of SINS, the spine surgery should be considered to prevent the SSM.

## Changes in paraspinal muscle characteristics assessed with MRI and functional outcomes following intensive exercise rehabilitation

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### Introduction

Low back pain (LBP) is a complex condition that affects between 65-85% of the general population throughout their lifetime [1, 2]. Chronic LBP has been associated with degenerative changes in the musculature of the lumbar spine. Typical nonoperative treatment in the form of physical rehabilitation has not consistently demonstrated significant improvement in muscle physiology, which has been attributed to insufficient intensity. MRI has traditionally been used to assess common metrics of muscle health related to function. However, these studies are typically limited to analysis of a single vertebral level, which does not accurately capture whole muscle health across multiple levels. Therefore, the purpose of this study was to examine changes in whole lumbar paraspinal muscle volume and fat fraction in association with changes in pain, disability, and strength following a 10-week intensive exercise rehabilitation program.

### Methods

Eight patients underwent an intensive outpatient rehabilitation program consisting of machine-based lumbar extension resistance exercises at a frequency of 2 visits/week for 20 visits. Pain (Visual Analogue Scale), LBP related disability (Oswestry Disability Index), and quality of life (EQ5D) were measured via questionnaire, and lumbar extension strength was measured using a MedX isokinetic dynamometer before and after treatment. T2-weighted MRI images of the lumbar spine (L1-S1) for patients were obtained before and after the program. Multifidus and erector spinae (ES) muscles were segmented bilaterally using OsiriX software. Regions of interest (ROIs) were then imported into Matlab to quantify muscle volume and fat signal fraction. Pre- and post-treatment measures were compared using paired t-tests. Correlations between functional outcomes and changes in muscle volume and fat were examined using Pearson's correlation coefficients.

### Results

All but one patient demonstrated increased muscle volume after treatment (Figure 1) for the multifidus (mean change (SD); 9.45 (29.6)mm<sup>3</sup>, p=0.40), and ES (22.45 (46.9)mm<sup>3</sup>, p=0.22) muscles. There were no significant changes in fat fraction for either multifidus (0.01(0.08), p=0.72) or ES (0.02 (0.10), p=0.61) muscles (Figure 2). There were trends in associations between decreased VAS and increased ES volume ( $r = -0.62$ ,  $p = 0.10$ ) as well as between decreased VAS and paraspinal fat fraction (M:  $r = -0.58$ ,  $p = 0.13$ ; ES:  $r = -0.64$ ,  $p = 0.08$ ).

### Discussion

Examination of MRI for these 8 patients who underwent 10 weeks of intensive exercise rehabilitation demonstrated consistent, but insignificant increases in both muscle volume and fat fraction of the multifidus and ES muscle groups with treatment. Relationship trends were observed between muscle characteristics and pain, but not disability, quality of life, or strength, indicating that muscle physiology may play a role in LBP symptom changes with rehabilitation. More data is needed to confirm whether this intervention results in structural and functional change in the paraspinal muscles in individuals with LBP.

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### **Type 1 Modic changes in degenerative disc disease are associated with increased fatty infiltration of the lumbar paraspinal muscles over time**

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**INTRODUCTION:** Previous investigation has demonstrated associations between low back pain (LBP) and both lumbar paraspinal muscle atrophy, and fatty infiltration, which correlate with functional disability. Increased expression of the proinflammatory cytokines in paraspinal muscles after intervertebral disc injury in an animal study was shown to correlate with paraspinal muscle atrophy. In clinical studies, LBP has been associated with Modic-1 degenerative disc disease (DDD), which represent radiographic evidence of inflammatory changes after intervertebral disc injury. The relationship between Modic-1 DDD and lumbar paraspinal muscle changes in patients with LBP has not been investigated. In the present study, we aimed to (1) characterize changes in lumbar paraspinal muscle volume and fatty infiltration over time in patients with LBP and Modic-1 DDD and (2) compare such muscle changes at levels of Modic-1 DDD with levels lacking Modic 1 endplate changes.

**METHODS:** This cross-sectional cohort study with retrospective internal comparison was conducted at a single urban, academic, tertiary spine center. Patients with LBP who presented to our spine center with a prior baseline lumbar MRI that showed Modic-I DDD were enrolled and underwent a repeat MRI at least one year after baseline MRI. Patients with a body mass index (BMI) > 40 kg/m<sup>2</sup>, diabetes mellitus, spondylolisthesis, scoliosis, compression fracture, metastatic cancer, neuromuscular disorders, or previous spine surgery were excluded. Changes in lumbar paraspinal muscle volume and fatty infiltration were assessed within each individual by comparing baseline and follow-up MRI measurements. The volumes of the multifidi, erector spinae (ES), and psoas muscles were measured by manually defined contours using IPP®, and fatty infiltration was quantified on T1-weighted axial MRI using Goutallier and Quartile classifications, which are highly reproducible (ICC:0.893-0.918). The Wilcoxon rank-sum test was used to make comparison between baseline and follow-up MRI results.

**RESULTS:** Nine patients (median±interquartile range [IQR] age: 43±21 years; seven females) were included in the study. The median time between MRIs was 17 months (IQR ±11). The total volume of the multifidi and psoas muscles from L1 to sacrum decreased significantly from baseline to follow-up MRI (p<0.023). At the level(s) of Modic-I DDD, the percentage of fatty infiltration in the multifidi and psoas muscles was significantly higher compared to levels without Modic-I DDD (p<0.040).

**DISCUSSION:** These data suggest that Modic-I DDD is associated with adjacent paraspinal muscle atrophy and fatty infiltration in patients with LBP. A larger study is warranted with a comparison group that lacks the radiographic finding of Modic-1 DDD, as well as longitudinal assessment of physical function in relation to paraspinal muscle changes. Further investigation is needed to determine the ability of targeted physical therapy to prevent paraspinal muscle changes in patients with Modic I DDD and to assess the effect on LBP symptoms and physical function.

## Disc height changes of the fusion and adjacent segments – an in-vivo lumbar patient investigation

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**Introduction** Radiographic follow-up studies revealed that **39 to 86%** of lumbar patients treated with fusion may develop progressive adjacent segment degeneration (ASD) and **5-38%** were reported to receive second operation within 2 to 10 years after surgery. Altered vertebral kinematics after fusion are widely assumed to cause ASD, but, no data has been reported on the intrinsic relationship between the fusion and adjacent segments before and after surgery. We investigated the changes of lumbar disc heights of patients before and 3 years after fusion surgery using a validated 3D imaging technique.

**Methods.** Five patients with discogenic low back pain from L4-S1 were investigated. Pre-operatively, the lumbar spine of each subject was MRI scanned for construction of 3D models of the vertebrae (Fig. 1a). The lumbar spine was then imaged using a dual fluoroscopic imaging system (DFIS) at a weightbearing, standing position of the body before and 3 years after the fusion surgery. The captured fluoroscopic images and the 3D vertebral models were used to reproduce the vertebral positions of the index segments of L4-5 and L5-S1 and the adjacent segment of L3-4 during the standing position using a 2D-3D matching technique. Disc heights before and after the surgery were calculated at the anterior, central and posterior locations of the disc (Fig. 1b). The relationships between the pre-operative index disc heights and the post-operative changes of the disc heights of the index and adjacent segments were specifically analyzed.

**Results.** On average, the fusion increased the heights of the index discs and reduced the height of the adjacent disc L3-4 ( $p > 0.05$ ). The changes of the disc heights of the two index discs after fusion are strongly, negatively associated to the corresponding pre-operative index disc heights ( $p < 0.05$ ), i.e., a lower pre-operative index disc height corresponds to a larger increase in the disc height after fusion surgery. The changes of the disc height of the adjacent disc L3-4 after fusion are moderately associated to the pre-operative height of the index disc L4-5, i.e., a lower pre-operative height of the index disc L4-5 corresponds to a larger reduction of the adjacent disc height after surgery (Fig. 2). No correlation was found between the height changes of the disc L3-4 and the pre-operative height of disc L5-S1.

**Discussion.** The data indicated that the fusion surgery affect the disc heights of the index and adjacent segments, but depending on the pre-operative disc heights of the index segments. A low pre-operative index disc could result in a large reduction in heights of the adjacent disc and thus an increase of compressive stresses inside the disc. However, a high pre-operative index disc minimally affects the adjacent segment. It has been shown that an excessive increase of disc stresses can cause damage to the disc biological structures and lead to disc degeneration. Therefore, the data of this study could be instrumental for future investigation of biomechanical factors that are associated to post-operative ASDs and for improvement of fusion surgeries that can delay or prevent second operation.

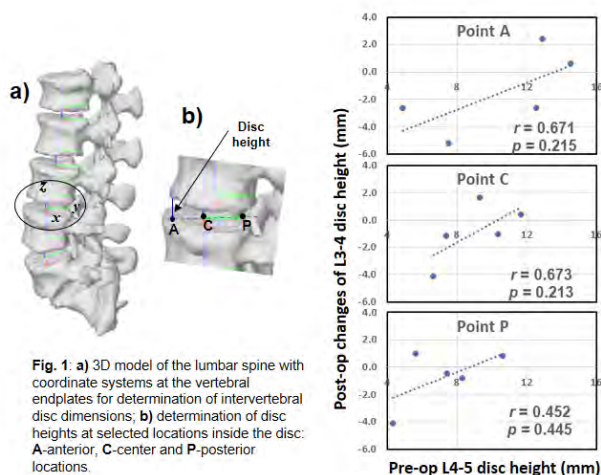


Fig. 2. Correlations of the pre-operative heights of the index disc L4-5 with the changes of the disc heights of adjacent disc L3-4 at different locations inside the disc after fusion surgery.



## Hemoglobin A1c as a predictor of surgical site infection following single level lumbar/lumbosacral posterior fusion in patients with diabetes

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**INTRODUCTION:** Diabetes mellitus (DM) is a prevalent disease of glucose dysregulation that has been associated with an increased risk for postoperative infection following spine surgery. The status of preoperative blood glucose management may affect the risk of surgical site infection (SSI). In the present study, we evaluated the association between preoperative glycemic control as indicated by hemoglobin A1c (HbA1c) in patients with diabetes and incidence of postoperative SSI following single level lumbar/lumbosacral posterior fusion. Furthermore, we calculated a threshold level of HbA1c above which the risk of SSI after posterior lumbar/lumbosacral arthrodesis increases significantly in diabetic patients.

**METHODS:** From January 2009 to December 2015, total 92 patients who underwent single level lumbar/lumbosacral posterior fusion with diabetes and had preoperative HbA1c recorded within 4 weeks of surgery were included in the study. Patients were divided into two groups according to whether they had SSI, and then demographic/clinical data were compared. A receiver operating characteristic (ROC) and area under the curve (AUC) analysis was conducted to define the cut-off value of HbA1c above which the risk of SSI was significantly increased. Including this value, potential variables were verified by multiple logistic regression analysis.

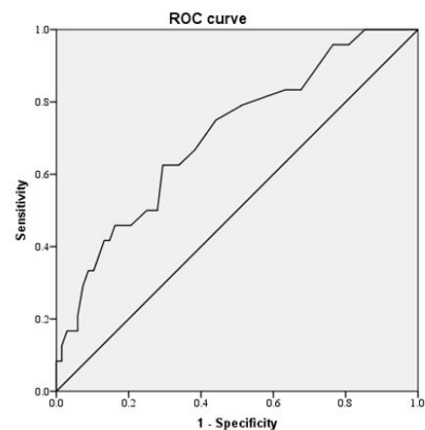
**RESULTS:** Twenty four patients were treated for SSI and 68 patients maintained noninfectious condition within 1 year. Three of the 24 (12.5%) patients developed SSI in the deep layer requiring operative irrigation and debridement. The preoperative HbA1c value was significantly higher in patients with SSI (6.8%) than in those without SSI (6.0%;  $p=0.008$ ). The results of ROC analysis determined that  $HbA1c \geq 6.9\%$  could serve as a threshold for significantly increased risk of SSI ( $p=0.003$ ,  $AUC=0.708$ , sensitivity=62.5%, specificity=70.6%). After adjusting for confounding factors, there was a significant association between preoperative HbA1c and occurrence of SSI ( $p=0.008$ ,  $OR=4.500$ ,  $95\% CI=1.486-13.624$ ).

**DISCUSSION:** In patients with diabetes, the preoperative glycemic control as indicated by HbA1c is an independent risk factor for SSI following single level lumbar/lumbosacral posterior fusion. Particularly when preoperative HbA1c exceeded 6.9%, the risk of SSI significantly increased.

Table 1 Demographic and clinical characteristics of study groups

	S group	NS group	P-value
No.	24	68	
Sex (M:F)	13:11	25:43	0.137
Age (years)	70.0 ± 8.4	66.7 ± 8.6	0.108
Smoking	7	16	0.583
BMI (kg/m <sup>2</sup> )	25.71 ± 4.66	24.96 ± 3.44	0.404
HbA1c (%)	6.8 ± 1.3	6.0 ± 0.8	0.008*
Hospital stay (days)	45.8 ± 39.7	19.3 ± 7.5	0.003*
Follow-up duration (months)	25.0 ± 13.8	21.8 ± 9.0	0.190
ASA physical status classification			0.206
	2	18	59
	3	6	9
Procedure			0.768
	PLF	6	15
	PLIF	18	53
Fusion segment			0.483
	L4/5	17	53
	L5/S1	7	15
Transfusion	3	7	0.717
EBL (mL)	483.3 ± 312.7	459.6 ± 229.7	0.694
Operation time (min)	272.9 ± 45.7	266.7 ± 42.1	0.544

Student's t test, Mann-Whitney U test,  $\chi^2$  test or Fisher's exact test were used as appropriate



## **Skeletal hypoplasia (L5) and the anterior opening of the intervertebral disc caused lumbar hyperlordosis in patients with Crowe type 4 Completely Dislocated Hips**

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### **Introduction**

Recent studies investigating the relationship between the spine and the pelvis have refined our understanding of pelvic and spinal orientation. However, there have been few reports on the spino-pelvic alignment and the shape of vertebral body and the intervertebral disc in patients with Crowe type 4 completely dislocated hips (CDH).

### **Materials and Methods**

The subjects included 60 CDH patients (average age: 63 years) and 50 patients with idiopathic osteonecrosis of the femoral head (ION) (average age: 58 years) who underwent THA. All of the patients were female. Lateral whole spine radiographs of all patients were prospectively taken before surgery. The sagittal spino-pelvic alignment parameters that were examined included lumbar lordosis (LL: L1-S1), sacral slope (SS), the angle of the segmental vertebral body (VB angle: L1-L5) and the intervertebral disc angle (ID angle: L1/2-L5/S). Angles that opened anteriorly, had positive values; while those that opened posteriorly had negative values. The significance of the differences among the two groups was evaluated by Student's *t*-test. P values of <0.05 were considered to indicate statistical significance.

### **Results**

The mean LL, SS, VB angle and ID angle in the CDH and ION groups were 66° and 48°, 52° and 38°, L1VB: -5° and -2°, L5VB: 12° and 9°, L1/2: 7.2° and 4.4° L2/3: 10.1° and 6.5° L3/4: 12° and 7.0° L4/5: 11° and 9° L5/S: 15.9° and 11.7°, respectively (P<0.01).

### **Conclusion**

Our study had 2 main findings. In patients with CDH: 1) The sagittal alignment of the spine in patients with CDH was characterized by the anterior angulation of the pelvis and lumbar hyperlordosis. Pelvic morphology with CDH may affect lumbar hyperlordosis and these may be compensatory changes that occur to maintain the body balance. 2) Skeletal hypoplasia (L5) and the anterior opening of the intervertebral disc caused lumbar hyperlordosis in patients with CDH. Among the patients with L5 hypoplasia, there seemed to be a group in which developmental compensation occurred during the gestational period as a result of genetic or other factors which resulted in pelvic anteversion and skeletal hypoplasia from the lumbosacral spine to the pelvic and hip joint.

## The RANK/RANKL/OPG system is expressed by human intervertebral disc cells

Tomohiko Sano, Koji Akeda, Norihiko Takegami, Junichi Yamada, Kazuma Nakase, Takao Sudo, Akihiro Sudo

**INTRODUCTION:** The receptor activator of nuclear factor kappa B (NF- $\kappa$ B) ligand (RANKL) is well known to regulate bone metabolism. Binding of RANKL to its receptor RANK induces differentiation and activation of osteoclasts through NF- $\kappa$ B pathways. Osteoprotegerin (OPG) is a soluble decoy receptor for RANKL. It has recently been reported that the RANK/RANKL/OPG system is expressed in human articular cartilage and is associated with the progression of knee osteoarthritis. Therefore, we hypothesized that the expression of the RANK/RANKL/OPG system will be associated with the progression of intervertebral disc (IVD) degeneration. The purpose of this study was (1) to examine the mRNA and immunohistochemical expressions of the RANK/RANKL/OPG system in the human IVD, (2) to examine the expression of the RANK/RANKL/OPG system under stimulation by interleukin-1 $\beta$  (IL-1 $\beta$ ), and (3) to evaluate the effect of RANKL on the expression of a pro-inflammatory cytokine and matrix-degrading enzymes with/without IL-1 $\beta$  stimulation.

**METHODS:** Human IVD tissues (n=7, average age: 46.6 years-old) obtained from spine surgeries were used in this study. Annulus fibrosus (AF) and nucleus pulposus (NP) cells were separately isolated by sequential enzyme digestion and cultured in monolayer. The expression of the RANK/RANKL/OPG system by human AF and NP cells was examined using real-time polymerase chain reaction (PCR) and immunohistochemistry. To evaluate the effect of IL-1 $\beta$  stimulation on the mRNA levels of the RANK/RANKL/OPG system, AF or NP cells were cultured with or without recombinant human IL-1 $\beta$  (rhIL-1 $\beta$ ) at 0.1, 1.0 or 10 ng/ml for an additional 24 hours. To evaluate the effect of RANKL on the mRNA expression of a pro-inflammatory cytokine and matrix-degrading enzymes, the cells were cultured with or without recombinant human RANKL at 10 ng/ml in the presence or absence of rhIL-1 $\beta$  (1.0 ng/ml) for an additional 48 hours. The expression of the pro-inflammatory cytokine IL-1 $\beta$  and matrix-degrading enzymes [matrix metalloproteinase (MMP) -3, -13, and a disintegrin and metalloproteinase with thrombospondin motifs-5 (ADAMTS-5)] were examined using real-time PCR. Differences in quantitative outcome measures were established using one-way analysis of variance with Fisher's Least Significant Difference test.

**RESULTS:** Immunoreactivity to and mRNA expressions of RANK, RANKL and OPG were clearly identified in monolayer cultures of AF and NP cells. IL-1 $\beta$  significantly stimulated the mRNA expression of RANKL, but not that of RANK and OPG, by both AF and NP cells. Treatment with RANKL did not induce significant changes in the mRNA expressions of IL-1 $\beta$ , MMP-3, -13 and ADAMTS-5 by both AF and NP cells. However, the expressions of MMP-3, -13, ADAMTS5 and IL-1 $\beta$  by both AF and NP cells were significantly upregulated by RANKL stimulation in the presence of IL-1 $\beta$ .

**DISCUSSION:** This study demonstrated that the RANK/RANKL/OPG system was expressed by human IVD cells. The expression of RANKL was significantly upregulated by IL-1 $\beta$  stimulation. RANKL enhanced the expression of a pro-inflammatory cytokine and matrix-degrading enzymes in the presence of IL-1 $\beta$ . The results of this study suggest the possibility that the RANK/RANKL/OPG system plays a role in the process of disc degeneration by accelerating the expression of cytokines and matrix-degrading enzymes.

## Postural adjustments following walk slip perturbation with a handheld task in subjects with recurrent low back pain

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**Introduction:** Slip-related balance deficits during walking lead to increased fall risks and major concerns in the health care system. Trunk sway response while holding a tray could be critical following walk slip perturbations in subjects with recurrent low back pain (LBP). This study was to investigate reaction time, trunk sway angle, and velocity following treadmill-induced slip perturbation while the subjects held or did not hold a tray during walking between subjects with and without recurrent LBP.

**Methods:** There were 28 subjects with LBP and 39 control subjects who participated in the study. Three levels of consecutive treadmill-induced walk slip perturbations were introduced based on the duration, velocity, and displacement. The reaction time (seconds) was determined as the time between onset of the treadmill motion and recovery after toe-off. The peak trunk sway angle, and velocity were compared with tray usage between the groups.

**Results:** The LBP group demonstrated slower peak trunk sway ( $t = -2.59$ ,  $p = 0.01$ ) and increased peak trunk flexion angle ( $t = -2.57$ ,  $p = 0.01$ ) while holding a tray at the first walk slip perturbation. Although the reaction time was not significantly different between groups, the levels of perturbation and tray usage demonstrated a significant interaction on the peak sway velocity ( $F = 4.81$ ,  $p = 0.03$ ). The LBP group was able to compensate for their balance deficits with tray usage by enhancing control over trunk sway angle and velocity following the perturbation.

**Discussion:** The trunk sway angle and velocity were not significantly correlated with reaction time while holding a tray; however, the LBP group demonstrated significantly delayed trunk flexion velocity at first perturbation without holding a tray. The novelty of the walk slip perturbation test with a handheld task revealed compensation strategies used by the LBP group during the higher magnitudes of perturbation.

**Key words:** kinematic; walk; slip; perturbations; low back pain; motor learning; compensation; biomechanics; balance; trunk; reaction time.

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## **Significance of conservative treatment for lumbar spinal canal stenosis: surgical outcome for patients with recurrent symptoms after successful conservative treatment**

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### **INTRODUCTION**

Lumbar spinal canal stenosis (LSS) is almost always initially treated with conservative treatment in the absence of severe symptoms such as severe motor disturbances or bowel and/or urinary dysfunction. Although good outcomes were reported with conservative treatment against LSS, we experienced surgeries for cases of recurrent symptoms even after successful conservative treatment. However, the outcomes of such cases are still unknown.

### **AIM**

To investigate the surgical outcome for patients with recurrent symptoms after successful conservative treatment compared to that for patients with failed conservative treatment at initial hospitalization.

### **METHODS**

Nineteen patients who had symptoms relief with initial inpatient conservative treatment from 2005 to 2010 but underwent surgeries later because of recurrent symptoms were included in this study (Group R, 12 males, 7 females, mean age: 67 years old, mean follow-up period: 8.1 years). Forty five patients who did not have symptoms relief with initial inpatient conservative treatment in the same period and underwent surgeries were also included as control (Group C, 29 males, 16 females, mean age: 67 years old, mean follow-up period: 8.5 years). The Japanese Orthopaedic Association (JOA) score and JOA score recovery rate were used to evaluate the clinical outcome.

### **RESULTS**

The mean JOA score of Group C at final follow-up showed significant improvement compared to that on initial admission (20.7 and 13.8 points, respectively,  $p < 0.05$ ). The mean JOA score on initial admission between Group R and Group C did not show significant difference (15.6 and 13.8 points, respectively). Although the mean JOA score of Group R at discharge after successful conservative treatment (21.2 points) showed significant improvement compared to that on initial admission ( $p < 0.01$ ), they underwent surgeries mean 25.3 months after discharge. The mean JOA score of Group R at the time of recurrent symptoms (12.2 points) showed significant deterioration compared to that at discharge ( $p < 0.01$ ) but did not show significant difference compared to that of Group C on initial admission. The mean JOA score of Group R at final follow-up (19.4 points) showed significant improvement compared to both that on initial admission and that at the time of recurrent symptoms ( $p < 0.05$ ). The mean JOA score recovery rate between Group C and Group R at final follow-up did not show significant difference (42.9% and 39.4%, respectively). None of the following factors such as difference of surgery (decompression with/ without fusion), type of clinical classification (radicular, cauda equina or mixed), duration of recurrence, coexistence of deformity (scoliosis, spondylolisthesis) affected the outcome.

### **DISCUSSION**

The surgical outcome for Group R did show similar outcome compared to that for Group C even after 8 years follow-up. Our study suggests LSS patients with successful conservative treatment could get similar benefit of surgery even after the recurrence of symptoms. Therefore, if symptoms allow, enough conservative treatment, which have much less side effects than surgery, would be recommended before performing surgery for LSS.

## **BMP-3 growth factor stimulates stem cells and disc cells in 3D co-culture to a higher proteoglycan production**

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**Introduction:** In western countries, low back pain (LBP) is one of the most common pain disorders and the main cause of LBP is believed to be degeneration of intervertebral discs (IVDs). Transplanting cells such as human mesenchymal stem cells (hMSCs) into the intervertebral disc (IVDs) to influence the residing disc cells (DCs) in the degenerated discs is suggested as potential treatment options. BMP-3 growth factor is known to promote chondrogenesis and has been proven effective in the enhancement of chondrogenesis in hMSCs pretreated with IL-1 $\beta$  cytokine stimulation (found in abundance in degenerated IVDs) cultured in hydrogel [1]. 3D co-cultures of hMSCs and DCs has previously further been demonstrated to result in increased proteoglycan production [2].

**Aims:** The aim was to study the effects of BMP-3 on hMSCs, DCs as well as hMSCs/DC in co-culture in a pellet system, both as single treatment and after pre-treatment of IL-1 $\beta$ , in terms of proteoglycans accumulation.

**Method:** Cell pellet cultures (200,000 cells/pellet) were performed with hMSCs and DCs, and co-culture pellets were performed with hMSCs and DCs in 1:1 ratio. The cells were obtained after informed consent from 6 patients undergoing spine surgery. The pellets were stimulated with BMP-3 in two different concentrations, 10ng/mL or 100ng/mL. For pre-treatment, cell pellets were first stimulated with IL-1 $\beta$ , concentration 10ng/mL or 100ng/mL for 24 hours, the media was then discarded and replaced with media containing BMP-3 with concentrations 10ng/mL or 100ng/mL. The pellets were harvested at day 7, 14, and 28, fixated, sectioned and Alcian blue van Gieson stained. Cell viability test was carried out with cell counting kit-8 to ensure survival of cells in pellets stimulated with IL-1 $\beta$ . Microscopic evaluation was performed for proteoglycans accumulation.

**Results:** Cell viability was observed in all pellet regardless of cell type and stimulation. Higher proteoglycan accumulation was observed in all co-culture pellets compared to both hMSCs and DCs pellets, regardless of stimulation. Stimulation with BMP-3 at a concentration of 10 ng/mL did not demonstrate any clear increase in proteoglycan production in either hMSCs, DCs or the co-cultures. However, BMP-3 stimulation with 100ng/mL resulted in increased proteoglycan accumulation in the co-cultures both compared to controls and stimulation with 10ng/mL, however in the hMSC and DC pellets no clear effect was seen. After pre-treatment with IL-1 $\beta$  a similar effect of BMP 100 ng/mL was seen as without pre-treatment.

**Discussion:** Stimulation with BMP-3 in 100 ng/mL concentration was demonstrated to result in increased proteoglycans production when hMSC and DC were co-cultured regardless of pre-exposure to IL-1 $\beta$ . These results indicate the possibility to use BMP-3 as an enhancer in cell therapy treatment of degenerative discs.

1. [1] D. Hingert, H. Barreto Henriksson, H. Brisby, Human mesenchymal stem cells pre-treated with IL-1beta and stimulated with BMP-3 enhance chondrogenesis, *Tissue engineering. Part A* (2017).
2. [2] T. Svanvik, H.B. Henriksson, C. Karlsson, et al., Human disk cells from degenerated disks and mesenchymal stem cells in co-culture result in increased matrix production, *Cells, tissues, organs* 191(1) (2010) 2-11.

**GP160**

**Preemptive multimodal analgesia for postoperative pain management after lumbar fusion surgery - a randomized controlled trial**

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Publish consent withheld

**GP161**

**Gender- and age-specific analgesia for early postoperative pain management after lumbar discectomy : A Randomized Clinical Trial**

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Publish consent withheld



## Efficacy of early intervention of balloon kyphoplasty for thoracolumbar osteoporotic vertebral fracture

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**Introduction:** Along with the recent increase in osteoporotic vertebral body fracture (OVF) in the super aging society, it is necessary to consider treatments aiming for early social reintegration to OVF. The purpose of this study was to investigate the efficacy of early intervention of percutaneous balloon kyphoplasty (BKP) for OVF.

**Methods.** A total of 51 patients (mean age, 75.5 years) who underwent BKP for OVF at thoracolumbar level at the authors' institute were recruited. The patients with the following image findings, which reported as causing vertebral fracture progression or pseudoarthrosis, underwent BKP within 4 weeks after injury (early group). They were 1. a confined high intensity or a diffuse low intensity area in the fractured vertebrae on T2-weighted MR images (Tsuji T et al., Spine, 2011), 2. a diffuse low intensity area in the fractured vertebrae on T1-weighted MR images (Kanchiku T, et al., J Spinal Disord Tech, 2014). Other patients underwent BKP due to residual of ADL disorders after conservative therapy for more than 1 month, or delayed bone union or pseudoarthrosis (late group). Patients were divided into two groups (early or late group) according to the timing of BKP. The items were investigated as follows: local kyphotic angle, collapse rate of fractured vertebrae, occurrence of the adjacent fracture vertebrae, and postoperative hospital stay. Those items were analyzed between two groups ( $p < 0.05$ ).

**Results.** There were 32 patients (male/female 6/26, age 74.6 years) in the early group and 19 patients (male/female 4/15, age 77.1 years) in the late group. The periods from the onset to BKP were 15.8 days in the early group and 59 days in the late group. The preoperative bone mineral density T score was -2.12 in the early group and -2.28 in the late group ( $p = 0.646$ ). The postoperative hospital stay was 15.1 days in the early group and 31.9 days in the late group ( $p < 0.05$ ). The local kyphotic angle (preoperative / operation / final) was -11.3 / -6.7 / -12.2 in the early group and -27.6 / -19.8 / -28.4 in the late group ( $p < 0.001$ ). There was no significant difference in the local kyphosis between the preoperative and the final follow-up in both groups ( $p = 0.692$ ,  $p = 0.794$ ). The collapse rate of vertebral fracture (preoperative / operation / final) was 0.81 / 0.91 / 0.83 in the early group and 0.69 / 0.77 / 0.72 in the late group. In both groups, the final collapse rate was equivalent to that before surgery ( $p = 0.322$ ,  $p = 0.346$ ). The occurrence of adjacent vertebral fracture was significantly higher in the late group (3/32 patients in early group, 9/19 in late group,  $p < 0.05$ ).

**Conclusion.** Even with BKP intervention, global spinal alignment and vertebral body collapse was the same as before surgery in both groups. From these results, early BKP intervention before vertebral body collapse was important from the viewpoint of maintaining global spinal alignment. Moreover, early BKP intervention enabled early social reintegration and reduced occurrence of adjacent vertebral fractures.

1. Tsujio T, et al. Characteristic radiographic or magnetic resonance images of fresh osteoporotic vertebral fractures predicting potential risk for nonunion. Spine 2011; 36(15): 1229-1235.
2. Kanchiku T, et al. Usefulness of an early MRI-based classification system for predicting vertebral collapse and Pseudoarthrosis after osteoporotic vertebral fractures. J Spinal Disord Tech 2014; 27(2): E61-65.

## Role of semaphorin 3A in intervertebral disc degeneration

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**INTRODUCTION:** Several factors, including inflammatory cytokines, oxidative stress, innervation, and angiogenesis, cause intervertebral disc (IVD) degeneration. Vascular endothelial growth factor (VEGF) plays an important role in the progression of IVD degeneration through angiogenesis. Semaphorin 3A (SEMA3A) shares the receptor neuropilin 1 with VEGF. However, the role of SEMA3A in IVD degeneration is unclear. The main objectives of this study were to clarify the expression and function of SEMA3A in IVD degeneration and to determine whether SEMA3A can be used as a therapeutic target.

**METHODS:** Animal model of IVD degeneration: Eight-week-old Wistar rats were anesthetized, and disc puncture was performed using a 23-gauge needle at the 3<sup>rd</sup> to 10<sup>th</sup> coccygeal vertebrae (ref). Annulus fibrosus (AF) cell culture: Rat AF cells were isolated and cultured as previously reported (ref). Human IVD samples: Informed consent for the experimental use of surgical samples was obtained from each patient according to the ethical guidelines. Statistical analysis: All measurements were performed in triplicates. Differences between the groups were analyzed using the Student's t-test (\*p < 0.05).

**RESULTS:** Immunohistochemistry of surgically obtained human IVD samples showed that the expression of vWF, a marker of vascular endothelial cells, increased with the progression of degeneration (figure), suggesting that vascularization is associated with IVD degeneration. Real-time RT-PCR analysis showed that the mRNA expression of SEMA3A was predominantly higher in rat AF than in rat nucleus pulposus (NP). The mRNA expression of SEMA3A was significantly reduced in the rat model of IVD degeneration than in the sham model. Next, we treated cultured rat AF cells with inflammatory cytokines, including TNF-alpha, IL-1beta, and IL-6, and evaluated the mRNA expression of SEMA3A. Real-time RT-PCR analysis showed that the expression of SEMA3A was significantly reduced by treatment with these cytokines, while the expression of VEGF was significantly increased. Treating AF cells with IL-6 resulted in the greatest reduction in the expression of SEMA3A; hence, we examined the downstream signaling of IL-6 by inhibiting the JAK/STAT, p38, JNK, and ERK pathways. Real-time RT-PCR analysis showed that the IL-6 mediated reduction in the expression of SEMA3A was significantly neutralized by the inhibition of the JAK/STAT and p38 pathways. Finally, to examine the role of SEMA3A in IVD degeneration, we treated cultured rat AF cells with rhSEMA3A and IL-6 and evaluated the expression of inflammatory cytokines and catabolic factors. Interestingly, we found that rhSEMA3A significantly abolished the IL-6 mediated induction of MMP3, IL-6, and TNF-alpha.

**DISCUSSION:** Our results showed that the expression of SEMA3A was physiologically higher in AF than in NP and that the expression of SEMA3A had an inverse relationship with vascularization in IVD degeneration. These results indicate that SEMA3A may be an anti-angiogenesis factor in IVD. We also found that SEMA3A blocked the catabolic shift in IL-6 treated AF cells. These findings indicate that SEMA3A maintains tissue homeostasis in IVD and that SEMA3A may be a therapeutic target for IVD degeneration.

1. Suzuki S, Fujita N, et al. Arthritis Res Ther 2015;17:316.

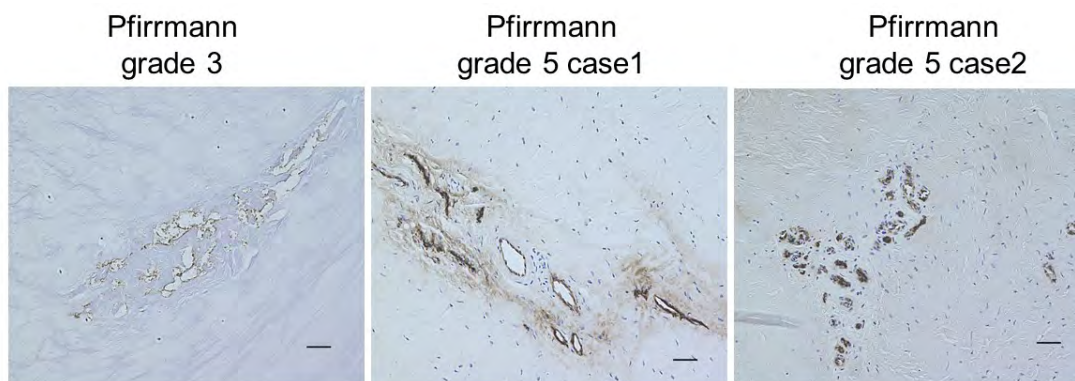


Figure. Immunohistochemistry of vWF in the IVD samples from DLS patients.

## MRI examination of the L2-S1 level retroperitoneal oblique corridors in Japanese

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### Introduction

Among the minimally-invasive anterior lumbar interbody fusion (LIF) techniques, the oblique lumbar interbody fusion (OLIF), which takes a retroperitoneal approach by approaching the intervertebral disc via the oblique corridor anterior to the major psoas, takes a different route from the extreme lateral interbody fusion, which involves entering the major psoas muscle. Therefore, it is important to evaluate whether or not this approach is possible preoperatively. The purpose of this study is to evaluate the oblique corridor in Japanese patients by magnetic resonance imaging (MRI).

### Methods

Of the 1480 patients who underwent lumbar MRI testing at our institute between April and August 2017, patients with previous history of lumbar spine and retroperitoneal surgery, transitional vertebra, lumbar scoliosis with a curvature of  $\geq 30$  degrees, or age under 20 years old were excluded from this study. We excluded L2-S intervertebral disc levels that are insufficient at one level or that can not be accurately evaluated with MRI axial images. The subjects of this study were the 364 remaining Japanese patients aged 20–90 years whose axial and sagittal images at the four intervertebral disc levels (L2/3–L5/S1) were confirmed in a 1.5 TESLA MRI. 169 of the subjects were males, and 195 were females with a mean age of 52 (20–89) years. According to Molinares's method, the L2-5 oblique corridor was defined as the distance between the left lateral border of the aorta or iliac artery and the anterior border of the psoas, and the L5-S1 oblique corridor was defined transversely from the midsagittal line of the inferior endplate of L5 to the medial border of the left common iliac vessel. We evaluated oblique corridor distances in the L2/3, L3/4, L4/5, and L5/S1 intervertebral disc levels and level of the aortal bifurcation measured in imaging diagnoses using the axial MRI image and the distance from the bifurcation to the L5/S intervertebral disc measured on the sagittal MRI image. The presence or absence of the rising psoas sign, an indicator of abnormal major psoas muscle anatomy, was also evaluated.

### Results

The oblique corridors measured were L2/3 = 17.1 mm (males: 16.6, females: 17.5), L3/4 = 16.4 mm (males: 15.7, females: 16.9), L4/5 = 13.0 mm (males: 12.5, females: 13.4), and L5/S = 10.4 mm (males: 9.4, females: 11.3). The bifurcation of the aorta was 1.6% at L3, 4.1% at L3/4, 55.5% at L4, 24.2% at L4/5, and 14.6% at L5. The rising psoas sign was found in 5.2% of the patients (males: 7.7%, females: 2.4%).

### Discussion

The results of this study verified that the retroperitoneal oblique corridor at the L2–S1 levels in Japanese individuals on the MRI were L2/3 = 99.4%, L3/4 = 100%, L4/5 = 91.5%, and L5/S = 69.8%. These findings resulted in supporting the previous report by Molinares et al. The oblique corridor evaluation by MRI is therefore a very useful tool for preoperative OLIF planning.

## Clinical assessment of simultaneous diffusion tensor imaging and T2 relaxometry of lumbar nerve roots in patients with low back pain

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**PURPOSE:** Diffusion Tensor Imaging (DTI) based on single-shot Echo Planner Imaging sequence (EPI-DTI) is promising method to evaluate lumbar nerve roots for assessment of low back pain using quantitative parameters such as fractional anisotropy (FA) value, mean diffusivity, radial diffusivity, and apparent diffusion coefficient (ADC) values. Alternatively, T2 value, which obtained by multi-echo EPI sequence with multiple-acquisition, has also been reported for evaluation of lumbar nerve roots.

In this study, we developed a single-shot dual-echo EPI-DTI sequence (Diffusion-Relaxation Matrix: DRM) that can simultaneously provide the diffusion tensor parameters and T2 values. The purpose of this study was to investigate the clinical feasibility of DRM for the lumbar nerve roots in patients with low back pain.

**METHODS:** All subjects were examined with 1.5T whole-body clinical system (Ingenia, Philips Healthcare). Fifty-five low back pain patients with unilateral neurological symptom (median age, 58.2 years; range, 24–72 years), underwent DRM sequence.

To assess the diffusion parameters and T2 values quantitatively, regions of interests (ROIs) were placed both proximally and distally to the lumbar foraminal zone at the levels responsible for symptoms. Quantitative values obtained from DRM including FA value, ADC value, and T2 value (Fig.2) were compared between symptomatic and asymptomatic side. Imaging parameters were; Axial, voxel size=3.33× 2.21× 3.50mm<sup>3</sup>, FOV=320×253mm<sup>2</sup>, 50 slices, b-value=0,800s/mm<sup>2</sup>, MPG=15 directions, TR=10900ms, TE=54, 120ms, and total acquisition time=6m00s.

**RESULTS AND DISCUSSION:** Average FA values of symptomatic side were significantly lower than those of asymptomatic side ( $p < 0.05$ ). Also, average ADC values and T2 values of symptomatic side were significantly higher than those of asymptomatic side ( $p < 0.05$ ) (Fig.3). FA values were negatively correlated with each quantitative value (correlation coefficient of FA values and ADC values was 0.448. correlation coefficient of FA values and T2 values was 0.448.) (Fig.4). Prolongation of T2 values were observed in case of abnormally enlarged nerve roots (Fig.5). Therefore, addition of T2 evaluation might be able to further assess the condition of edema in the nerve roots.

**CONCLUSION:** Simultaneous acquisition of diffusion tensor imaging and T2 map by using DRM technique might be able to evaluate the extent of nerve disorders more accurately.

**Fig.1** Sequence diagram of diffusion-relaxation matrix (DRM) sequence consists of dual-echo single-shot DW-EPI without prolongation of acquisition time.

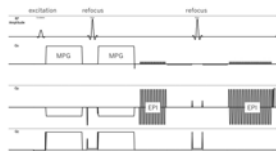


Fig.1

**Fig.2** Representative quantitative FA map (A), ADC map (B), and T2 map(C) obtained from diffusion-relaxation matrix (DRM) sequence



Fig.2

**Fig.3** Comparison of quantitative values between symptomatic side and asymptomatic side acquired by diffusion-relaxation matrix (DRM) (FA values (A), ADC values (B), and T2 values(C)).

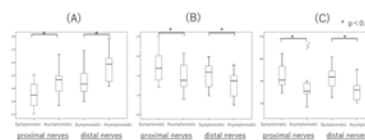


Fig.3

**Fig.4** Correlation of quantitative values acquired by diffusion-relaxation matrix (DRM) (FA values and ADC values (A), FA values and T2 values (B))

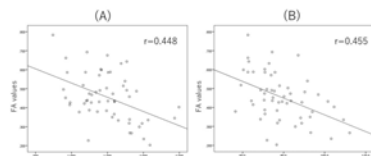


Fig.4

**Fig.5** Representative MRI images with abnormally enlarged nerve roots at the L3 levels (arrow) (MIP image of iso-diffusion weighted image (A), iso-diffusion weighted image (B), and T2 map(C)). T2 value is visually prolonged at the enlarged area probably due to edema.

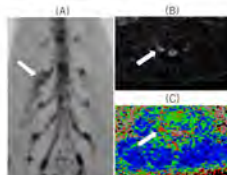


Fig.5

## The effect of one-level fusion on the occurrence of disc degeneration at the adjacent and skip level

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### Introduction

The relationship between the acceleration of adjacent disc degeneration and the lumbar fusion has been proved by many researches. However, there has been no research regarding the change at the skip level. Also, there is a paucity of literature regarding the influence of one-level fusion on the disc degeneration. The aim of this study was to investigate the effect of one-level fusion on the occurrence of disc degeneration at the adjacent and skip level.

### Methods

We retrospectively reviewed 169 patients (M:F=79:90, age=49.1±15.7 years) who had the degenerative lumbar disease at L4-5 disc. Depending on the treatment methods, we divided the subjects into fusion (n=97) and non-fusion group (n=73). We classified each group into mid-term group (postoperative 3 months-5 years, n=59 vs. 44) and long-term group (more than 5 years, n=38 vs. 29). Disc degenerations at the upper and lower adjacent segment and the upper skip segment were evaluated using Pfirrmann grade in MRI. The occurrences of disc degeneration were compared between groups.

### Results

There was no difference in demographic factors including sex (P=0.062), age (P=0.445), preoperative diagnosis (P=0.221), initial disc degeneration status at the upper and lower adjacent segments and the upper skip segment (P=0.133-0.726). Between fusion group and non-fusion group, there were no differences in the occurrences of disc degeneration at the upper (22.7% vs. 15.1%, P=0.214) and lower adjacent segment (22.7% vs. 11.0%, P=0.066) and the upper skip segment (14.4% vs 13.7%, P=0.892). Between mid-term group (Mean follow-up length, 31.1±14.6 months) and long-term group (Mean follow-up length, 90.4± 26.9 months), there were significant differences in the occurrences of disc degeneration at the lower adjacent segment (6.8% vs 25.4%, P=0.001) and the upper skip segment (11.6% vs 25.4%, P=0.040). There were no differences between mid-term and long-term non-fusion group. All results are shown in the table.

### Discussion

Fusion may influence on the level of disc degeneration, which may occur at the upper adjacent segment in mid-term and at the upper skip and lower adjacent segment in the long-term, rather than the occurrence of disc degeneration.

Table1. Disc degeneration at adjacent and skip levels depending on follow-up length and fusion

	Skip level	Upper adjacent level	Lower adjacent level
<b>Fusion vs non-fusion</b>	14.4% vs 13.7%	22.7 % vs 15.1%	22.7% vs 11.0%
<b>Mid-term fusion vs mid-term non-fusion</b>	5.1% vs 9.1%	22.0% vs 13.6%	15.3% vs 9.1%
<b>Long-term fusion vs long-term non-fusion</b>	28.9% vs 20.7%	23.7% vs 17.2%	34.2% vs 13.8%
<b>Mid-term vs long-term</b>	11.6% vs 25.4% *	18.4% vs 20.9%	6.8% vs 25.4% *
<b>Mid-term fusion vs long-term fusion</b>	5.1% vs 28.9% *	22.0% vs 23.7%	15.3% vs 34.2% *
<b>Mid-term non-fusion vs Long-term non-fusion</b>	9.1% vs 20.7%	13.6% vs 17.2%	9.1% vs 13.8%

Note: \* means P < 0.05

## Comparison of different spinal cage materials and bone graft techniques for posterior lumbar interbody fusion

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**Introduction:** Polyetheretherketone (PEEK) and titanium are widely used as spinal cages during posterior lumbar interbody fusion (PLIF), however, controversies remain about which material is superior. In addition, various bone graft methods for PLIF are being performed, but no standardized protocols have been established yet. Therefore, this study aimed to establish optimal spinal cage material and bone graft technique for PLIF by comparing surgical outcomes using two different bone graft techniques with PEEK or titanium spinal cages.

**Methods:** We retrospectively reviewed 104 consecutive patients (49 male and 55 female, aged > 60 y) who had undergone single-level PLIF between 2006 and 2015. Minimum follow-up period was 2 years. We transplanted the local chip bone with a block bone derived from the lamina (B+) or only the chip bone (B-) into the interbody space using either a PEEK cage (PB+ group: 28 patients, PB- group: 25 patients) or a titanium cage (TB+ group: 26 patients, TB- group: 25 patients). Baseline clinical data, including gender, age, body mass index (BMI), and follow-up period, were collected for all four groups. Preoperative and final scores of the Japanese Orthopaedic Association (JOA) and JOA recovery rate were used for analyzing clinical outcomes. Using lateral view of plain radiographs, the bone union was evaluated at the final follow-up, and the height of interbody space (HIS) was assessed at 1 week postoperatively and at the final follow-up.

**Results:** There were no significant differences in gender ratio, age, and BMI among the four groups (ratio of males, age, and BMI for PB+ group: 53.6%, 66.4, 22.6; PB- group: 44.0%, 67.3, 23.5; TB+ group: 53.9%, 63.8, 23.4; and TB- group: 36.0%, 62.5, 22.1, respectively). JOA scores and recovery rate showed no significant differences among the four groups at any stage assessed (preoperative, final follow-up, and recovery rate for PB+ group: 13.6, 26.6, 83.5%; PB- group: 14.2, 26.6, 83.5%; TB+ group: 12.0, 27.1, 88.0%; and TB- group: 14.3, 26.4, 82.5%, respectively). In addition, bone union rate showed no remarkable difference among four groups (PB+ group: 92.8%, PB- group: 96.0%, TB+ group: 92.3%, and TB- group: 90.9%). On the other hand, differences between HIS at 1 week postoperatively and final follow-up were significantly larger in the TB- group than in the TB+ group but not in the two PEEK groups (PB+ group: 1.26 mm, PB- group: 1.83 mm, TB+ group: 1.67 mm, and TB- group: 2.32 mm).

**Discussion:** In the case series of single-level PLIF, sufficient bone union was achieved regardless of the spinal cage material or bone graft technique used. However, cage subsidence was more common with the titanium cage. Interestingly, we found that the block bone derived from the lamina remarkably protected against subsidence in patients fitted with a titanium cage, suggesting that the block bone graft technique can efficiently avoid subsidence, particularly in titanium cage implantation.

## Correlation between lumbar spinal deformities and abdominal trunk muscle strength in the elderly women

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**Introduction:** We developed an innovative exercise device for abdominal trunk muscles that also measures muscle strength. This device enables patients to perform abdominal trunk muscle exercises in a sitting position without requiring movement of the painful lower back. It has a built-in measurement system for abdominal trunk muscle strength. We investigated the correlation between abdominal trunk muscle strength and spinal deformity in the lumbar spine in the elderly women.

**Methods:** Eighty-eight elderly women, who were scheduled to have surgeries for degenerative diseases of the lower extremities in our hospital. Before surgery, body height, body weight, body-mass index, grip strength, knee extensor muscle strength, and bone mineral density of the lumbar spine were measured. Abdominal trunk muscle strength was also measured using our device. The Pearson correlation coefficient analysis was used to evaluate the correlations between the abdominal trunk muscle strength and the other measurements. A full-spine standing radiogram was taken in all subjects. According to the findings of the radiogram, the subjects were divided into the 4 groups consisting of the normal group (n = 57) without specific findings, the spondylolisthesis group (n = 17) with degenerative spondylolisthesis at sagittal plane in the lumbar spine, the scoliosis group (n = 8) with degenerative scoliosis in the lumbar spine, and the fracture group (n = 6) with vertebral compression fracture in the lower thoracic or lumbar spine. A Tukey-Kramer honestly significant differences test was used to compare all the measurements including the abdominal trunk muscle strength in the 4 groups.

**Results:** There was a moderate positive correlation ( $r = 0.40$ ,  $p < 0.05$ ) between abdominal trunk muscle strength and grip strength, and a mild positive correlation ( $r = 0.31$ ,  $p < 0.05$ ) between abdominal trunk muscle strength and knee extensor muscle strength. The average age in the scoliosis group was significantly higher than that in the normal group (72 years vs 63 years). The average abdominal trunk muscle strength was 6.5 kPa in the normal group, 5.6 kPa in the spondylolisthesis group, 3.2 kPa in the scoliosis group, and 3.1 kPa in the fracture group. Those in the scoliosis and fracture groups were significantly lower than that in the normal group. There was no significant difference in the other measurements among the 4 groups.

**Conclusion:** Abdominal trunk muscle strength measured using our device was correlated with other muscle strength. The results indicated that weakness of the abdominal trunk muscle strength in the elderly women was associated with degenerative scoliosis and vertebral fracture in the lumbar spine.

## Morphological evaluation of lumbar nerve root using diffusion-weighted MR neurography

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### INTRODUCTION

Nerve root anomalies are relatively uncommon. However, they are frequently undiagnosed on preoperative imaging studies including conventional MRI. The presence of those root anomalies represents a significant potential for neurologic injury when the nerve root is required to be mobilized during spinal procedures. The purposes of this study were to examine morphological changes of the lumbar nerve roots such as anomalies and high take-off angles using the DW-MRN, and evaluate its utility.

### METHODS

All DW-MRN images taken during 10 months' period of consecutive symptomatic 366 patients (175 men and 191 women, mean age: 59.8 years old) were retrospectively analyzed. All patients complained LBP and/or LP. All images were obtained using a clinical 1.5 T MRI system [Intera, 1.5 T; Philips Healthcare, Best, The Netherlands; Motion probing gradient single plane (A-P), B-value (s/mm<sup>2</sup>) = 800, TR/ TE/ TI (ms) = 5000/ 80/ 180, Flip angle (°) = 90, Slice thickness/gap (mm) = 5/ 1, Field of view (FOV) (mm) = 300, Matrix = 256, Scan time = 2min 50s], and Philips' Achieva 3.2 were used for image analysis. We investigated (1) the congenital variations of the lumbar nerve roots and classified them by Neidre & MacNab criteria, and (2) prevalence of patients with nerve roots with the taken-off angle of 60 degrees or more.

### RESULTS AND DISCUSSION

Among the 366 images, three images were excluded due to the metal artifacts and/or low signal intensity. A total of 363 images of 363 patients were analyzed in this study. (1) Lumbar nerve root anomalies were identified in 7 images (2.0%). All anomalies were conjoined nerve root (Type 1 of the Neidre & MacNab criteria). (2) 171 patients (47.1%) had nerve roots with the taken-off angle of 60 degrees or more. In addition, those patients were significantly older compared with patients with the taken-off angle of less than 60 degree.

Based on the results of this study using DW-MRN, 2.0% prevalence of lumbar nerve root anomalies in symptomatic patients were identified though it was unclear whether the anomalies were corresponded to their symptoms. Nerve root anomalies are well-known to be easily damaged by intraoperative manipulation compared with normal nerve root due to poor mobility. In this point, preoperative identification of them using is very important. DW-MRN can be provided in approximately 3 minutes using 1.5T MRI system. Thus, we recommend it should be taken routinely in addition to the conventional images.

In the present study, 47.1% prevalence of the nerve roots with the taken-off angle of 60 degrees or more were found, which indicates those MRI findings are commonly seen and may be unreliable in old patients. However, once they are overlooked due to difficulty of diagnosis by conventional MRI, they may cause postoperative failed back syndrome.

Thus, in addition to the non-invasiveness, there are several advantages on the DW-MRN such as clear visualization of the nerve roots, and short exposure time. DW-MRN is recommended to examine the preoperative nerve root.



## The effect of combination pharmacotherapy on low back pain

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**Introduction:** Combination pharmacotherapy is an important modality for managing low back pain. Monotherapy with nonsteroidal anti-inflammatory drugs, opioids, skeletal muscle relaxants, or analgesics was shown to have small to moderate effects; however, the effect of combination pharmacotherapy is rarely described. Therefore, we aimed to evaluate the difference between combination pharmacotherapy and monotherapy on low back pain.

**Methods:** We searched PubMed, Embase, and Cochrane Central Register of Controlled Trials databases up to March 14, 2017. Randomized controlled trials (11 trials, 1875 patients) comparing the effect of low back pain combination pharmacotherapy to monotherapy or placebo were included. We performed this meta-analysis in accordance with PRISMA. Two authors independently extracted the data and assessed the validity of included trials. Fixed or random effect models were used based on the  $I^2$  value.

**Results:** 12 randomized controlled trials comparing the effect of low back pain combination pharmacotherapy to monotherapy or placebo were included. In chronic low back pain, combination pharmacotherapy was more effective than placebo in pain relief ( $p < 0.001$ ; SMD = -0.50 [95% CI, -0.70 to -0.29;  $I^2=0\%$ ]) and function improvement ( $p < 0.001$ ; SMD = -0.27 [95% CI, -0.41 to -0.13;  $I^2=0\%$ ]) and showed improved pain relief compared to monotherapy ( $p < 0.001$ ; SMD = -0.82 [95% CI, -1.10 to -0.54;  $I^2=0\%$ ]). Combination pharmacotherapy did not outperform monotherapy pain relief and function improvement in acute low back pain. Additionally, risk of adverse events of combination pharmacotherapy was much higher compared to placebo ( $p < 0.05$ ; RR = 1.80 [95% CI, 1.33-2.42;  $I^2 >50\%$ ]) and monotherapy ( $p < 0.05$ ; RR = 1.44 [95% CI, 1.01-2.06;  $I^2 >50\%$ ]) in both settings.

**Discussion:** This study reported that combination pharmacotherapy can improve pain relief in chronic low back pain, compared to placebo or monotherapy. Furthermore, combination pharmacotherapy improved function in chronic low back pain settings. In contrast, for acute low back pain, combination therapy did not outperform monotherapy in either category. Additionally, we confirmed that combination pharmacotherapy carries increased risk of adverse events compared to placebo or monotherapy.

## The movement of the transverse abdominal muscle and the muscles of the pelvic floor muscles during expiration

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**Introduction:** Clinically, not only the transverse abdominal muscles (TrA) but also the pelvic floor muscles (PFM) are weakened in patients with low back pain. It constitutes "the inner unit" with the TrA, the PFM, the diaphragm, and the multifidus muscles. Considering the mechanism by which this muscle functions, the action of a unilateral TrA alone cannot possibly stabilize the spine. However, few reports about timing analysis between the TrA and the PFM were presented. Thus, the objective of the present study was to measure the location of the muscles during expiration in order to elucidate cofunction between the TrA and the PFM in healthy subjects.

**Methods:** The subjects were 16 young adult males without low back pain (all male, mean age: 20.8±1.2 years, mean height: 169.8±4.9 cm, mean weight: 60.9±4.1 kg). This study was conducted with the prior approval of the Institutional Review Boards of the universities involved, and consent was obtained from the subjects after providing them with descriptions of the study. Two diagnostic sonography devices (TOSHIBA, MyLab Five) were synchronized to an analog/digital converter (BioResearch, Power Lab) and moving images of the subjects' right transverse abdominal muscles and muscles of the pelvic floor were recorded. We used the 2D image analysis software (DITECT, DIPP-Motion V/2D) to analyze the trajectories of the movement of the muscles. Using the time point at which the transverse abdominal muscle is closest to the surface of the body as a standard, we measured the time point at which the TrA is at its deepest point and the time point at which the muscles of the PFM are at their closest to the surface of the body during expiration, respectively. We obtained the mean values for some stable measurements taken during 30 secs of respiration. The values for the TrA and the PFM were compared using the unpaired t test, and we calculated Pearson's correlation coefficient. In all cases, the standard of significance was set at 5%.

**Results and discussion:** The mean time point at which the TrA was at its deepest point was 2168.5±546.7 msec, and the mean time point at which the PFM were at their most cranial to the surface of the body was 2031.6±765.7 msec. The difference between the values for the TrA and the PFM was 136.9±476.5 msec, indicating that there was no significant difference. A significant correlation was found between the time point at which the TrA was at its deepest point and the time point at which the PFM were at their closest to the surface of the body ( $r=0.79$ ,  $p<0.001$ ). Although the PFM are not accessory respiratory muscles, the results of this study elucidated the fact that they move in conjunction with the TrA during expiration. Further studies are needed in order to reveal about the characteristics of patients with low back pain.

## The influence of pelvic incidence on the lumbar lordosis in patients with hip osteoarthritis

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### Introduction:

Hip-spine syndrome (HSS) was first described by Offierski and MacNab in 1983. They illustrated that the flexion contracture of the hip osteoarthritis (HOA) may result in compensatory lumbar hyperlordosis. Since the introduction of the pelvic incidence (PI), which represents a constitutional anatomic parameter in each individual, studies on the sagittal spino-pelvic alignment (SSPA) have been increasing. However, there was no reports concerning the association between lumbar hyperlordosis and flexion hip contracture or PI.

The objectives of the present study were to investigate the association between lumbar hyperlordosis and flexion hip contracture or PI.

### Methods:

The subjects included female patients with an average age of years treated by total hip arthroplasty due to HOA. The objects were divided into two groups. High LL group (n= 197) included patients over 60 degree and non-high LL group (n=564) included those under 60 degree.

Lateral whole spine radiographs were prospectively taken of all patients before surgery.

The parameters of SSPA examined were PI and LL. Hip joint's range of motion arc (hip ROM arc) was measured. Questionnaire of pain by Japanese Orthopaedic Association hip score of pain (JOA hip score of pain) was carried out in these patients. The data were analyzed using the Student's test. A p-value<0.05 was considered to be statically significant.

### Results:

The mean LL in high LL group and non-high LL group were 66.4and 42.0 degrees.The mean PI was significantly greater in high LL group compared with non-high LL group. (62.0vs 51.0 degrees,P<0.01 ) However, there were no significant differences in hip ROM arc and JOA hip score of pain between the two groups. (P=0.81, 0.08)

### Discussion:

In patients with HOA, these findings suggest that the development of lumbar hyperlordosis may be affected by the presence of higher pelvic incidence and not by flexion hip contracture.

## Lumbar disc degeneration activates microglia in the spinal cord: CSF1/CSF1-receptor signaling may take a role

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**Introduction:** Although lumbar disc degeneration has long been regarded as a major contributor to back pain, how disc degeneration leads to back pain remains unknown. Microglia, the resident immune cells in the central nervous system, plays an important role in neuropathic pain. Previous studies observed that disc degeneration can activate microglia in the spinal cord, suggesting microglia may be involved in back pain. Using a mouse model of lumbar disc degeneration, the current study aims to characterize changes of spinal microglia in disc degeneration and to determine the role of colony-stimulating factor 1 (CSF1), a key regulator of myeloid lineage cells, in microglial activation.

**Methods:** The microglia reporter mouse line Cx3cr1<sup>GFP/+</sup> mice (male, 3-month old) were used in experimental (n=18) and control (n=18) groups. Under anesthesia, a posterolateral retroperitoneal approach was used to expose the L3/4 disc. The disc was punctured using a needle to induce disc injury in the experimental group but remained untouched in the control group. Three or four mice from each group were sacrificed at baseline, and each week after the surgery up to 4 weeks. The L3/4 disc, lumbar spinal cord, and L3 dorsal root ganglions (DRG) were obtained for histological examinations and immunofluorescence analysis. Spinal cord microglia were visualized and images collected with confocal microscopy. Morphometric measurements, including somatic volume, process length, and ramification degree were analyzed for microglia in the dorsal horn using the Imaris program. Expression of CSF1 in DRG sensory neurons and CSF1-receptor (CSF1R) in L3 spinal cord were examined using immunostaining. T-tests were used to compare the number and morphological measurements of microglia at each week between the experimental and control groups.

**Results:** Histological studies revealed that the punctured disc underwent progressive disc degeneration, including nucleus bulging, annulus loosening and disc space narrowing. In disc injury mice, microglia in the spinal cord were accumulated in the superficial layers of the dorsal horn. The number of microglia was significantly higher in experimental group than that in the control group at postoperative week 1, 2, 3 and 4 ( $P < 0.05$  for all). Moreover, microglia exhibited larger soma size, shorter processes distance, less ramification, and increased cell number density ( $P < 0.05$  for all) in disc injury mice. In experimental mice, CSF1 was upregulated in the sensory neurons of L3 DRG, so did CSF1R in spinal microglia.

**Conclusions:** In mice, disc puncture and consequent disc degeneration led to microglial accumulation and activation in the lumbar spinal cord. Disc degeneration likely activates spinal microglia through the CSF1/CSF1R pathway to contribute to back pain.

## Immunohistochemical analysis of 5-Hydroxytryptamine receptors in human intervertebral discs

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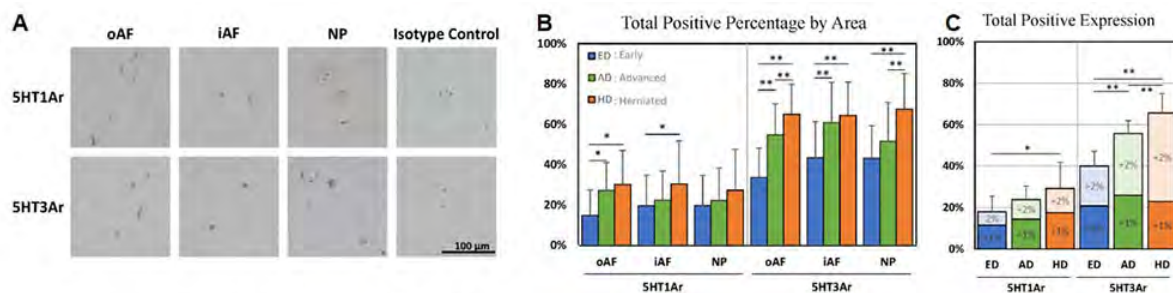
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**INTRODUCTION:** Serotonin [5-Hydroxytryptamine (5-HT)] is a neurotransmitter found in the central nervous system (CNS) and blood platelets. Studies show that serotonergic receptors are expressed in human articular chondrocytes and that serotonin released in injured tissues is somehow involved in inflammation. Recently, 5-HT3A antagonists have been reported to produce anti-inflammatory effects in human articular chondrocytes, suggesting a role in the inflammatory response. Intervertebral disc (IVD) degeneration is due to elevated levels of inflammatory mediators and matrix-degrading enzymes. The aim of this study was to analyze the presence of 5-HT1A and 5-HT3A receptors in human IVD tissues with various stages of degeneration and herniated IVD tissues, and to reveal the relationship of these receptors to the degenerative/inflammatory status of the disc tissue.

**METHODS:** With IRB approval, human IVD tissues were obtained and categorized using MRI, Pfirrmann's classification, and verification of disc herniation during surgery: Early Degeneration (ED: n = 15, grades 2-3), Advanced Degeneration (AD: n = 15, grades 4-5), and Herniated Disc Tissue (HD: n = 9). The samples were embedded in paraffin, and serial 5- $\mu$ m sections were used for Safranin-O/HE staining and immunohistochemical analysis. Each sample was divided into nucleus pulposus (NP), inner annulus fibrosis (iAF), and outer annulus fibrosis (oAF). The results were quantified using the mean percentage of immunopositive cells from five fields of microscopic images per sample at 400x magnification. Stained cells were counted and categorized with a semi-automated script in ImageJ. Differences in percentage of immunopositive cells were tested using a one-way ANOVA with a Bonferroni post hoc correction (significance level,  $p < 0.05$ ).

**RESULTS: 5HT1A receptor:** The total percentage of immunopositive cells was significantly higher in HD than in ED tissues ( $p < 0.05$ ). More specifically, the iAF region had a significantly higher percentage of immunopositive cells in HD than in ED tissues while that of the oAF region was significantly less in ED compared to AD and HD tissues. There were no significant differences in the NP region. **5HT3A receptor:** The total percentage of immunopositive cells was significantly different among all three degrees of degenerated disc tissues (ED, AD, HD,  $p < 0.01$ ). All three regions (iAF, NP, and oAF) had a significantly lower percentage of immunopositive cells in ED than in AD and HD tissues. The significantly highest percentage of immunopositive cells in the oAF region was observed in HD tissues ( $p < 0.01$ ).

**DISCUSSION:** The present study showed a general trend for a larger presence of both 5HT1Ar and 5HT3Ar immunopositive cells in advanced stages of degeneration, especially in herniated disc tissues, compared to those in early stages of degeneration. A direct quantitative comparison of the two receptors should be performed by western blot or gene expression studies for these receptors and their ligands to reveal the role of serotonergic receptors in IVD degeneration/inflammation. The results of this study suggest that the increased expression of 5HT1Ar and 5HT3Ar receptors could be involved in the progression of disc degeneration induced by an inflammatory response.



A: Immunopositive stains for 5HT1Ar and 5HT3Ar in outer AF (oAF), inner AF (iAF) and nucleus pulposus (NP)

Comparison of percentages of immunopositive cells for each stage of degeneration, B: Zonal, C: Total \*  $P < 0.05$ , \*\*  $P < 0.01$

## Prevalence and risk factors for low back pain in healthcare and non-healthcare university students: a large-scale, multi-center study

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**INTRODUCTION:** Low back pain (LBP) is the world's most disabling condition affecting every population, including healthcare professionals. Studies have shown that when LBP manifests at a young age, the severity and impact of LBP may compound itself later in life. However, little is known regarding LBP development in young, healthcare students. Specifically, no study has compared the prevalence and risk factors of LBP between healthcare and non-healthcare students. Therefore, this large-scale study addressed the 12-month prevalence rates and risk factors of LBP in healthcare and non-healthcare undergraduate university students.

**METHODS:** A research group was formed to formulate questions for an online survey based on expert opinions and literature regarding LBP and its risk factors. Following, a self-administered online survey was distributed to undergraduate healthcare and non-healthcare students by email at two Hong Kong universities in September of 2017. Students were invited to participate via their respective schools and residential halls within the university. The survey collected data on demographics and study major/focus, as well as episodes, duration and intensity of LBP in the last 12 months. Various potential risk factors were also recorded, such as but not limited to perceived stress from family and peers, study-associated stress, exercise habits, smoking and drinking profiles, type and duration of computer use, schoolbag use, study environment, etc. Additionally, anxiety, depression and insomnia were assessed by anxiety and depression subscales in the Depression Anxiety Stress Scale, and the Insomnia Severity Index, respectively. Univariate and multivariate analyses were performed.

**RESULTS:** A total of 785 respondents completed the survey (Table 1). The 12-month prevalence of LBP in healthcare students (42.9%) was significantly higher than that in non-healthcare students (30.8%) ( $p < 0.01$ ). In healthcare students, the multivariate analysis revealed that females (odds ratio (OR)=2.32), backpack usage (OR=1.86), mild difficulty in sleeping (OR=1.66), senior year of study (OR=1.32 per year) and taller students (OR=1.05 for each cm) were significant independent risk factors for LBP. Among non-healthcare students, desktop users in comparison to laptop users doubled the odds of experiencing LBP. Likewise, students studying in bed doubled the odds of having LBP than those using desks. High perceived stress (OR=1.22) and prolonged usage of electronic devices (OR=1.08) were associated with LBP development. However, senior non-healthcare students were less likely to have LBP (OR=0.70 per year).

**Table 1. Demographic data of respondents**

	Healthcare Students (n = 431)	Non-healthcare Students (n = 354)	p value
Age	21.2 + 2.5	20.9 + 2.4	0.21
Gender (% female)	64.6%	60.5%	0.23
Height (cm)	165.0 + 8.4	166.6 + 8.3	< 0.01
Weight (kg)	56.3 + 9.6	58.9 + 11.2	< 0.01

**DISCUSSION:** This is the first large-scale study to compare the 12-month prevalence of LBP and associated risk factors between healthcare and non-healthcare undergraduate students. Healthcare students had significantly higher prevalence of LBP than non-healthcare students. High physical loading and poor sleep quality increased the risk of LBP in healthcare students (e.g. physiotherapy students), while computer usage and work surface were significant determinants of LBP in non-healthcare students. The mismatch of LBP risk factors between these students may be attributed to their nature of study. Since early-onset LBP may increase the risk of chronic/recurrent LBP in future, our findings highlight that specific education/prevention programs should be tailored for these distinct student groups. A larger study is underway to validate our findings among various ethnicities worldwide.

## Signal intensity changes of the posterior elements of the lumbar spine in symptomatic adults

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**Introduction.** Hypointense signal changes (SCs) on T1-weighted imaging (WI) and hyperintense SCs on T2-WI of bone are generally considered to indicate bone marrow edema or inflammation. Modic type 1 changes around the vertebral endplate of the lumbar spine are well known to indicate inflammation; however, the clinical significance of similar SCs of the posterior elements has not been elucidated.

**Methods.** Six hundred ninety-eight MRIs of patients with complaints of low back and/or leg pain were retrospectively examined. Target SCs in this study were hypointensity on T1-WI and hyperintensity on T2-WI or short tau inversion recovery sequences showing the same signal patterns seen in Modic type 1 change of the lumbar posterior elements. We analyzed the (1) Prevalence, symptom, and age distribution of SCs, (2) Localization of SCs and their association with Modic type 1 changes, (3) Spinal-level distribution of SCs, (4) Association between SCs and disc degeneration of the affected spinal level, and (5) Association between SCs and lumbar alignment.

**Results.** (1) Among 698 adult patients, 36 (16 men, 20 women) exhibited SCs (5.2%). No SCs were identified in patients age < 40 years. (2) Of the 36 SCs, 9 (25%) were localized at a single spinal level, while 27 (75%) were found at neighboring spinal levels across the facet joint. Thirteen SCs (36.1%) had continuity with Modic type 1 changes around the vertebral endplate, while 23 (63.9%) were localized to the posterior elements. (3) SCs were frequently identified in the lower lumbar spine below the L4 level. (4) More than 80% of the SCs involved disc degeneration. (5) Spondylolisthesis was associated with more than 90% of SCs in double-level, and scoliosis or axial rotation was associated with SCs in unilateral side.

**Discussion.** SCs were common at lower lumbar spinal levels accompanied by lumbar disc degeneration in patients age >40 years. SCs that occurred at double spinal levels across the facet joint were mainly associated with degenerative change of the facet joint or secondary to intervertebral disc degeneration. On the other hand, SCs that occurred at localized single spinal level is possibly associated with osteoporosis or abnormal stress of subchondral bone of endplate.

This study has some limitations. Because this study is a cross-sectional study, a prospective study is required to clarify the pathomechanism of the findings of SCs. This study did not include control subjects without symptoms. If similar findings were obtained in asymptomatic subjects, it would indicate that the observed SCs may be regarded as simply indicating an aging process. Also, we could not confirm whether SCs indicated the source of the patients' pain; this would require a procedure such as xylocaine injection into the affected facet.

**Conclusion.** The prevalence of SCs in symptomatic adults was 5.2%. On the basis of observed disc degeneration, 75% of SCs were considered to indicate inflammation or bone marrow edema around the facet joint.

## **Xray vision: the accuracy and reliability of a technology that allows clinicians to see spinal x-rays superimposed on a patient's back**

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**Introduction:** Clinicians of all disciplines learn to visualize internal anatomy to enhance diagnostic accuracy and reduce iatrogenic injury. Unfortunately, the performance of this skill is poor.<sup>1</sup> To address this issue, our team developed technology that superimposes diagnostic images on to a patient's skin while minimizing distortion caused by patient topography. The result is that clinicians can immediately visualize their patient's underlying anatomy while freeing their hands to conduct clinical procedures such as palpation, injections or even surgery. In this project, we assess the accuracy and reliability of this projection system.

**Methods:** Sample size was calculated prior to recruitment (PASS15 software,  $n = 13$ , power = 0.91, alpha 0.05). Enrolled participants had an existing anteroposterior lumbar spine x-ray taken within 5 years and did not have any lumbar surgery or major trauma since the films were taken. In the prone position, the participant's x-ray was projected on to their back using customized software to drive mixed media goggles (Hololens, Microsoft). The software was then used to translate and scale the image until the projected iliac crests were aligned with those observed. The resulting location of each projected spinous process was then marked with red ink and the procedure repeated two more times. Three more trials were then performed with green ink for a generic anteroposterior lumbar x-ray obtained from the internet. The examiner then employed ultrasound to identify the centre of each lumbar spinous process and marked those locations with black ink. A standardised photograph of the markings was taken together with a calibration object to determine the vector of the projected spinous location from the actual spinous location as determined by ultrasound.<sup>2</sup> These procedures were repeated 1-5 days later. The projected location of any spinous process was judged to be accurate or "on target" if its location was within known spinous dimensions for that specific level.<sup>3</sup>

**Results:** All 13 participants had their own lumbar images with an additional 4 participants who films could not be obtained in time (14 males and 3 females, mean age = 37.6 years, mean BMI = 25.9 kg/m<sup>2</sup>). Overall, the percentage of "on target" projections using the generic image was 73.94% and for the patient-specific image was 74.40%. While these pooled results were not statistically different, generic and patient-specific results differed in that patient-specific projections were more reliable between days (80.00% matched) than the generic results (68.75% matched).

**Discussion:** The projection system tested here shows promise as a unique technology to assist clinicians in locating internal anatomy. While there are presently many sources of error including those from the device (resolution), viewer (inaccurate marking and placement) x-ray (magnification) and patient (when using generic images), we anticipate these errors can be mitigated, if not corrected, in future studies to provide an accurate and reliable way for clinicians to visualize patient-specific anatomy while allowing their hands to move freely.

1. Downey et al. *Physiotherapy* 89.
2. Mieritz et al. *JMPT* 39.
3. Shaw et al. *Spine J.* 15



## Low back pain related disability and MRI findings in the elderly: a cross-sectional and prospective one-year follow-up in the community

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Introduction: It is well known that degenerative changes do not always induce symptoms. There is still unknown the detail of relationship between degenerative findings in MRI of lumbar spine and low back pain (LBP). The purpose of this study was to clarify the relationship between LBP related disability and lumbar spinal MRI findings in the elderly of community setting.

Method: 172 people (av. age:64.4 years old) in community individuals agreed to participate in this study. They were received conventional MRI of lumbar spine (T1 sagittal, T2 sagittal and axial). LBP related disability was determined by Japanese version of Roland and Morris Disability Questionnaire (RDQ). A Japanese version of the RDQ was available for both the original score and also the standardized score (deviation score) of the national norm (20-79 years old, male/female). In the present study, disability was evaluated by the standardized RDQ score which was worse than the national norm or not. Fatty degeneration of paraspinal muscle was evaluated by three grades (none, slight, severe) (Kjaer 2007). Paraspinal muscle atrophy was evaluated by lumbar indentation value (Takayama 2016). And other anatomical factors such as vertebral fracture (Genant 1993), endplate change (Viedeman 1995), DDD score (Kawaguchi 1999, Cheung 2006) and dural sac cross-sectional area (DCSA) (L1/2-L5/S1) were also assessed.

The standardized RDQ score which was worse than the national norm or not at the initial analysis and one-year follow-up were analyzed using a multiple logistic regression analysis with the following independent variables: gender, age, fatty degeneration of paraspinal muscle, paraspinal muscle atrophy, vertebral fracture, endplate change, DDD score and DCSA. A p-value of less than 0.05 was considered statistically significant.

Result: 1) In cross-sectional study, only female negatively affected LBP-related disability (OR:2.989, 95%CI: 1.368-6.532)(p=0.0060).

2) In one-year follow-up, only female negatively affected LBP-related disability (OR:3.119, 95%CI: 1.220-7.978)(p=0.0176).

Discussion and conclusion: In this study, only gender affects LBP-related disability. This result indicates that abnormal MRI findings do not always affect LBP-related disability.

## Evaluation of real neurologic intermittent claudication using accelerometer device in patients with lumbar spinal stenosis: pilot and feasibility study

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### Introduction

Neurologic intermittent claudication (NIC) is the crucial factor when we diagnose or decide surgical treatment in lumbar spinal stenosis. Although NIC is the key when we decide treatment options, we usually get the information about NIC by asking to the patients, such as "How long can you walk without stopping or taking a rest?". Some literature suggest the methods measuring the accurate NIC, they were complex and hard to apply in outpatient clinic. Therefore, in this study, we aimed to evaluate the feasibility of measuring NIC using accelerometer device in patients with lumbar spinal stenosis.

### Method

Prospective cohort study was performed. Patient group included 20 patients who were diagnosed as Lumbar spinal stenosis with NIC and admitted for the surgery. The control group included 20 patients who were admitted to the outpatient clinic with simple back pain without complaining of NIC or gait difficulty. In this study, over 60 year old patients were included in both groups. Patients with neurological disorders that may affect gait, such as Parkinson's disease and also lower extremity fractures or severe arthritis were excluded. We worn Accelerometer (Actigraph, FL, Pensacola, FL) on the waist of the patients and recorded a 30 minutes walking experience in the hospital and analyzed recorded gait patterns. The hand grip strength, core muscle strength, and ODI questionnaires were also examined to evaluate functional status including demographic data such as age, sex and BMI.

### Result

During the gait time measured using the accelerometer, the percentage of resting time duration were 28.0% in the patient group and 16.9% in the control group. Patients group was statistically significantly longer. ( $P=0.011$ ) The interval time when patients started to walk until took rest was defined as NIC and the average value of the NIC interval was calculated within the measurement time. The mean NIC of the patient group was 9.2 minutes and the control group was 17.2 minutes. ( $p=0.025$ ) Evaluation of functional status showed significant differences in core muscle strength and ODI score between both groups, but there was no statistical difference in hand grip strength. During the gait time, the patient's percentage of resting time was longer as the core muscle strength got weaker ( $r=-0.404$ ,  $p<0.05$ ) and patients with a high ODI score had a longer resting time. ( $r=0.50$ ,  $p<0.01$ ) (pearson correlation). The measured NIC showed a negative correlation with ODI score ( $r=-0.431$ ,  $p<0.05$ )

### Discussion

NIC is an important factor in diagnosing lumbar spinal stenosis, assessing severity, and determining treatment policy. So far, we have evaluated the functional status indirectly through history taking and questionnaire. However, it is expected that NIC can be evaluated by analyzing actual patient's activity and gait by developing mobile device and big data processing technology. In this study, we conducted a pilot and feasibility study to measure the NIC using an accelerometer. The difference between the patient group and the control group was clearly revealed and as correlation with ODI and core muscle strength was shown, we could confirm that further improved research can be possible.

## Assessment of sleep quality in patients with degenerative lumbar spinal disease

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### INTRODUCTION

Recent studies have also reported nocturnal leg pain or leg cramps in patients with lumbar spinal stenosis (LSS). Therefore, the patient with degenerative spinal disease might have sleep disruption and poor sleep quality with pain during the night. To our knowledge, however, there has been no study regarding the association between sleep disturbance and degenerative spinal disease, which has yet to be regarded as a risk factor of sleep disturbance. Therefore, the purpose of this study is to 1) identify the incidence of sleep disorder in patients with degenerative spinal disease, 2) establish relationship between sleep disorder and nocturnal leg pain patients with LSS from analyzing the cause of sleep disorder.

### METHODS

The study included the patients with degenerative lumbar spinal disease including LSS and lumbar disc disease without stenosis (LDD). Initially, 169 patients were assessed for eligibility between August 2017 and November 2017. Based on the diagnosis, the enrolled patients were assigned to either the LSS group or the LDD group. For assessment of sleep quality, Pittsburgh Sleep Quality Index (PSQI) was used. For clinical outcome assessment, VAS for back and leg pain, nocturnal pain, ODI, and EQ-5D were assessed.

### RESULTS

A total of 95 and 74 patients were assigned to LSS and LDD group, respectively. Among the enrolled patients, 49 (51.6%) and 37 (50.0%) patients was considered to be poor sleeper (5 or higher of PSQI score) in the LSS and LDD group, respectively. There was no difference of ratio of poor sleeper between the both groups. Compared ODI and EQ-5D between poor sleeper and non-poor sleeper, poor sleeper group showed significantly higher ODI scores and lower EQ-5D in both LSS and LDD group ( $P < 0.001$  for all variables in both groups). In addition, PSQI scores were significantly correlated with the ODI and EQ-5D scores ( $P=0.033$  and  $0.002$  in ODI and EQ-5D, respectively).

### DISCUSSION

The present study shows that both LSS and LDD with stenosis is significantly associated with poor sleep quality. The prevalence is almost 50% of poor sleeper. In addition, poor sleeping has negative influence on the disability and quality of life in both LSS and LDD groups.

## Neuromuscular activity during gait in patients with sacroiliac joint pain

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**Introduction:** The sacroiliac (SI) joint is cited as the source of pain in 15% to 30% of patients presenting with low back pain. Without previous lumbar fusion appearance for situation that indicates up to 47% in those patients. However, the diagnosis of SI joint dysfunction is difficult to make because presenting symptoms can be similar to other etiologies of low back pain. Several physical exam maneuvers have been described in an effort to distinguish sacroiliac joint pain from other causes but a gold standard is lacking, illustrating the need for a deeper understanding of SI joint pathology. Knowledge of neuromuscular adaptations that occur in patients with SI joint dysfunction is scarce and may improve our understanding of the disease and have implications on rehabilitation for these patients. The purpose of this study was to determine neuromuscular activity during gait in patients diagnosed with sacroiliac joint pain compared to controls.

**Patient Sample:** Fifteen patients with symptomatic SI joint pain who have been deemed appropriate surgical candidates compared with 20 healthy controls.

**Outcome Measures:** Spine and lower extremity of integrated electromyography (iEMG) and time to max EMG activity.

**Methods:** Clinical gait analysis was performed the week before surgery. External Oblique (EO), Multifidus(Mf) at the level of L<sub>5</sub>, Erector Spinae(ES) at the level of L<sub>1</sub>, Gluteus Maximus(GM), Rectus Femoris(RF), Semitendinosus(ST), Tibialis Anterior(TA), and Medial Gastrocnemius(MG) neuromuscular activity were measured and recorded during the gait analysis session. Each subject performed a series of over-ground gait trials at a comfortable self-selected speed. iEMG activity is a graphic representation of the sum total EMG activity over a defined period of time. One-way ANOVA analysis was used for the statistical analysis.

**Results:** Compared to controls, patients with SI pain demonstrated significantly less activation of the EO ( $3.43 \pm 2.3$  vs  $0.35 \pm 0.1$  mV;  $p=0.044$ ), GM ( $2.76 \pm 4.1$  vs  $0.33 \pm 0.1$  mV;  $p=0.050$ ), and Mf ( $3.40 \pm 4.2$  vs  $0.57 \pm 0.4$  mV;  $p=0.049$ ). Time to max EMG muscle activity was significantly longer in the EO ( $0.03 \pm 0.0$  s vs  $0.01 \pm 0.0$  s;  $p=0.050$ ), ES ( $0.01 \pm 0.0$  s vs  $0.00 \pm 0.0$  s;  $p=0.048$ ) and the ST ( $0.03 \pm 0.0$  s vs  $0.02 \pm 0.0$  s;  $p=0.046$ ) in patients with SI joint pain compared to healthy controls.

**Conclusions:** The sacroiliac joint is responsible for load transfer from the pelvis to the spine, and does so through a complex interaction of static and dynamic stabilizers. Dysfunction in the SI joint often causes pain and limits one's ability to stand, walk and sit. Impaired anticipatory and compensatory motor function is beginning to garner attention as an underlying contributor to SI joint pain, yet there are few studies characterize individual muscle function and time-to-max EMG in patients with this disease. This study found impairment in activation and time-to-max EMG for several trunk and lower extremity muscles in patients with SI joint pain, suggesting there is a pain avoidance mechanism leading to poor neuromuscular function and coordination. In addition to our findings, this study contributes to existing knowledge on EMG muscle activity in patients with SI joint pain and will be useful in future studies investigating neuromuscular function of patients with SI joint pain after both nonsurgical and surgical treatment options.

## Metabolic and musculoskeletal conditions correlated with lumbar intervertebral disc degeneration

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**INTRODUCTION:** Considering that a growing economic burden is being imposed on our aging societies by the increasing health care costs for managing degenerative spinal disorders, there is an urgent need to develop prophylaxis for intervertebral disc (IVD) degeneration. Past studies have shown that age is a risk factor for IVD degeneration. Obesity, hyperlipidemia, and impaired glucose tolerance have been also reported to be associated with the development of lumbar IVD degeneration. However, apart from such studies, there has been no systematic research exploring the association of age-related musculoskeletal diseases and metabolic disorders with IVD degeneration. We aimed to clarify potential associations between IVD degeneration and other common metabolic and musculoskeletal disorders.

**METHODS:** Clinical data of consecutive subjects undergoing a musculoskeletal examination in addition to regular medical screening between July 2012 and March 2016 were retrospectively reviewed. Examinations included blood tests, radiography of the knee joint and lumbar spine, MRI of the lumbar spine, abdominal CT, and DXA. A total of 276 subjects, comprising 134 men and 142 women, were assessed. Pfirrmann grades 1–3 changes indicated no IVD degeneration (ND group) and grades 4 and 5 changes IVD degeneration (DD group). Cross-sectional areas (CSAs) of trunk muscles and visceral adipose tissues were measured using CT. To examine for independent associations of metabolic syndrome and musculoskeletal disorders (sarcopenia; osteoporosis; the mass of the psoas major, paraspinal, and anterolateral abdominal muscles; and knee OA) with IVD degeneration, we constructed a logistic regression model including all above variables, age, sex, and lifestyle, and estimated ORs and 95% CIs for IVD degeneration.

**RESULTS:** IVD degeneration was positively correlated with age. Aside from a higher high-density lipoprotein cholesterol in men in the DD group, the prevalence of metabolic disorders did not differ significantly between the groups. Mean hand grip strength and appendicular skeletal muscle mass were significantly lower in men in the DD than the ND group. The average CSA of the paraspinal muscles was significantly lower in the DD than in the ND group in both men and women. Logistic regression analysis revealed that paraspinal muscle CSAs were significantly correlated with IVD degeneration at L3/4 (OR = 0.28, CI = 0.08–0.96), L4/5 (OR = 0.26, 95% CI = 0.08–0.88), and L5/S (OR = 0.15, 95% CI = 0.05–0.47). Osteoporosis was negatively correlated with IVD degeneration at L3/4 (OR = 0.37, 95% CI = 0.15–0.93) and L4/5 (OR = 0.19, 95% CI = 0.07–0.51).

**DISCUSSION:** The results of the present study show that lumbar IVD degeneration had a negative correlation with higher CSAs of paraspinal muscles and with a diagnosis of osteoporosis in the subjects who underwent a medical screening examination at our facility. Contrary to prior studies which indicated an association between IVD degeneration and metabolic disorders, we found no significant correlation between IVD degeneration and any of the metabolic conditions assessed in our study. Given the limitations of the present study, our results must be cautiously interpreted. Nevertheless, the findings may contribute to further investigation of the etiology of IVD degeneration.

## A systematic review of the effectiveness of weight loss programs in non-specific low back pain

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**Introduction:** There is a large number of studies suggesting that high BMI or obesity are risk factor for spine degeneration and low back pain. In fact, weight loss is often suggested by researchers and clinicians as an important component of management strategies in low back pain.

However, there is a lack of information on the role of weight loss interventions in mitigating the negative consequences of low back pain. Thus, objective of this study was to systematically review studies evaluating the effectiveness of weight loss programs in decreasing pain, disability and increasing function and quality of life in patients with chronic non specific low back pain.

**Methods:** Relevant studies were search on MEDLINE, EMBASE, CINAHL, and OVID PsycINFO). Given the scarcity of high quality studies randomized controlled trials, quasi randomized controlled trials and quasi-experimental designs were eligible for inclusion. Studies had to include patients with chronic non specific low back pain (>12 weeks), evaluate a weight loss program and use outcomes of pain, function, disability or quality of life.

**Results:** A total of 5 studies were eligible for inclusion. There were no randomized controlled trials and only 5 pre-test post test studies from which 4 evaluated bariatric surgery (188 patients) and 1 evaluated non surgical multidisciplinary intervention (46 patients). All four studies evaluating bariatric surgery demonstrated that weight loss was associated with a decrease in pain in the short term (Mean difference from -1.3 to -3.4 VAS on a 0-10 point scale). Furthermore, the results of these studies suggest that the benefits of bariatric surgery are not maintained in the long term, likely due to a subsequent observed increase in body weight. Additionally, there is very low-quality evidence for a single one arm study that a multidisciplinary intervention decreases pain at intermediate term only (MD = -1.6, 95% CI = -2.6 to -0.6) but this change is not likely clinically significant.

**Discussion:** Results suggest that weight loss on significantly obese individuals undergoing bariatric surgery may be effective in reducing pain in patients with non-specific or recurrent LBP in the short term. A multidisciplinary intervention in overweight individuals may also be effective in reducing pain although there are questions regarding a clinical significance. Definitive conclusions cannot be drawn due to lack of high quality randomized controlled trials. Clinicians should be cautious when instructing patients on the benefits of weight loss on LBP specially when considering those that are overweight and not obese.

## Plaster cast fixation for patients with osteoporotic compression fractures: comparison of two methods of reduction, standing posture and dorsal suspension reduction in a supine position

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### Introduction

Vertebroplasty (VP) and kyphoplasty (KP) have been reported as minimally invasive surgical treatments for patients with osteoporotic vertebral compression fracture (OVCF) that can quickly relieve pain. However, VP and KP are reportedly associated with higher risks of secondary VCF at both adjacent vertebrae and another segment. Conservative treatments are therefore recommended for early treatment of OVCF. Plaster cast fixation (PCF) should be recommended because conservative treatment of OVCF requires rigid fixation. As reduction methods for PCF with OVCF, reduction in standing postures (standing method, STM) and dorsal suspension reduction in a supine position (suspension method, SUM) have been used for many years. This retrospective study aimed to compare STM and SUM in terms of utility for PCF of OVCF.

### Material and Methods

Subjects in this study comprised 49 patients with osteoporosis confirmed by DEXA or NTX, and in whom a single vertebral fracture had been identified on X-ray, MRI, and/or CT. The STM group comprised 22 patients (78.4 years), and the SUM group comprised 27 patients (76.0 years). After PCF, we confirmed a reduced position of the OVCF from X-rays in a standing position. Level of the fractured vertebra, collapse rate, and local kyphosis angle before and after PCF were determined from X-rays. Investigation of the interval to reduction of pain after PCF, hospital stay, and period with the plaster cast were determined.

### Statistical analysis

Statistical analyses were performed using R 2.8.1 software on a personal computer. Age, hospital stay, and interval to reduction of pain were compared between groups using independent-sample t-testing. And stepwise regression analysis was conducted. In all tests, values of  $P < 0.05$  were deemed statistically significant.

### Results

No significant difference in mean duration of disease (STM, 4.7 days; SUM, 4.4 days) was apparent between groups. Mean collapse rate before PCF was higher for SUM (30.6%) than for STM (24.5%). However, aggravated collapse rate after PCF was 30.6% for STM cases, compared to 26.1% for SUM cases. Local kyphosis angle tended to improve more in SUM ( $15.2^\circ \rightarrow 10.0^\circ$ ) than in STM ( $14.1^\circ \rightarrow 16.3^\circ$ ) after PCF. However, no significant difference was recognized between these two groups. Both hospital stay and interval to reduction of pain were significantly shorter with SUM than with STM ( $p < 0.05$  each). Multiple regression analysis identified degree of collapse of the posterior vertebral wall before PCF as a factor influencing the interval to reduction of pain ( $p = 0.03$ ).

### Conclusion

In general, conservative treatment is continued for 3 weeks to 3 months. We perform PCF for patients with OVCF. Patients start walking with a walker after PCF, which avoids bed-rest and allows for early rehabilitation and an early return home. In this study, PCF performed with SUM achieved earlier reduction of pain and a short duration of hospitalization. For conservative therapy of VCF, we therefore recommend PCF with SUM. VP and KP exert influences at adjacent vertebrae and at all segment overall by reinforcing the vertebral body. As the first line of conservative treatment, PCF with SUM for OVCF suggests that we should try methods with rigid external fixation.

## **Lumbar spinal canal stenosis in patient with diffuse idiopathic skeletal hyperostosis. Surgical outcome of the spinous process – splitting laminectomy**

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### Introduction

Although spinal fracture in the patient with ankylosing spinal disorder had been discussed, there was little knowledge about the impact of diffuse idiopathic skeletal hyperostosis (DISH) on lumbar degenerative disorder. The purpose of this study was to evaluate the surgical outcome of posterior decompression surgery for lumbar canal stenosis in the patient with DISH.

### Methods

From 2011 to 2015, 184 patients (132 males and 52 females, mean age 72.0 year-old, mean follow-up period 30.7 months) who underwent lumbar spinous process-splitting laminectomy for lumbar spinal canal stenosis were included into this single-center retrospective study. Based on the lateral whole spine radiographs, subjects were classified into two groups of DISH (D) group and non-DISH (N) group. If the patient has spinal ankylosis more than three continuous segments, the patient was classified into the D group. Age, gender, pre-operative physical status classification of American Society of Anesthesiologists (ASA classification), number of decompressed segments, operation time, estimated blood loss, requirement of revision surgery were evaluated on the charts. On the radiographs, decrease disc space narrowing (>2mm), increase of angulation >5° in flexion, increase of translation >5 % in flexion were evaluated between the preoperative and at final follow up radiographs. Japanese Orthopedic Association Back Pain Evaluation Questionnaire (JOABPEQ) were used for clinical outcome.

### Results

Mean age was 73.6 year-old in D group and 71.6 year-old in N group. Preoperative ASA classification was 2.2 in D group, 1.9 in N group, meanwhile gender (male%) was 87.5% in D group, 67.6% in N group ( $p = 0.016$ ). Mean number of decompressed segments was equivalent between the two groups (2.3 in D group, 2.2 in N group), however, operation time was longer in D group (89.0 minutes) than that in N group (73.7 minutes) ( $p = 0.036$ ), and estimated blood loss was larger in D group (98.7g) than that in N group (51.9g) ( $p = 0.006$ ). The revision surgeries were more frequent in D group (9.8%) compared with that in N group (4.8%). At final follow-up, decrease of disc space narrowing (>2mm) was more frequent in D group (26.5%) than that in N group (19.8%). Frequency of change in translation >5 % was significantly larger in D group (33.3%) than that in N group (17.3%) ( $p = 0.021$ ). Each domain in JOABPEQ were also improved in the both groups without significance between two groups.

### Discussion

Although development of anterior translation in decompressed segment after decompression surgery in DISH patients, the surgical outcome was equivalent with non-DISH patients. Higher frequency of revision surgery may be impacted by post-operative spinal instability.



## The effect of active knee extension in sitting on lumbopelvic curvature in individuals with clinically tight hamstring muscles: a cross-sectional reliability study

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**INTRODUCTION:** There has been increasing interest in relative flexibility between the lumbar spine and its adjunct body regions in the evaluation for control of the lumbar spine. One clinical method for relative flexibility of the lumbar spine is to evaluate lumbopelvic movement during active knee extension to 10° flexion of the knee with the hip in 90° flexion and the ankle in full plantar flexion in a sitting position (AKEiS).<sup>1</sup> However, a quantitative measure of lumbopelvic curvature during AKEiS has not been established yet, nor has reliability for this test been reported and thus its establishment was the aim of the current study.

**METHODS:** Convenience sampling of individuals with clinically tight hamstring muscles, who showed movement of the lumbar spine during AKEiS was undertaken. Other inclusion criteria were individuals: 1) ≥ 18 years of age, 2) without lower limb symptoms or limitation of hip, knee or ankle range of motion and 3) without scoliosis. The measurement side was right and individuals who had symptoms in relation to the peripheral nerve in the right lower leg during the AKEiS were excluded.

The lumbopelvic curvature was evaluated in the AKEiS (Figure 1) on 15 occasions using a flexible ruler and ImageJ1.6 software (Figure 2) on 2 separate sessions. To investigate inter-examiner reliability, 2 examiners participated in data collection and analysis, which were blinded to each examiner. To investigate inter-session reliability, participants were asked to attend 2 separate sessions on consecutive days.

To determine the minimum number of repetitions, we first calculated mean values for the angle of the lumbopelvic curvature using an increasing number of successive repetitions from 2 to 15 with data collected by one examiner, and then calculated the absolute difference in mean value with successive inclusion of additional repetitions (i.e. difference between mean value calculated from 3 vs. 2 repetitions; 4 vs. 3 repetitions, and so on). The minimum number of repetitions was defined as the number of repetitions at which the successive difference values plateaued (i.e. no further reduction in difference between repetitions could be achieved by the addition of more repetitions). Intraclass Correlation Coefficients (ICC) were evaluated for the inter-session reliability and inter-examiner reliability. A Minimum Detectable Change (MDC) was also calculated.

**RESULTS:** Fourteen men and 13 women participated in the study (mean ± SD years of age = 21.1 ± 2.8 years). Three participants (11.1 %) had low back pain. There was no statistical difference ( $P > 0.05$ ) in the mean absolute difference between the mean value of N-1 and N repetitions ( $6 \leq N \leq 15$ ) in the lumbopelvic curvature angle (Figure 3), indicating that 5 was considered the minimum number of repetitions. ICC<sub>(1,5)</sub> for the inter-session reliability and ICC<sub>(2,5)</sub> for the inter-examiner reliability was 0.97 and 0.93, respectively, indicating excellent reliability. The MDC was 7.3°.

**DISCUSSION:** The measure for the lumbopelvic curvature during AKEiS, which was established in the current study, will be a foundation for further research regarding the relative flexibility of the lumbar and adjunct regions.

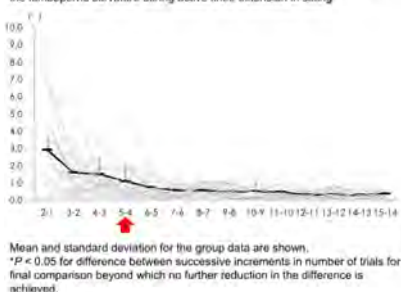
Figure 1. Standardization of knee flexion/extension angle during measurement using a metal orthosis.



Figure 2. Schema for calculation of the angle of the lumbopelvic curvature during active knee extension in sitting (S) on ImageJ1.6 software.



Figure 3. Group mean (black) and individual (grey) data of the absolute difference between the mean value of N-1 and N repetitions ( $2 \leq N \leq 15$ ) in the lumbopelvic curvature during active knee extension in sitting.



## Impact of psychological problems on health-related quality of life in patients with residual kyphotic deformity after osteoporotic vertebral fractures

**kazuya kishima, keishi maruo, toshiya tachibana, fumihiro arizumi, kazuki kusuyama, shinichi yoshiya**

### Introduction:

Residual kyphotic deformity after osteoporotic vertebral fractures (OVFs) may cause chronic low back pain (LBP). Previous studies have reported that chronic LBP is associated with states of depression and anxiety. However, a relationship between psychiatric problems and LBP after OVFs has not been established. The purpose of this study is to assess the relationship between psychological problems and health-related quality of life (HRQOL) in patients with residual kyphotic deformity after OVFs.

### Material and methods:

A total of 95 patients with residual kyphotic deformity after OVFs were enrolled in this study. Patients with painful new (within three months) OVFs, nonunion, pathological fracture, and a previous history of spine surgery were excluded from the study. The mean age was 78 years, and there were 8 males and 87 females. Radiographical parameters included thoracic kyphosis (TK), lumbar lordosis (LL), lower lumbar lordosis (LLL), thoracolumbar kyphosis (TL), sagittal vertical axis (SVA), T1 pelvic angle (TPA), pelvic tilt (PT), and pelvic incidence (PI). Clinical outcomes included Oswestry Disability Index (ODI), Japanese Orthopedic Association Back Pain Evaluation Questionnaire (JOABPEQ), and visual analogue scale (VAS). The Brief Scale for Psychiatric problems in Orthopaedic Patients (BS-POP) was used as a screening test to detect these psychiatric problems. The abnormal group was defined as 10 or more physician version points and 15 or more patient version points.

### Results:

A total of 29% (28/95) of the patients were classified into the abnormal group. The mean BS-POP score for physician version was  $9.4 \pm 1.6$  points and the patient version was  $15.5 \pm 3.8$  points. The median ODI (24 vs 51,  $P < 0.001$ ) and median VAS LBP (29 vs 57,  $P < 0.001$ ) were significantly worse in the abnormal group. All domains of JOABPEQ, including lumbar spine dysfunction (58 vs 30,  $P < 0.001$ ), social life dysfunction (78 vs 51,  $P < 0.001$ ), psychological disorders (62 vs 37,  $P < 0.001$ ), gait disturbance (57 vs 25,  $P < 0.001$ ), and pain-related disorders (43 vs 14,  $P < 0.001$ ), were significantly worse in the abnormal group. However, there were no significant differences in any of the radiographic parameters, including median TK ( $38^\circ$  vs  $38^\circ$ ,  $P = 0.54$ ), TL ( $32^\circ$  vs  $36^\circ$ ,  $P = 0.42$ ), LL ( $35^\circ$  vs  $30^\circ$ ,  $P = 0.265$ ), LLL ( $35^\circ$  vs  $37^\circ$ ,  $P = 0.861$ ), SVA (48mm vs 60mm,  $P = 0.576$ ), TPA ( $23^\circ$  vs  $27^\circ$ ,  $P = 0.117$ ), between the two groups.

### Discussion:

Health-related quality of life in patients with similar kyphotic deformity after osteoporotic vertebral fractures was significantly worse in the abnormal group.

Table 1 BS-POP Questionnaire

Questionnaire for medical personnel (BS-POP for use by physicians), English version

Questions	Responses and scores		
1. The patient's pain appears uninterrupted	1 That is not the case	2 The pain is intermittent	3 The patient appears to be almost always in pain
2. The patient has a specific way of indicating the symptomatic area(s)	1 That is not the case	2 They rub the symptomatic area(s)	3 Without instruction, they begin to remove their clothes and show the symptomatic area(s)
3. The patient appears to have pain over the whole symptomatic area	1 That is not the case	2 They sometimes do	3 Almost all the time
4. When examination or treatment is recommended, the patient becomes badly tempered, easily angered, or argumentative	1 That is not the case	2 They show slight resistance	3 They show significant resistance
5. When having their senses assessed, the patient responds excessively to stimulation	1 That is not the case	2 Their response is slightly excessive	3 Their response is quite excessive
6. The patient repeatedly asks questions regarding their condition or surgery	1 That is not the case	2 They sometimes do	3 Almost all the time
7. The patient changes their attitude depending on the medical staff member	1 That is not the case	2 They do somewhat	3 They do significantly
8. The patient wishes that their symptoms were gone, even with regard to slight symptoms	1 That is not the case	2 They do somewhat	3 They do significantly

Questionnaire for patients (BS-POP for use by patients), English version

Questions	Responses and scores		
1. Do you ever feel like crying, or do you cry?	1 No	2 Sometimes	3 Almost all the time
2. Do you always feel miserable and unhappy?	1 No	2 Sometimes	3 Almost all the time
3. Do you always feel nervous and irritated?	1 No	2 Sometimes	3 Almost all the time
4. Do you feel annoyed and aggravated over small things?	1 No	2 Sometimes	3 Almost all the time
5. Do you have a normal appetite?	3 No	2 I sometimes lose my appetite	1 Yes
6. Are you in your best mood in the morning?	3 No	2 Sometimes	1 Almost all the time
7. Do you get somewhat tired?	1 No	2 Sometimes	3 Almost all the time
8. Are you able to put your usual effort into your work?	3 No	2 I sometimes can't	1 Yes
9. Do you feel satisfied with the sleep you are getting?	3 No	2 I sometimes don't feel satisfied	1 Yes
10. Do you have trouble falling asleep for any reason other than pain?	1 No	2 Sometimes	3 Almost all the time

## Trunk movement during gait in patients with knee osteoarthritis before and after total knee arthroplasty

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**INTRODUCTION:** Previous studies have indicated that the kinematics of the knee joint affect the trunk and pelvis during gait. However, the factors that influence trunk movement in patients with knee osteoarthritis (OA) during gait after surgery remain unclear. Here, we examined the effect of total knee arthroplasty (TKA) on trunk movement during gait by comparing patients with knee OA with healthy controls.

**METHODS:** Fourteen patients with medial knee OA who underwent initial unilateral TKA and 11 control subjects participated in this study. Kinematic data during gait were acquired using a three-dimensional motion analysis system with 16 infrared cameras (VICON MX; Vicon Motion Systems, Oxford, UK). All participants walked along 10-m walkway at self-selected speed. Thirty-five passive reflective markers were placed. Knee and hip joint flexion and trunk and pelvic tilts during gait were calculated. Knee joint range of motion (ROM), the Japanese Orthopaedic Association (JOA) score of the knee OA, and the Numeric Rating Scale (NRS) for knee pain during gait were obtained to assess the patient-based clinical outcomes. Kinematic data and clinical outcomes were collected preoperatively and 1 year postoperatively for patients with knee OA. For the controls, only a gait analysis was performed.

**RESULTS:** Knee extension ROM, the JOA score, and the NRS significantly improved 1 year postoperatively compared with preoperative stages ( $p = 0.001$ ,  $p < 0.001$  and  $p = 0.001$ , respectively). Before TKA, the peak knee flexion during the stance phase and knee range of motion during gait were significantly smaller in patients with OA than in controls ( $p < 0.001$  and  $p < 0.001$ , respectively). Also, the peak anterior tilts of the trunk and pelvis during the stance phase were significantly larger in preoperative OA patients than in controls ( $p = 0.002$  and  $p < 0.001$ , respectively). After TKA, knee range of motion during gait was significantly larger and the peak anterior trunk tilt during the stance phase was significantly smaller than at the preoperative stages ( $p = 0.027$  and  $p = 0.003$ , respectively). No significant differences in knee range of motion during gait and the peak anterior trunk tilt were observed between the postoperative OA patients and controls ( $p = 0.206$  and  $p = 0.995$ , respectively).

**DISCUSSION:** Patients with knee OA walked with greater anterior tilts of the trunk and pelvis before surgery compared to controls. Furthermore, as clinical symptom such as unilateral knee joint ROM improved, the anterior trunk tilt during gait decreased 1 year postoperatively, and the trunk movement of the patients with knee OA after TKA was approximately equal to that of the healthy subjects.

## Perioperative surgical complications related to oblique lumbar interbody fusion (OLIF) in adult spinal deformity

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**Introduction:** Lumbar interbody fusion has been popularized for the surgical treatment of degenerative lumbar spine diseases. According to the direction of approach, various surgical techniques have been used, and each technique has the unique advantages and disadvantages. Especially, oblique lumbar interbody fusion (OLIF) approach is considered the solution to the troubles of anterior and lateral lumbar interbody fusion techniques. However, current studies are limited to small cohort sizes, short-term follow-up, and short level correction for degenerative lumbar diseases but adult spinal deformity should be correct much more lumbar lordosis or long level fusion. The purpose of this study is that surgeons have caution and conduct OLIF carefully through investigate the unexpected perioperative complication of OLIF technique.

**Methods:** From April 2015 to May 2017, we retrospectively reviewed 37 patients who were diagnosed with adult spinal deformity and had OLIF surgery. All patients underwent staged operation by one spine surgeon. First, patients had OLIF surgery 1 or 2 or 3 level to correct lumbar lordosis and to support anterior body. After 1 week from OLIF, they had secondary operation via posterior approach with or without pedicle subtraction osteotomy (PSO) depending on demand of target correction angle of lumbar lordosis. During 1 week after OLIF surgery, acute perioperative complication was investigated. A complication classification based on the relation to surgical procedure and effect duration was used. Moreover, the collected data were classified into radiological states and clinical symptoms. Radiologic results including the cage location and sagittal alignment were also assessed with plain radiography.

**Results:** A total of 43.2% (16/37) of patients who underwent OLIF surgery experienced a perioperative complication. Patients were age  $69.69 \pm 7.4$ . The procedure was performed in the lumbar spine at L1-L2 in 7, L2-L3 in 33, L3-L4 in 30, and L4-L5 in 21 patients. It was done at 1 level in 2, 2 levels in 10, and 3 levels in 23 patients. The most common complications were subsidence (37.8%), and other complication such as postoperative ileus (16.2%), incisional pain (8.1%), transient hip flexor weakness (10.8%), and transient thigh pain/numbness (5.4%) were reported. No patient suffered permanent neurologic injury. No cases of superficial or deep infection, ureteral injury, sympathectomy affecting the lower extremities, or visceral injury were seen.

**Discussion:** 14 patients, 20 segments experienced cage displacement, or sinking down of cage. These means acute end plate injuries were occurred commonly. It because patients had poor bone quality, and technical issues. We have to be prepared endplate carefully before cage insertion. But adult spinal deformity patients often had wedge shape disc space because of degenerative scoliosis, furthermore, when we used bigger size of cage to get more lordosis, end plate could get damage during preparation.

**Conclusion:** Many studies demonstrated OLIF technique has lots of advantages. However, in treatment modalities for adult spinal deformity, there were only few study reported about perioperative complication of OLIF surgery. So, immoderate cage insertion to correct too much lumbar lordosis could make unexpected perioperative complication. Thus, surgeons should have caution and recognize limitation of OLIF technique.

## Effects of skill training versus strength and flexibility exercise on functional limitations and pain in people with chronic low back pain over a 6-month period

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**INTRODUCTION:** People with chronic low back pain (CLBP) often seek treatment because they have difficulty performing daily activities but there is no consensus on which treatment is most effective for improving performance. Strength and flexibility exercises commonly are used. Skill training, an intriguing alternative based on challenging, progressive practice of a skill in an effort to learn or relearn the skill, merits investigation. In this study, our purpose was to compare the effects of skill training (ST) and strength and flexibility exercise (SF) on LBP-related functional limitations and pain over 6 months in people with CLBP.

**METHODS:** Participants with CLBP (n=149; 39% males; mean age 42.5±11.7 years) who were not in an acute flare-up were randomly assigned to one of two treatments: SF exercise of the trunk and lower extremities or ST involving challenging, progressive practice of daily activities limited due to CLBP. Both groups received 6 hours of treatment, 1 hour/week for 6 weeks. The modified Oswestry Disability Questionnaire (mODQ; 0-100%) and the numeric pain rating scale (average pain over prior 7 days; 0-10) were administered weekly in the treatment phase and monthly in a 6-month follow-up phase. A mixed random effect repeated measures analysis was conducted on each outcome for each phase with baseline mODQ or pain values included as covariates.

**RESULTS:** *Treatment Phase.* Treatment group differences for mODQ varied with time (p=0.0004). mODQ scores were not different at treatment visits 1 or 2 (p>0.36) but were lower for ST compared to SF at treatment visits 3 through 6 (p<0.017). At completion of the treatment phase, mODQ scores for ST were 7.89±1.60 points lower than for SF (p<0.0001). Pain decreased linearly over time (p<0.0001) and this decrease was not different between treatment groups (p=0.65). Averaged over the treatment phase, pain ratings for ST were 0.76±0.15 points lower than for SF (p<0.0001). *Follow-up Phase.* On average, mODQ scores for ST were 7.01±1.30 points lower than for SF (p<0.0001) across the follow-up phase. Treatment group differences in mODQ did not vary with time (p=0.724). Pain ratings for ST were 0.57±0.18 points lower than for SF (p=0.002) on average across the follow-up phase, but between group differences in pain did not vary across time (p=0.44).

**DISCUSSION:** During the treatment phase, the ST group's 14.96 point decrease in mODQ scores demonstrated a clinically important improvement in function. By contrast, the SF group's 6.83 point decrease in mODQ scores did not meet the criterion value for clinical importance. Both groups maintained their improvements in function up to 6 months after treatment. During the treatment phase both the ST and SF groups displayed decreases in average pain of 2.47 and 2.15, respectively; the improvements were clinically important and were maintained up to 6 months after treatment. Compared to strength and flexibility exercise, challenging, progressive practice in daily activities that are limited due to CLBP appears to be a more effective treatment for attaining and maintaining clinically important improvement in *both* function and pain in people with CLBP.

## Lubricin expression in the lumbar endplate and its association with Modic changes (MCs)

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**Introduction:** Our study is to explore the expression and distribution of lubricin in the lumbar endplate and its association with Modic changes (MCs).

**Methods:** Human endplate specimens were harvested during surgery from patients undergoing surgery for thoracolumbar spine fractures or from patients undergoing lumbar interbody fusion. These patients were then divided into two groups based on preoperative magnetic resonance imaging of the spine: the first had normal endplates (normal group) and the second all showed MCs (MCs group). Lubricin expression was examined by immunohistochemistry, and differences between the groups were analyzed using real-time PCR (RT-PCR). Lubricin expression and distribution, as well as differences between endplates with MCs and normal endplates, were confirmed using a rabbit model where MCs were initiated by injecting *Propionibacterium acnes* (*P. acnes*) into the discs. In a final experiment, endplate chondrocytes were co-cultured with *P. acnes* supernatant fluid (at concentrations of 1%, 2%, 4%) for 48h and the expression of lubricin, aggrecan, collagen-type-II, sox9, and several matrix degrading enzymes were evaluated.

**Results:** Lubricin was found in human endplates and its expression was lower in the MCs group compared to the normal group. In the rabbit model, lubricin was found in the bony endplate and, at higher levels, in the cartilage endplate. In rabbits injected with *P. acnes* (the MCs group), lubricin expression was decreased compared to the normal group. In cultures of endplate chondrocytes, the expression of lubricin, aggrecan, sox9 and collagen-type-II decreased significantly, while that of MMP-1 and ADAMTS5 increased significantly, when cells were co-cultured with *P. acnes*.

**Discussion:** Lubricin is present in both the bony and cartilage endplate where it may have an anti-inflammatory role. *P. acnes* infection inhibits lubricin expression by cartilage endplate cells and this may facilitate the progression of MCs and endplate degeneration.

**Keywords:** Lubricin, Modic changes, lumbar endplate, *P. acnes*

## Clinical and radiological outcome of muscle-preserving interlaminar decompression for lumbar spinal canal stenosis in patients with or without kissing spine

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**【Introduction】** While it is known that the complex of spinous process is involved in spinal stability in lumbar spinal canal stenosis (LSCS), precisely how is unclear. Kissing spine (KS), also called Baastrup's disease, refers to contact between adjacent spinous processes resulting in associated bone sclerosis; but its clinical significance has not been clarified. There have been reports of favorable outcomes obtained using muscle-preserving interlaminar decompression (MILD), a less invasive surgical decompression procedure developed to treat LSCS. In this procedure, surgery is performed on part of the spinous process and supraspinous and interspinous ligaments. In KS cases, there are concerns that with this procedure, invasion of the spinous process complex leads to deterioration of clinical result, disc height and segmental stability. This study clarifies the image characteristics of LSCS with KS, and examines mid-term outcomes and postoperative segmental instability in cases with and without KS.

**【Methods】** Eighty-four patients treated for LSCS with MILD were divided into KS and non-KS groups. KS was defined as an interspinous distance of less than 2 mm with bone sclerosis in lateral views of lumbar radiographs. The JOA score improvement rate, spinous process length, total lumbar lordosis angle, segmental lordosis angle and range of motion, and disc height index were evaluated. Statistical analysis was performed using the Mann-Whitney test and a significant p value of <0.05.

**【Results】** There were 30 patients in the KS group and 54 in the non-KS group. In the KS group, age, spinous process length and number of decompressed intervertebral disc levels were greater than in the non-KS group. The JOA score improvement rate was 61.2% in the KS group and 69.5% in the non-KS group, which was not a significant difference. Total lumbar lordosis, segmental lordosis and range of motion were the same in the two groups before and after MILD. Postoperative disc height index was significantly decreased in both groups.

**【Discussion】** In this study, 36.0% of cases undergoing surgery for LSCS had KS, spinous process height was high due to old age, and there tended to be multiple canal stenosis. No clear relationship was observed between the presence or absence of KS and preoperative lumbar alignment, lumbar range of motion or disc height. It is thought that KS is a change that occurs as a result of spinous process enlargement as age increases. In recent years, there has been debate about the significance of preserving the complex of spinous process when performing less invasive decompression surgery. It has been showed that the presence or absence of KS does not influence the clinical outcome of MILD. We also demonstrated that MILD did not affect postoperative lumbar alignment and segmental stability regardless of the presence or absence of KS. Although it is clear that using MILD involves invasion of the complex of spinous process, the effect of this could not be seen as radiographic changes. These results indicated that MILD was useful for treating LSCS less invasively.

## Inconsistence description of lumbar multifidus morphology and function. A systematic review

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### Introduction

There is still debate about the role of low back muscles in etiology and therapy of non-specific Low Back Pain (nLBP), particularly, with regards to the stabilizing contribution of the Lumbar Multifidus (LM) (1,2). Because of the complex morphology of the LM and variability in research methodology, it is unclear how LM studies should be interpreted. Additionally, it is unclear how results of anatomy studies of LM are represented in anatomy atlases.

### Aim

1. To systematically review the literature on LM morphology and research methods.
2. To compare research literature findings with the presentation and description in anatomy atlases.

### Methods

1. Relevant studies were searched in PubMed (Medline) and Science Direct.
2. Anatomical atlases were retrieved from multiple university libraries and online. Comparisons were made by five items: visuals present(y/n), quality of visuals(in-/sufficient), correct labeling multifidus(y/n), clear description of region of interest(y/n), description of plane has been described(y/n). This risk of bias assessment tool was developed to assess the quality of description of anatomy, since existing risk of bias tables have only been developed to assess the methodology of studies.

### Results

1. In total 69 studies and 19 anatomical atlases were included. LM morphology was mostly described by MRI, ultrasound or drawings.
- 2.1 Main outcome in multiple studies: 52 of 69 studies showed the LM as a superficial muscle at the levels L4 – S1. However, others presented the LM as deep intrinsic muscle.

From the 69 studies, 29 studies scored a total of five points at the risk of bias assessment, which is low risk of bias. 2.2 Main outcome of the anatomy atlases is that LM is shown as a deep intrinsic back muscle covered by m. erector spinae. Overall, anatomy atlases presented the LM from cervical to sacrum level similarly. However, this is different from the outcome of the studies. The most anatomical atlases (8/19) had a score of three points at the risk of bias assessment. The other atlases had a score lower than three points.

### Discussion

Anatomy atlases reported different LM morphology compared to anatomical studies. Between studies, there appears to be inconsistent reporting in LM anatomy. Most consistent anatomy descriptions were found in Deng et al. (2015), Rosatelli et al (2008), Beneck et al. (2012), which, therefore should be regarded as gold standard references for LM morphology and functional studies(3-5).



## Is L5-S1 motion segment different from the rest? A radiographic kinematic assessment of 72 patients with chronic low back pain

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**INTRODUCTION:** The relationship between biomechanical instability and degenerative changes in the lumbar spine in Chronic Low Back Pain (CLBP) patients remain controversial. The main objectives of this retrospective radiographical study were:

- To examine the association between the occurrence of disc degeneration and facet joint osteoarthritis at different lumbar levels in CLBP patients.
- To evaluate the changes in kinematics at different lumbar levels with progressive grades of disc degeneration and facet joint osteoarthritis in CLBP patients.

**METHODS:** Using standing neutral and dynamic flexion/extension (Fx/Ex) radiographs (n=72) of the lumbar spine, *in vivo* segmental kinematics at L1-L2 through L5-S1 were evaluated in consecutive CLBP patients (mean age: 43 years; mean symptom duration: 152 weeks) with no spinal deformity, no prior spine surgery, and no pathology that may be an indication for surgery based on clinical and radiographic assessments. Disc degeneration was quantified using changes in signal intensity and central disc height on mid-sagittal T2-weighted magnetic resonance (MR) scans. Additionally, presence or absence of facet joint osteoarthritis was noted on T2-weighted axial MR scans. Angular measurements were made on digitised images of the radiographs using Surgimap software (vers. 1.2.1.82). For reliability analyses, measurements on radiographs and MR scans were performed by two independent observers, and repeat measurements were performed by the first observer three weeks after the first measurements.

**RESULTS:** Disc degeneration and facet joint osteoarthritis were more prevalent at the lower lumbar levels (L4-L5 and L5-S1) when compared with the upper levels, with the highest prevalence observed at the L5-S1 level (Table 1). Chi-square tests showed that at the L5-S1 level, disc degeneration and facet joint osteoarthritis occurred independent of each other (p=0.188). However, at the L3-L4 and L4-L5 levels, an association was found between the occurrence of disc degeneration and facet joint osteoarthritis (p<0.05 and p<0.001 respectively). In the absence of facet joint osteoarthritis, the L5-S1 motion segment exhibited a smaller range of motion (ROM) in Fx and a greater ROM in Ex ( $0.6^\circ \pm 4.2^\circ$ ,  $3.3^\circ \pm 3.6^\circ$  respectively, p<0.05 for all comparisons) when compared with upper lumbar levels, but the differences diminished in the presence of facet osteoarthritis. In the absence of facet joint osteoarthritis, no change in L5-S1 kinematics was observed with progressive disc degeneration; but in its presence, Ex ROM decreased from  $7.2^\circ \pm 5.6^\circ$  in the mild disc degeneration state to  $2.3^\circ \pm 3.9^\circ$  in the severe disc degeneration state (p<0.05).

**DISCUSSIONS:** Amongst lumbar motion segments, the L5-S1 level is unique because of the presence of iliolumbar and lumbosacral ligaments, coronally oriented facets and laminae, wedge-shaped disc and its junctional location. Our results show that the L5-S1 motion segment exhibits unique degenerative and kinematic characteristics compared with the upper lumbar motion segments. Disc degeneration and facet joint osteoarthritis occurred independent of each other at the L5-S1 level, but not at the other lumbar levels. Compared with the mild disc degeneration state, severe disc degeneration in the presence of facet joint osteoarthritis biomechanically re-stabilised the L5-S1 motion segment.

**Table 1.** Number of patients (n) with different grades of disc degeneration in the absence (Fac 0) and presence (Fac 1) of facet joint osteoarthritis. Lower lumbar levels (L4-L5 and L5-S1) experienced more degeneration compared with the upper levels. Cells highlighted in gray depict lumbar levels and degeneration grades that were excluded from the study due to inadequate sample size for statistical analyses.

		Disc degeneration grades (0:nil; 4:severe)----->				
		0	1	2	3	4
L1-L2	Fac 0	67	1	1	1	0
	Fac 1	0	0	1	1	0
L2-L3	Fac 0	61	6	4	0	0
	Fac 1	0	0	0	1	0
L3-L4	Fac 0	46	9	5	1	0
	Fac 1	3	2	5	1	0
L4-L5	Fac 0	20	7	8	2	1
	Fac 1	3	4	15	8	4
L5-S1	Fac 0	10	4	8	6	5
	Fac 1	5	5	12	9	8

## Stiffness matters: PART I - the effects of plate stiffness on the biomechanics of acdf in vitro

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**Introduction:** The goal of spinal arthrodesis is to create an environment which facilitates sufficient stability and the "right" biomechanical conditions to foster the formation of bridging bone. In an anterior cervical discectomy and fusion (ACDF), the instantaneous axis of rotation (IAR) and the load-sharing characteristics are dictated by the stiffness of the plate. The ideal cervical plate is sufficiently stiff to limit interbody motion but is compliant enough to facilitate load-sharing rather than stress-shielding. The relationship between cervical plate stiffness, load-sharing, and the IAR is complex. The purpose of this study was to measure the effects of anterior cervical plate stiffness on (i) interbody load-sharing, (ii) instantaneous axis of rotation, and (iii) poster element strain in both human and goat cervical spinal motion segments *in vitro* following ACDF. Each parameter was measured under both simulated immediate post-operative conditions as well as conditions to simulate early-stage interbody fusion.

**Methods:** Anterior cervical plates across a range of bending stiffnesses were applied to human and goat cervical motion segments following ACDF. A validated custom force-sensing interbody implant was placed in the disc space to measure load-sharing in the spine. Strain gages were mounted to the posterior elements as a relative indicator of facet loading. Instrumented motion segments were subjected to physiologic range-of-motion testing *in vitro*. Interbody loads, posterior element strain, and the IAR were measured during flexion/extension for each plate.

**Results:** Load-sharing in the interbody space, posterior element strain, and the location of the IAR were all significantly affected by plate stiffness. Stiff plates resulted in an IAR located at or near the ventral margin of the disc, less consistent load-sharing during ROM, and higher posterior element loading. More compliant plates resulted in more load sharing, less posterior element strain, and a more dorsally located IAR relative to stiffer plates. Simulating fusion reduced the forces transmitted through in the interbody implant.

**Discussion:** A more compliant plate fosters more consistent load-sharing through the entire range of flexion/extension motion. This is clinically significant because load-sharing through the interbody space stimulates bone formation and maturation and may ultimately lead to better outcomes. A more compliant plate causes less posterior element strain which may reduce facet joint loads and in turn reduce facet joint arthrosis. An ideal plate may be one that is stiff enough to minimize interbody motion and yet compliant enough to allow consistent load-sharing and minimal increase in posterior element strain. Results also demonstrated that as new tissue forms, the loads through the interbody cage diminish. In this way, measuring interbody loads *in vivo* could be an indicator of the progress of fusion.

## Sociodemographic characteristics of distinct patterns of low back pain.

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**Introduction.** Most previous research on patient characteristics of back pain classification has focused on clinical factors. This study presents new and original findings that concentrate on sociodemographic traits. The purpose of this study was to compare sociodemographic characteristics based on a syndrome or clinical pattern classification approach to low back pain (LBP).

**Methods.** This retrospective review of prospectively collected LBP cases in Saskatchewan. Patient enrolment occurred between January 2014 and June 2017. Baseline data was recorded at the initial assessment across a range of sociodemographic variables for each patient (age, gender, chronicity, functional status, smoking, medication use, sleep disturbance, lawyer involvement, work status). All patients had mechanical LBP as determined by the Saskatchewan Spine Pathway triage methodology. There were 1913 patients:

Pattern1 PEP (relieved with prone extension)=703 (36.7%); Pattern1 PEN (not relieved with prone extension)=813 (42.5%); Pattern2 (relieved with flexion)=297 (15.5%)

\*Pattern3=72 (3.8%), \*Pattern4=28 (1.5%) (\* excluded from this study).

**Results.** The mean age of the cohort was 42.1 years (SD=13.03) with 56% males; average symptom duration was 83.01 days (SD=152.2, median=25.5).

Multivariable logistic regression revealed different characteristics for each pattern:

Pattern1 PEP: younger (odds ratio (OR) = 0.984), males (OR=1.29) with high baseline functional status (OR=0.984) were associated with greater odds of this pattern.

Pattern1 PEN: females (OR=1.54) who were not working (OR=1.52) were associated with greater odds of this pattern.

Pattern2: older (OR=1.014) patients, who continued to work (OR=1.57) but had chronic symptom duration (OR=1.49) were associated with greater odds of Pattern2.

**Discussion.** These data further suggest that LBP is a heterogeneous entity that not only has distinct clinical markers, but sociodemographic characteristics too; thus, a classification approach to LBP is warranted in both clinical and research settings.

The results provide a unique contribution to the literature because little has been published on socio-demographic differences (similarities and differences) of low back pain subgroups.

## Use of hemivertebrae for *in vitro* motion segment testing: a feasibility study

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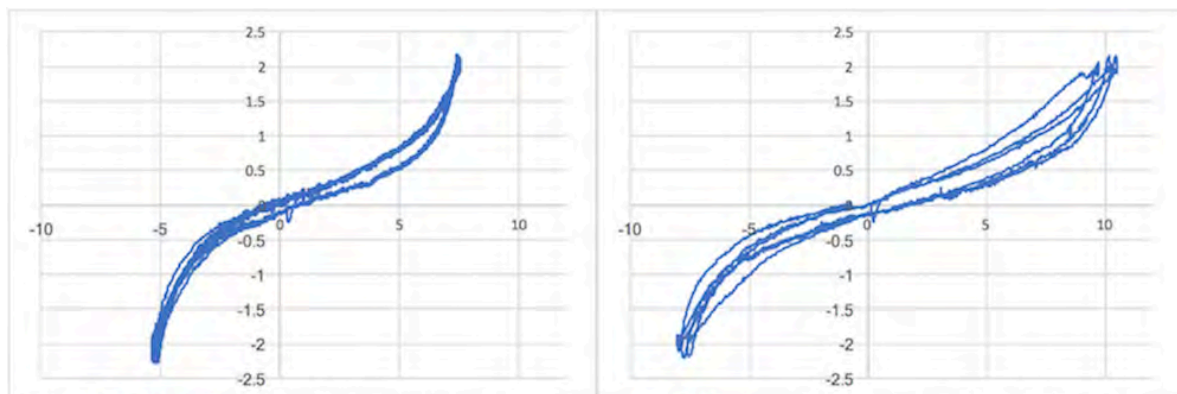
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**Introduction:** Two main challenges plague *in vitro* testing of lumbar motion segments. The first is maintaining the desired motion trajectory when test conditions change (i.e. ligament removal). The second is that current body-disc-body preparations yield only two motion segments per lumbar spine thereby wasting two additional intervertebral discs. If half of the vertebral body could be used in motion segment evaluation (hemivertebra-disc-hemivertebra), all discs in the lumbar spine would be available for testing. Unfortunately, this approach provides much less bone for anchoring (i.e. potting) the vertebra during testing. Given the above, the objective of this project was to determine if hemivertebrae segments provide sufficient stability during force control robotic testing.

**Methods:** In this study, 10 canine lumbar spine segments (L5-L7) were prepared by transecting all vertebral bodies in half with a handsaw resulting in two motion segments bounded by hemivertebrae (L5<sup>1/2</sup>-disc-L6<sup>1/2</sup> and L6<sup>1/2</sup>-disc-L7<sup>1/2</sup>). This created 20 motion segments. To each hemivertebra, a series of 6 screws (3 of #4 x 3/4 inch, 3 of #6 x 1 inch) were inserted as a radial pattern with ~5/8-3/4 inch left to protrude. Each segment was then lowered into a plastic pot while controlling specimen alignment. Dental stone (Modern Materials, Heraeus Kulzer) was then added to the pot and allowed to harden. Intervertebral disc dimensions were measured by caliper and 3D scanning (Structure Sensor, Occipital) to calculate the centre of rotation (posterior 1/3 at mid-disc level). The specimen was then inverted and the potting procedure repeated. The cephalad pot was then fixed to a stationary beam, while the caudal pot was fixed to a six-axis load cell (MC3A-100, AMTI) mounted to a parallel hexapod (R-2000, Mikrolar). Custom software (LabVIEW, National Instruments) was used to control robot movement. Force and moment targets were achieved by adjusting the velocity on each axis in proportion to force or moment errors while limiting the maximum velocity of the system. Flexion, extension, lateral bending and axial rotation were performed with three cycles each. Testing velocity was 0.1 degree per second with the maximal moment of 2.0 Nm. The resulting angle vs. moment data were then evaluated for signs of specimen loosening or damage.

**Results:** Of the 20 motion segments tested, only one was found to have loosened during testing as evidenced by discontinuities in the moment/angle graphs (Figure 1) as well as post-testing examination for cement loosening. The onset of loosening occurred during testing of axial rotation.

**Discussion:** Overall, hemivertebrae segments of a canine lumbar spine provided sufficient stability for typical moments applied during force control robotic testing. For moments larger than those applied here, these conclusions may not apply. In addition, precautions should be considered to reduce loosening during axial rotation testing by increasing the angle of anchoring screws to further resist this motion. As such, this technique allows for all intervertebral discs within the lumbar spine to undergo robotic testing thereby reducing waste while creating possibilities for additional test segments or within-animal control segments.



**Figure 1:** The left is an example of angle-vs-moment graph of a successful flexion/extension motion testing; the right is an angle-vs-moment graph from the loose pot during the same motion. The x-axis is the angle in degrees, and the y-axis is the moment in Nm.

## Telomerase activity after spinal cord injury

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**INTRODUCTION.** Telomere is a crucial part of chromosome to protect DNA damage. Telomerase provides DNA stability by maintaining telomere length. These have largely been investigated for their roles in cancer and cellular senescence in mitotic cells. Moreover, recent studies have presented their protective roles of DNA damage and cellular apoptosis in neurologic disease. However, the roles in spinal cord injury have not been studied. The purpose of this study is to investigate the interaction of telomerase activity and telomere length on the effect of neuro-protection or neuro-degeneration after spinal cord injury (SCI).

**METHODS.** Contusive SCI was made using 86 Sprague-Dawley rats, and each 7 rats were allocated into the acute phase (1, 3, 8, 24 and 48 hours), and the sub-acute and chronic phase (1, 2, and 4 weeks). Telomerase activity were assessed by telomerase reverse transcriptase (TERT) and telomeric-repeat binding protein (TERF) 1 and 2. Differentiation of the activated neural stem cells was also investigated by coexpression of neuronal/glia cell markers (GFAP, Neu N and CC-1). Expression of apoptosis were also investigated by caspase-3, 8 and 9 using terminal dioxynucleodidyl transferase dUTP nicked-end labeling (TUNEL) staining. Immunofluorescence staining and western blotting were performed for quantitative analyses, and these results were compared with those in the control group.

**RESULTS.** Expression of TERT increased gradually until post-injury 24 hours, and decreased following SCI. However, the overall expression of TERT was not significantly higher than that of the normal spinal cord. TERF 2 also showed gradual increase following SCI until post-injury 24 hours and decreased with time. And these TERF 2 expression was significantly higher than that of the normal spinal cord. Apoptosis analysis showed persistent high expression of caspases -3, -9, and -8 during the observation period compared with control group.

**DISCUSSION.** Increased activity of TERT and TERF 2 was noted in the acute phase of SCI. These findings suggest that increased telomeric activity may also be related to neuro-protective mechanisms for subsequent apoptosis (via the inhibition of apoptosis) resulting from the DNA damage after acute SCI.

## Spinal stiffness evaluation using latent class and functional data analyses

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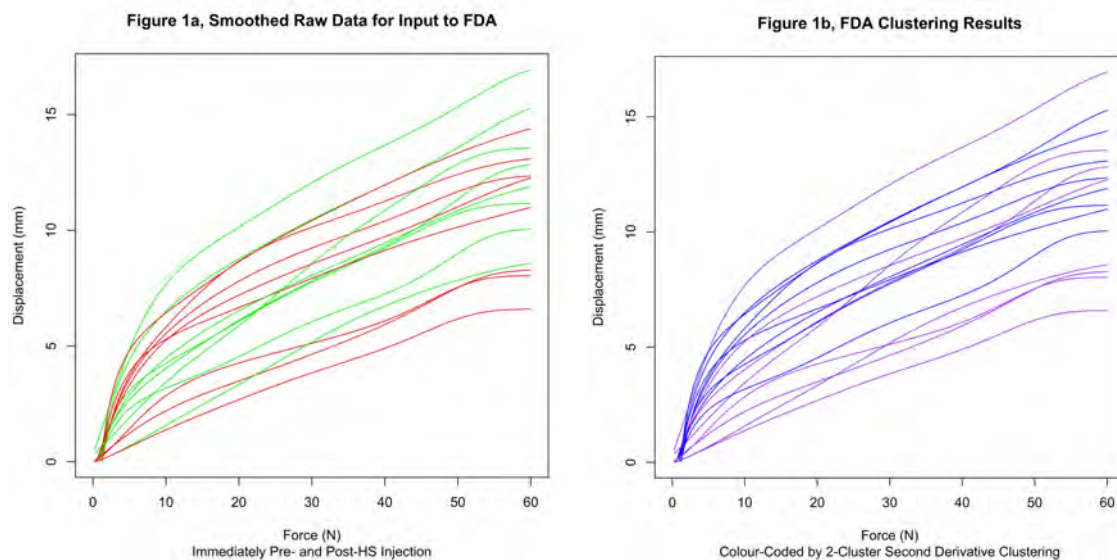
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**Introduction:** Recently, our lab has shown that instrumented L3 indentation generates force-displacement data that is positively associated with patient-reported measures of disability<sup>1</sup>. Specifically, several single value representations from these plots (e.g. terminal stiffness, regional stiffness) are discriminatory variables. Unfortunately, this approach does not evaluate the entire plot; doing so may reveal new sources of clinically significant data. Given the above, we have shown that advanced analytical techniques such as functional data analysis (FDA) and latent class regression analysis (LCRA) can discriminate between types of simulated force-displacement curves. In this project, we build on our past work by applying these techniques to previously published clinical force-displacement data that shows no change in terminal stiffness and regional stiffness with a control intervention, but a significant change in these same variables with an experimental intervention. Specifically, we hypothesize that FDA and LCRA will result in these same group distinctions using the entirety of the force-displacement curve.

**Methods:** Previously collected force-displacement data obtained through L3 indentation before and after subcutaneous saline injections were used as input for the FDA and LCRA. Specifically, the control intervention of isotonic saline (NS) produced no significant change in terminal or regional stiffness. Alternatively, a significant difference in these same variables followed an injection of hypertonic saline (HS). The data was first monotonically smoothed then normalized to a starting position of 0mm displacement at 4N of force. The terminal and regional stiffness values were calculated and compared with the previously published results to the smoothing was valid. Next, the curves were analysed by the FDA method (R v.3.3.1, The R Project for Statistical Computing) and LCRA method (Latent GOLD v.5.1, Statistical Innovations). Outputs of each were evaluated against known clinical pain and recovery cases.

**Results:** As expected, the FDA method grouped force-displacement plots by rate-of-change features that discriminate by plot shape (Fig 1). This unfortunately did not correlate to known patient traits from the clinical study. In contrast, LCRA discriminates by both shape and the end value of the plot. The dimensionality of force-displacement data required prevented an analysis by injection type, due to insufficient degrees of freedom. A grouped analysis of all plots for all subjects did not result in meaningful clusters.

**Discussion:** Our overall goal was to determine if known sub-groups can be identified from spinal stiffness curves using advanced analytical techniques. While our results here did not achieve this goal, an important outcome was realized; subsections of force-displacement data (e.g. terminal stiffness or linear slope) retain important clinical information about patient status. It should be noted that the sample size for this work was small. One limitation of clustering algorithms used in FDA and LCRA is their sensitivity to sample size. An investigation with a larger cohort is underway.



1. Wong, A.Y.L., et al., Does experimental low back pain change posteroanterior lumbar spinal stiffness and trunk muscle activity? A randomized crossover study, *Clinical Biomechanics*, 2016. 34: p. 45-52.

## The association of type 1 Modic changes, paraspinal muscle atrophy, pain and function in individuals with lumbar disc herniation

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**INTRODUCTION:** The relationship between radiographic findings in the lumbar spine and low back pain (LBP) is incompletely understood. Atrophy and fatty infiltration of the paraspinal muscles are often observed in individuals with LBP, and have been shown to correlate with poor physical performance. Prior investigation demonstrates a correlation between Modic-1 changes and LBP. However, a relationship between Modic-1 changes, lumbar paraspinal muscle changes, and functional status in patients with lumbar disc herniation has not previously been investigated. The aim of this study was to investigate these relationships in individuals with symptomatic disc herniations.

**METHODS:** This was a cross-sectional matched case-control study conducted at an urban, academic, tertiary spine center. Consecutive patients with Modic-1 changes and patients without Modic-1 changes, all of whom who were scheduled to have a discectomy for disc herniation, were enrolled into this study. Pre-surgical data were collected, including Visual Analogue Pain Scale (VAS) and Oswestry Disability Index (ODI) scores. Lumbar multifidus and erector spinae (ES) atrophy and fatty infiltration were assessed by T1-weighted axial MRI at L1-2, L2-3, L3-4, L4-5 and L5-S1 disc levels. The expected cross-sectional area (CSA) and the functional CSA of these muscles (area of fatty infiltration subtracted from the total CSA) were calculated using free hand technique on OsiriX®. Fatty infiltration of these muscles was graded using Goutallier and Quartile classifications.

**RESULTS:** Nine participants with Modic-1 changes (three female) and 12 without Modic-1 changes (six female) were included. The groups were similar in age (median 37, interquartile range  $\pm$ [IQR] 19; median 41, IQR $\pm$ 10 years; respectively,  $p=0.118$ ). Participants with Modic-1 changes had a higher percentage of atrophy in the multifidi at the L2-3, L3-4 and L4-L5 levels compared to those without Modic-1 changes ( $p<0.002$ ). Six patients had Modic-1 changes at the L5-S1 and three patients had at the L4-5 levels. In participants with Modic-1 changes, greater fatty infiltration the L2-3, L3-4 and L4-L5 multifidi and ES muscles was associated with higher pre-surgical VAS (multifidi  $r=0.733$   $p=0.025$ ; ES  $r=0.846$ ,  $p=0.004$ ) and ODI scores (multifidi  $r=0.773$ ;  $p=0.015$ ); this relationship did not exist in participants without Modic-1 changes (multifidi  $r=-0.370$ ,  $p=0.236$ ; ES  $r=0.363$ ,  $p=0.246$ ; ODI  $r=0.528$ ,  $p=0.078$ ).

**DISCUSSION:** In this cohort of patients with symptomatic lumbar disc herniations, an association between Modic-1 changes, greater atrophy and fatty infiltration in the lumbar multifidi, as well as higher pain and functional disability scores was observed. This relationship did not exist in individuals without Modic-1 changes. These data suggest the need for a larger longitudinal study in order to determine if a causal relationship exists between Modic-1 changes, lumbar paraspinal muscles changes, and the influence of these factors on the magnitude of LBP and functional disability in patients with these findings.

**GP201**

**Infection as an etiology for pseudarthrosis in multilevel spinal fusions**

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**Introduction**

Pseudarthrosis following spinal surgery places an enormous burden on both the patient and the healthcare system as a driver of revision surgery. Pseudarthrosis can often be accompanied by infection and there is no systematic approach to treating both simultaneously. In order to help address infection-related pseudarthrosis, our study aims (1) to identify the prevalence of occult infection in patients with pseudarthrosis and (2) to identify risk factors associated with positive intraoperative cultures.

**Methods**

A retrospective review of a single institution's surgical registry identified adult (>18 years old) patients who were treated with revision spinal fusion for pseudarthrosis between August 2015 and August 2017. Demographic, surgical, and medical data were collected, including risk factors for spinal infection (obesity, diabetes, steroid use, immunosuppression, chemotherapy, previous surgical infection, infection at a remote site, alcohol abuse, and malnutrition). Special attention was given to identify patients with occult infection, defined as patients with positive intraoperative cultures in the absence of clinical signs of infection. Fisher's exact test and univariate logistic regression were used to identify risk factors for positive intraoperative cultures and risk factors for hardware failure.

**Results**

Fifty-one patients were included in our analysis. All patients had a revision spinal surgery with a diagnosis of pseudarthrosis, intraoperative cultures, and the absence of clinical signs of infection. The median age at surgery was 59 years old (range 52 – 70) and females comprised 55% of the cohort. A total of 17 patients (33%) had at least one risk factor for spinal infection. The prevalence of occult infection as defined by at least one positive intraoperative culture was 33% and prevalence as defined by two or more positive intraoperative cultures was 16%. A risk factor for having at least one positive culture was the presence of a risk factor for spinal infection (OR 2.55, 95% CI 0.61 - 10.7, p=0.20), but this value was not significant. Risk factors for having two or more positive cultures include male gender (female: OR 0.10, 95% CI 0.01 - 0.95, p=0.045) and the presence of hardware failure (OR 4.53, 95% CI 0.87 - 23.7, p=0.07), but this did not reach significance. Female gender was also associated with less hardware failure (OR 0.51, 95% CI 0.15 - 1.78, p=0.29), while increasing length of the most recent fusion had increased odds of hardware failure (OR 1.14, 95% CI 0.98 - 1.34, p=0.097), but neither of these values were significant.

**Discussion**

The patient who develops concurrent infection and pseudarthrosis after spinal surgery presents a challenging problem for which no clear treatment guidelines have been established. In patients undergoing revision surgery for pseudarthrosis, the incidence of sub-clinical infection can be as high as 33%, and risk factors include male gender, select comorbidities associated with infection, and hardware failure. Even in the absence of clinical signs of infection, surgeons should maintain a high degree of suspicion for occult infection in patients with pseudarthrosis who also have these risk factors and consider routine cultures on patients undergoing revision surgery for pseudarthrosis.



## Assessment of damage to the iliopsoas muscle from the oblique lateral interbody fusion approach

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**INTRODUCTION:** Lumbar lateral interbody fusion (LLIF) has been widely performed to achieve minimally invasive, rigid lumbar interbody fusion. LLIF via splitting psoas muscle tends to result in postoperative muscle weakness of the iliopsoas muscle and thigh numbness due to the damage to the psoas major muscle and lumbar plexus. Similar postoperative complications have been made on the LLIF via oblique lateral corridor (OLIF; oblique LLIF) approach, but the detailed perioperative changes in the psoas major muscle in the medium to long term are not clarified. The purposes of this study were to investigate the relationship between clinical symptoms and changes in the psoas major muscle before and after OLIF surgery.

**METHODS:** The subjects were 27 patients who underwent OLIF surgery under the diagnosis of degenerative lumbar disease between November 2013 and April 2015 in our hospital. The cross-sectional areas (CSAs) of the psoas major muscle on the approaching and contralateral sides were measured by using axial computed tomography of the surgical intervertebral space before, after, and 1 year after surgery. Change in the muscle property was also evaluated retrospectively by using axial magnetic resonance imaging of the same level. To evaluate the psoas major muscle in each period, the change in the CSA from before to after the surgery was compared, with the ratio of those in the approach side to the contralateral side, and the progression of fat degeneration, measured by fat cross-sectional area, were also measured. In addition, the relationship between these parameters and postoperative lower limb neuropathy was investigated.

**RESULTS:** The ratio of the CSA of psoas major muscle in each period was  $1.09 \pm 0.21$  before surgery,  $1.25 \pm 0.29$  immediately after surgery, and  $1.02 \pm 0.29$  one year after surgery. Significant swelling of the psoas major muscle on the approach side was observed immediately after the surgery. No significant difference was observed in mean total CSA before ( $1550 \pm 746$  cm<sup>2</sup>) and 1 year after surgery ( $1583 \pm 690$  cm<sup>2</sup>). No postoperative fat degeneration was observed either. Three cases of paresthesia in the front of the thigh were observed, but no muscle weakness in the iliopsoas muscle was observed. No association was found between any of the cases and the ratio of the approach side to the contralateral side and the changes in total CSA. The symptoms improved within 2 to 3 weeks after surgery.

**DISCUSSION:** The swelling of the psoas major muscle on the approach side was observed only immediately after surgery with no significant long-term prolongation. This is considered to be due to a temporary swelling after surgery caused by intraoperative muscle, which implies that OLIF approach has minimal effect on the psoas major muscle.

## Lumbar epidural lipomatosis is associated with visceral fat and metabolic disorders

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**INTRODUCTION** Lumbar spinal epidural lipomatosis (LEL) is a condition characterized by excessive deposition of epidural fat in the spinal canal. Metabolic abnormalities may be associated with LEL, but few validated reports exist. Thus, we investigated the association between LEL and metabolic disorders in this study.

**METHODS** A total of 218 patients were examined by abdominal computed tomography (CT) scans and blood tests. Using the CT data, the visceral fat area, subcutaneous fat area, the ratio between visceral and subcutaneous fat areas (V/S ratio), and abdominal circumference (AC) were evaluated. We also investigated body mass index (BMI), as well as serum uric acid (UA), total cholesterol, triglycerides, high-density lipoprotein, low-density lipoprotein, insulin, ferritin, and glycosylated hemoglobin levels. We comparatively analyzed these parameters in LEL and non-LEL patients.

**RESULTS** There were 58 LEL patients and 160 non-LEL patients. The LEL group was predominantly male ( $P=0.003$ ). Visceral fat area was significantly higher in both men and women in the LEL group ( $P = 0.041$  and  $<0.001$ , respectively). In the LEL group, UA ( $P = 0.043/0.003$ ) and insulin ( $P = 0.023/0.046$ ) levels were significantly higher in both men and women, respectively, and ferritin levels ( $P = 0.017$ ) were significantly higher in men.

**DISCUSSION** LEL patients had significantly more visceral fat and increased levels of insulin, UA and ferritin, which are closely related with metabolic disorders. This study indicated that the increased epidural fat seen in LEL patients is associated with metabolic disorders and abnormalities, as represented by the metabolic syndrome.

## Presence of redundant nerve roots affects the balance ability in patients with lumbar canal stenosis

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### INTRODUCTION

Falls in the elderly may lead to bedridden states due to bone fractures and contribute to mortality. Several reports have addressed the elevated risk of falls in patients with lumbar spinal canal stenosis. Patients with redundant nerve roots (RNR) exhibit more severe neurological deficits and worse surgical outcomes than patients without RNR. However, there has less been focus on the association between RNR and balance ability. It was hypothesized that RNR could be associated with low balance ability scores and high risk of fall. The main aim of the present study was to assess the relevance of RNR to the sway of the center of gravity and the risk of falls in patients with lumbar spinal canal stenosis.

### METHODS

Patients with lumbar spinal canal stenosis who were resistant to conservative therapy, had surgical indications, and were preoperatively able to stand for 30 s or longer with their eyes closed were selected as subjects. Patients with a history or clinical symptoms of intracranial diseases, otorhinolaryngologic diseases, and cervical stenosis, as well as those with arthroplasty of the lower legs were excluded. A total of 44 patients were categorized into two groups using sagittal T2-weighted lumbar spine images with magnetic resonance imaging: the group of patients with RNR (RNR group, n = 20 patients) and those without RNR (NRNR group, n = 24 patients). Their postural sway was recorded while they remained in a standing position with their eyes closed for 30 s. Environmental area (EA) and locus length per environmental area (L/EA) were measured. Furthermore, history of falls during the past year was recorded for both groups. Wilcoxon rank-sum or Fisher's exact test was used to determine the statistical significance defined as  $P < 0.05$ .

### RESULTS

The mean EA in the RNR and NRNR groups was 9.06 (range: 2.03-19.36)  $\text{cm}^2$  and 4.53 (range: 1.72-8.35)  $\text{cm}^2$ , respectively. The mean L/EA in the RNR and NRNR groups was 17.27 (range: 7.05-31.23)  $\text{cm}/\text{cm}^2$  and 22.04 (range: 10.90-35.21)  $\text{cm}/\text{cm}^2$ , respectively; statistically significant differences were observed for both EA and L/EA ( $P = 0.0001$ ,  $0.0392$ ). A history of fall was recorded in 21 of the 44 patients (47.7%). Comparison of the groups showed that 14 of the 20 patients in the RNR group and 7 of the 24 patients in the NRNR group had a history of falls. The number of patients with a history of fall was significantly higher in the RNR group ( $P = 0.0144$ ).

### RESULTS

The RNR group had poorer sway of the center of gravity parameters and a frequent history of falls compared to the NRNR group. Since the sway of the center of gravity and the risk of falls are greater in patients with redundant nerve roots, measures on fall prevention are needed.

## Prevalence of Postoperative Nausea and Vomiting in Patients Undergoing Spinal Surgery Under General Anesthesia

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[Objective] Postoperative nausea and vomiting (PONV) occur in approximately 30% of patients receiving general anesthesia. Although PONV is uncomfortable, hinders early ambulation, and greatly reduces patient satisfaction, there have been few reports of studies on the incidence of PONV after spinal surgery. This study investigated the prevalence of PONV in patients undergoing spinal surgery at our hospital to identify risk factors.

[Subjects and methods] This study included 276 patients who underwent spinal surgery under general anesthesia at our hospital between April 2014 and September 2017 (165 men and 111 women, mean age 60.9 years). The following parameters were retrospectively compared: the incidence of PONV, use of metoclopramide, sex, age, operative time, smoking status, use of postoperative intravenous patient-controlled analgesia (IV-PCA), predictive scores for PONV (i.e., the Apfel score, which is based on female sex, nonsmoking status, previous history of motion sickness or PONV, and use of postoperative opioids, and the Koivuranta score, which is based on female sex, nonsmoking status, previous history of motion sickness, previous history of PONV, and surgery lasting 60 minutes or longer), surgical site (i.e., cervical, thoracic, or lumbar spine).

[Results] PONV occurred in 88 patients undergoing spinal surgery under general anesthesia, with an incidence of 31.9%. The incidence was significantly higher in women, patients undergoing surgery lasting 120 minutes or longer, and those using postoperative IV-PCA. Metoclopramide for PONV was taken as needed by 55 patients, accounting for 19.9%. Use of metoclopramide was significantly higher in women and patients using postoperative IV-PCA. Apfel and Koivuranta predictive scores were correlated with the incidence of PONV in patients undergoing spinal surgery. No significant differences were observed according to surgical site.

[Discussion] PONV occurred in 31.9% of patients undergoing spinal surgery under general anesthesia, indicating this is a frequent postoperative complication. Despite this, PONV is often treated symptomatically after discharge from anesthesia care. Furthermore, drugs available for treatment of postoperative nausea are limited in Japan. This study found that Apfel and Koivuranta scores were correlated with the incidence of PONV. Thus, for prevention of PONV, it is necessary to selectively implement therapeutic and prophylactic measures through effective use of these scores in cooperation with anesthesiologists.

[Conclusion] Of 276 patients undergoing spinal surgery under general anesthesia, 88 developed PONV, with an incidence of 31.9%. The incidence was significantly higher in women, patients undergoing surgery lasting 120 minutes or longer, and patients using postoperative IV-PCA. Apfel and Koivuranta scores are useful for predicting the occurrence of PONV in patients undergoing spinal surgery under general anesthesia.

## SERUM METAL LEVELS AFTER REMOVAL OF SPINAL INSTRUMENTATION

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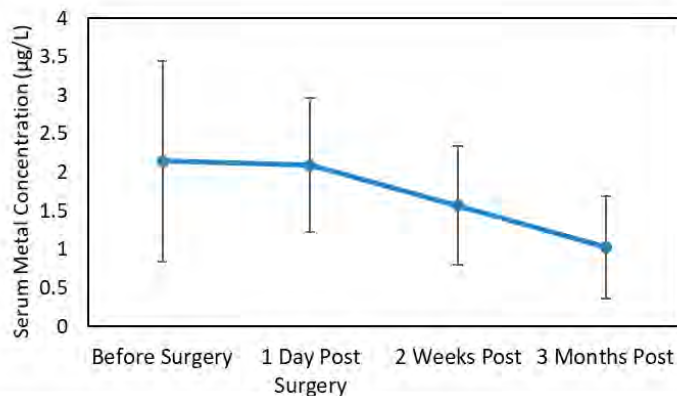
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**Introduction:** With the increasing use of spinal instrumentation, growing concern has been raised on the effects of degradation of prosthetic metal implants with subsequent increase in serum metal levels. Spinal surgery with titanium and chromium instrumentation has become increasingly common in degenerative conditions. Implant removal is not routinely carried out and is only performed for late operative site pain, infection, neurological complications or implant failure. Retrospective research has shown elevated metal ion levels after instrumented spinal fusion but no studies to our knowledge have prospectively investigated serum metal levels after removal of spinal instrumentation [1,2]. The primary aim of this study was the measurement of serum metal levels over time after removal of spinal instrumentation

**Methods:** This longitudinal cohort study measured serum titanium, chromium, nickel, and aluminium levels in 20 patients undergoing removal of spinal instrumentation due to late operative site pain, infection, or implant failure (removal) compared to baseline serum metal ion concentration levels in 20 patients undergoing surgery without spinal instrumentation (control). Serum samples were obtained pre-operatively and one-day post-operatively from both control and removal groups. Serum samples were also taken in the removal group at two weeks, three months, and one year post-op. to assess the pattern of metal ion release. Samples were analysed using high resolution inductively coupled plasma mass spectrometry to measure serum metal concentrations. A matched paired t-test was conducted to evaluate the effect of group and a repeated measures ANOVA was used to assess the effect of time in the removal group.

**Results:** An average of twelve metal implants (ten pedicle screws and two rods) were removed per patient. Our preliminary results showed significantly higher serum titanium levels in patients undergoing removal surgery (mean, 2.27 µg/l) against controls (mean, 1.01 µg/l, p=0.003). Patients within each group were matched for age and past exposure to metal implants. Serum aluminium (p=0.563), nickel (p=0.217) and chromium levels (p=0.221) were not statistically different between the two groups. A significant increase in aluminium levels was seen only after one-day post-surgery (p=0.006). Serum titanium levels increased slightly one-day post-surgery and decreased at 2 weeks and 3 months to levels lower than before surgery (Figure 1). Nickel and chromium levels remained constant at all four time points.

**Discussion:** Aluminium levels increased significantly one-day post-surgery, possibly due to intra-op. NSAID's but decreased within two weeks post-op to same levels as before surgery. No significant differences or trends were seen for nickel and chromium as implants were composed of titanium. Mean titanium levels before removal surgery were found to be 2.3 times higher than controls, similar to other studies [2] but much lower than in data from scoliosis patients where up to a 6-fold increase in titanium levels was seen, indicating increased metal instrumentation density leading to much greater metal ion serum levels [3]. Our preliminary data suggest that titanium levels can decrease by as much as 50% only three months after removal (Figure 1) and may continue to decrease at later follow-up.



**Figure 1.** Mean (SD) titanium serum levels from patients who underwent removal of metal surgery at four different time points (before surgery, 1-day, 2 weeks, and 3 months post op).

1. Mcphee, B., et al., Spine, 2007.
2. Richardson, T.D., et al., Spine, 2008.
3. Cundy, T.P., et al., Spine, 2013.

## RISK FACTORS OF LOW BACK PAIN IN MALE PATIENTS WITH OSTEOPOROSIS

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### INTRODUCTION:

It has been reported that the mortality rate of men after pathological osteoporotic fractures is higher compared with that of women. In recent years, the importance of treatment for male patients with osteoporosis has been acknowledged, although few reports evaluate its epidemiology and treatment. Elderly patients with osteoporosis, but without evidence of fresh pathological fractures, often complain of low back pain that impairs activities of daily living. In order to evaluate the risk factors associated with low back pain, the purpose of the current study was to elucidate the relationships among bone mineral density (BMD), muscle mass, bone turnover markers, spinal sagittal alignment, nutrition status, and low back pain.

**METHODS:** A total of 40 male patients (mean age: 75.1 years, range: 60–88 years) without evidence of fresh pathological vertebral fractures were included in this study. In all cases, we evaluated the following: BMD of the lumbar spine (LS), femoral neck (FN), and total hip (TH); trunk and limb muscle mass using bioimpedance analysis (TANITA MC-780A); bone turnover markers, including the bone formation marker BAP, the bone resorption marker TRACP5b, and the bone quality marker homocysteine; sagittal spinal alignment, including the sagittal vertical axis (SVA), pelvic tilt (PT), and pelvic incidence minus lumbar lordosis (PI-LL); controlling nutritional status (CONUT) score as a measure of nutrition; and low back pain in accordance with the Japanese Orthopaedic Association Back Pain Evaluation Questionnaire (JOABPEQ) and the Oswestry Disability Index (ODI). Correlations between a low back pain score and the previously mentioned factors were evaluated.

### RESULTS:

Significant positive correlations existed between FN BMD or TH BMD and the JOABPEQ score ( $r=0.64$  and  $r=0.62$ , respectively) whereas significant negative correlations were observed for BAP, homocysteine, SVA, PT, or CONUT scores and the JOABPEQ score ( $r=-0.47$ ,  $r=-0.33$ ,  $r=-0.41$ ,  $r=-0.31$ , and  $r=-0.41$ ). Significant negative correlations were identified between the BMD of the LS, FN, or TH, and the ODI score ( $r=-0.39$ ,  $r=-0.54$ , and  $r=-0.62$ ) although significant positive correlations were found for BAP, homocysteine, SVA, PT, PI-LL, or CONUT scores and ODI score ( $r=0.37$ ,  $r=0.33$ ,  $r=0.49$ ,  $r=0.56$ ,  $r=0.38$ , and  $r=0.59$ ). TRACP5b or muscle mass was not correlated with low back pain scores.

### DISCUSSION:

Teriparatide treatment has reportedly increased BMD and reduced severe back pain. Muscle fatigue, as a result of continuous paravertebral muscle contraction, in the patients with a sagittal spinal imbalance might induce low back pain as has been previously reported. Several reports suggest that high bone resorption and activated osteoclasts may induce low back pain, but the role of high bone formation and low bone quality in low back pain remains unclear. This is the first study to evaluate the correlation between nutritional status and low back pain. These findings indicate that a low BMD, high bone turnover, low bone quality, a sagittal spinal imbalance, and a low nutritional status were associated with the risk of low back pain in male patients with osteoporosis.

## REOPERATION RATES AFTER SURGERIES FOR DEGENERATIVE LUMBAR DISEASES ACCORDING TO FUSION PROCEDURES

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**INTRODUCTION:** There is an inherently low incidence of reoperation after surgery for lumbar degenerative disease. Therefore, it is difficult to sufficiently power studies to detect differences between reoperation rates of different lumbar fusion surgeries. National population-based databases provide large, longitudinally followed cohorts that may help overcome this challenge. The purpose is to compare the reoperation rates after surgery for degenerative lumbar diseases according to different surgical fusion procedures in a national population of patients.

**METHODS:** We used the Korean Health Insurance Review & Assessment Service national database to select our study population. We included patients with the diagnosis of degenerative lumbar diseases who underwent fusion surgeries from January 2011 to June 30, 2016. We assigned patients into two groups based on procedure codes: posterolateral fusion or posterior/transforaminal lumbar interbody fusion. The primary endpoint was reoperation. Age, sex, presence of diabetes, osteoporosis, associated comorbidities, and hospital types were considered potential confounding factors.

**RESULTS :** The reoperation rate was not different between the patients who underwent posterolateral fusion and those who underwent posterior/transforaminal lumbar interbody fusion. Old age, male gender, and hospital type were noted to be risk factors for reoperation.

**DISCUSSION :** The incidence of reoperation was independent of fusion method. We can help surgeons more accurately communicate risks of surgery to patients, so that all patients are able to make fully educated decisions about whether or not to undergo surgery.

## ASSOCIATION BETWEEN SKELETAL MUSCLE MASS AND BONE MINERAL DENSITY IN WOMEN OVER 40.

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**[Introduction]** Sudden recent increases in elderly patients have led to the need to treat osteoporosis and sarcopenia. Causes of osteoporosis include aging, genetics, diabetes mellitus, COPD, decreases in kinetic stress, and Vitamin D deficiency, but all of these are closely associated with the causes of sarcopenia. To prevent fractures, balance and mobility must also be assessed together. The objective of this study was to determine the correlation between bone mineral density and muscle mass within each age group.

**[Methods]** Participants comprised 1049 women between the ages of 40 to 96 years (mean age: 71.8 years) who had presented to our clinic between April 2015 and September 2016, and whose bone mineral density and skeletal muscle mass index were determined. Secondary osteoporosis was excluded from this analysis. There were 28 patients in their 40s (40-49 years), 96 in their 50s, 268 in their 60s, 424 in their 70s, 208 in their 80s, and 25 in their 90s. BMDs in the lumbar spine, total femur, and femoral neck were determined by DEXA (DPX Bravo, GE). Skeletal muscle mass was determined by BIA (Inbody720, BIOSPACE) and skeletal muscle mass index (SMI) was calculated. Spearman's rank correlation coefficient was used in the statistical evaluation where  $p < 0.05$  was considered statistically significant.

**[Results]** Mean BMD in patients in their 40s was 1.108 g/cm<sup>2</sup> in the lumbar spine, 0.818 in the total femur, and 0.805 for the femoral neck. In their 50s, numbers were: 1.053, 0.807, 0.776, respectively; in their 60s, it was 0.961, 0.769, 0.724; 70s: 0.967, 0.761, 0.713; and 80s: 0.979, 0.702, 0.658, 90s: 0.889, 0.640, 0.612. Mean SMI values for women in their 40s through 90s were 5.98, 6.02, 6.00, 5.85, 5.62, 5.53, respectively, in increasing age order. A positive correlation was noted between BMD and SMI in all subjects (correlation coefficients: lumbar spine 0.34, total femur 0.43, femoral neck 0.39) and individual numbers reached the level of significance. A positive correlation was noted between BMD and SMI in every age group and every bone area, with statistical significance observed in all patients in their 40s through 80s. For those in their 40s, the correlation coefficients were 0.46, 0.63, 0.58; for those in their 50s, it was 0.34, 0.54, 0.53; for those in their 60s, it was 0.46, 0.43, 0.39; for those in their 70s it was 0.28, 0.36, 0.32, and for those in their 80s it was 0.29, 0.39, 0.32. The younger the patient, the higher was the degree of correlation. Women in their 90s had mean correlation coefficients of 0.30 in the lumbar spine, 0.46 in the total femur, and 0.46 in the femoral neck. The correlation was statistically significant except for in the lumbar spine.

**[Conclusions]** A positive correlation between BMD and SMI can be observed in women in their 40s through 90s with a tendency towards higher correlation coefficients in younger patients. These results suggest that women can be screened for osteoporosis simply by measuring skeletal muscle mass, thus avoiding exposure to harmful x-rays.



## CAGE HEIGHT IN STAND-ALONE LATERAL LUMBAR INTERBODY FUSION HAS BIOMECHANICAL CONSEQUENCES: A FINITE ELEMENT STUDY

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**INTRODUCTION:** Improved stability seen after lateral interbody fusion (LIF) reconstruction has been attributed to preservation of ligamentous structures and low subsidence. No study exists that addresses the biomechanical consequences of using lateral interbody cages to establish varying degrees of disc height restoration. The aim of the current study was to examine the biomechanical effect of LIF cages of different heights which confers maximum stability for single level lumbar fusion procedures.

**METHODS:** A three-dimensional non-linear finite element model of an L1-S1 spine with grade 3 disc at L4-L5 was used in the study. A 22 mm cage (of Ti) was used to create models with cage height same as native L4-L5 disc height to 4 mm taller. Moments of 7.5 Nm in all the three principal directions were applied independently. Motions in the three principal directions, stresses at both the endplates of the fused disc as well as strains in all the ligaments were retrieved from the analyses.

**RESULTS:** At the fused level change in motion was nominal under flexion/extension, lateral bending (10% reduction) and torsion (25% increase) with cage height equal to native disc height while change in motion under flexion/extension and lateral bending (reduction of 70% to 90%) as well as under torsion (increase of 50%) was substantial as the cage height further increased. Small changes in motions at all the three discs superior to fused disc was observed in all cases studied. At level inferior to fused disc, a 60% increase in motion was seen as the cage height increased to 2mm taller than the native disc while a reduction in motion of 75% occurred with further increase in cage height. As the cage height increased, maximum contact stress at the L4-L5 endplates increased from 2 MPa to 12 MPa, ALL and PLL strain increased from 10% to 270% and CL strain increased from 10% to 100% of corresponding strain in the native disc.

**DISCUSSION:** The current analyses showed that when the cage replaced the native disc, it did not produce any appreciable change (less than 25%) in motion at the fused level, moderate increase in motion (about 60%) at inferior to the fused level leading to the conclusion that replacing the native disc by cage of equal height does not alter the biomechanics of the spine. Cages 2 mm taller than native disc made the fused segment, segment inferior to fused segment stiffer, induced endplate stresses of the order of 50% of its failure stress and produced strains in the posterior and anterior ligaments that are two times that of the strains in a normal disc leading to the conclusion that cages 2mm taller than native disc may alter the biomechanics of the degenerated segment. Minimal changes (about 0.5%) in the resulting biomechanics were observed when the cage made of PEEK was used rather than Ti cage. Additional cadaver tests have to be conducted to validate this conclusion.

## A CADAVERIC STUDY FOR ESTIMATING THE DOSE REDUCTION WHEN USING PULSED AND COLLIMATED X-RAY BEAMS IN PROCEDURES

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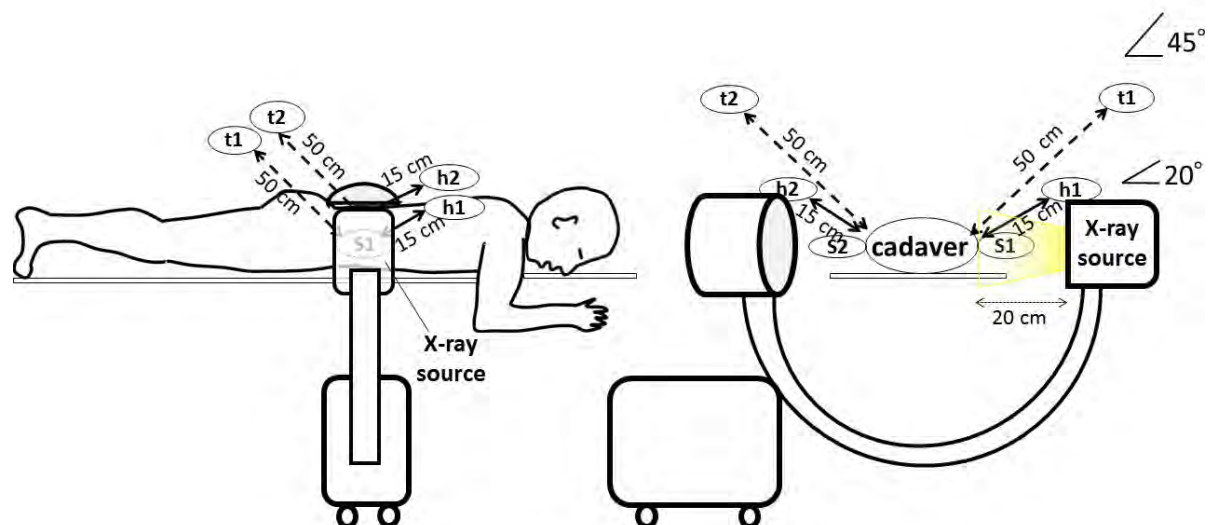
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**INTRODUCTION:** Awareness of the harmful effects of long-term low-dose radiation is rising. However, no comprehensive study has accurately simulated clinical situations to assess the required degree of reduction in the radiation exposure dose to medical staff and patients in fluoroscopic procedures.

**METHODS:** Seven fresh cadavers were irradiated for 5 min with C-arm fluoroscopy using pulsed and collimated X-ray beams. The X-ray sources were placed under the table, over the table, and lateral to the table. Radiation exposure doses were measured at different points, such as the center of the irradiation field on the cadaver, and the location of the surgeon's hand and thyroid gland. In addition, Monte Carlo simulation was performed to estimate the dose reduction and confirm the experimental results.

**RESULTS:** The radiation exposure doses using pulsed fluoroscopy (8 times/s) were reduced to about 30% for the patient and to about 70% for the surgeon's hand and thyroid gland as compared with that in continuous fluoroscopy. The radiation exposure doses using collimated X-ray beams were reduced to approximately 65% for the surgeon's hand and thyroid gland as compared with that in non-collimated fluoroscopy. These results were consistent with the simulation, and the phenomena could be appropriately explained by physics.

**DISCUSSION:** Our study revealed the effectiveness of pulsed and collimated X-ray beams in reducing radiation exposure doses from C-arm fluoroscopy. Surgeons should use the techniques of pulsed fluoroscopy and collimation to protect patients and themselves from radiation harm.



## BALLOON KYPHOPLASTY FOR LUMBAR SPINE TUMOR

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We report four cases of patients suffering from low back pain with lumbar tumor who were treated by Kyphon Balloon Kyphoplasty (BKP; Medtronic, Minneapolis, MI, USA) under fluoroscopic guidance.

Case 1 was a 44-year-old man whose primary lesion was salivary gland cancer. This patient felt low back pain at work which became so severe that it prohibited him from moving by himself. His performance status (PS) deteriorated to grade 4, and the pain continued for 1 month. Based on imaging studies and clinical findings, we diagnosed him with an L5 vertebral fracture. After performing L5 BKP, he was able to sit or walk for 10 minutes, and his PS improved to grade 2. However, his pain with motion did not completely resolve.

Case 2 was a 54-year-old man whose primary tumor was kidney cancer. After treating his cancer pain with radiotherapy, this patient still felt upper and lower lumbar pain. He desired surgical treatment because his PS was grade 2, and he was unable to ambulate for more than 10 minutes with a cane. Immediately after performing L1 and L5 BKP, his low back pain and posture during walking improved, but his groin pain remained and was an impediment in his daily life. Lidocaine injections into the sacroiliac joint were effective in controlling the groin pain.

Case 3 was a 65-year-old man whose primary tumor was lung cancer. This patient's lower back pain increased after 6 cycles of chemotherapy. Radiotherapy was performed to an osteolytic lesion of the L2 vertebral body, but his pain with motion was sustained. An L2 BKP was performed, and his symptoms were gradually alleviated as he had no problem in daily activities.

Case 4 was a 72-year-old man with the suspicious of L4 sarcoma. His low back pain prevented him from sitting during a meal for more than one month. Despite the use of radiotherapy, his symptom was lasting and PS remained grade 4. Total en bloc spondylectomy was considered impossible because of his heart disease. BKP was performed and he recovered to be ambulatory after two months with mild back pain.

Lumbar spine tumor often causes severe pain that can significantly disrupt a person's daily life. BKP has been used for osteoporotic vertebral fractures and has recently become an option for metastatic tumor pain. In the cases of our patients, partial pain relief was achieved, and their activity improved but not to normal levels. Although BKP was effective in reducing back pain, it was unable to relieve all symptoms. Currently, we are inclined to believe that BKP should be used in conjunction with other methods, such as block injection therapy, to manage metastatic lower back pain.

## SECONDARY THORACOLUMBAR VERTEBRAL END-PLATE LESIONS IN YOUNG GYMNASTS

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**Background:** We previously reported that the incidence of anterior thoracolumbar vertebral end-plate lesions was significantly higher in young gymnasts than that in non-gymnasts who played other sports (gymnasts 20%, non-gymnasts 2%, ISSLS 2013). And some reports have shown a high incidence of spondylolysis and/or spondylolisthesis in young gymnasts. However, few studies have focused on the association between thoracolumbar vertebral end-plate lesions and spondylolysis and/or spondylolisthesis. Sairyo et al. has defined secondary end-plate lesions as end-plate lesions resulting from biomechanical failure caused by spondylolysis and/or spondylolisthesis (Orthop. surg. traumatol. 2000).

**Purpose:** The purpose of this study was to investigate the incidence and the morphological features of secondary end-plate lesions in young gymnasts.

**Material:** The number of gymnasts who visited our hospital between 2010 and 2016 with a complaint of low back pain was 299. We divided them into three groups: 87 elementary school students, 137 junior high school students, and 75 high school students.

**Methods:** The incidences of spondylolysis, spondylolisthesis, and end-plate lesions were evaluated using X-ray. We limited screening of the end-plate lesions to anterior or posterior corners of the vertebral body. Secondary end-plate lesions were defined as those located on the lower edge of the vertebral body or the upper edge of the vertebral body adjacent to the caudal side of the vertebral body, at the same level as spondylolysis or spondylolisthesis. The incidence of secondary end-plate lesions was then compared among groups. These lesions were classified into 3 types based on morphology: Type 1, separation of an apophyseal region; Type 2, excavation of the apophyseal region; Type 3, wedging of the vertebral body.

**Results:** Secondary end-plate lesions were observed in 2 vertebral bodies of 2 (2%) elementary school students, 11 vertebral bodies of 9 (7%) junior high school students, and 3 vertebral bodies of 3 (4%) high school students. No significant difference was found among the groups. These lesions were observed in 1 L2 vertebral body, 1 L3 vertebral body, 1 L4 vertebral body, 3 L5 vertebral bodies, and 10 S1 vertebral bodies. Morphologic classification identified no type 1, 4 type 2, and 12 type 3 vertebral end-plate lesions.

**Conclusion:** Secondary end-plate lesions were observed in young gymnasts. Lesion incidence was not influenced by age. These lesions most commonly affected S1. The most common morphological classification was type 3, which involved severe deformity of the vertebrae. In some cases, gymnasts with type 3 were forced to prematurely retire owing to severe low back pain and/or neuropathic pain in the lower extremity. For solving these problems, it is necessary to prevent spondylolysis and/or spondylolisthesis from progressing. Therefore, early detection and early treatment intervention are essential.



**Fig.** Lateral lumbar radiography showed wedging of the vertebral body (Type3) of S1 and spondylolisthesis at the upper level.

## Alpha 2-macroglobulin as the dual regulator for both anabolism and catabolism in the cartilaginous endplate of intervertebral disc

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**Introduction:** Alpha 2-macroglobulin ( $\alpha 2M$ ) is an endoprotease inhibitor that is as a master inhibitor of cartilage degrading factors that attenuates post-traumatic osteoarthritis progression. But its function for the cartilaginous endplate (CEP) of intervertebral disc (IVD) is unknown. The objective is to illustrate if supplemental alpha-2 macroglobulin ( $\alpha 2M$ ) has beneficial effects on the CEP that may slow the progression of IVD degeneration.

**Methods:** Firstly, we confirmed degenerative CEP characters by H&E staining and Safranin O fast green staining and detected the increasing level of  $\alpha 2M$  and MMP-13 in the degenerative CEP in contrast to relatively normal CEP by immunohistochemistry. Then, the effects of exogenous  $\alpha 2M$  mainly on TNF- $\alpha$ -induced CEP catabolic enzyme MMP-13 and anabolic molecules were evaluated by qRT-PCR, Western blotting and ELISA in cultured CEP cells obtained from the rats. Furthermore, suppression of  $\alpha 2M$  on TNF- $\alpha$ -induced activation of the NF- $\kappa B$  signaling pathway was measured by Western blotting and immunofluorescence. In addition, function of  $\alpha 2M$  on TNF- $\alpha$ -treated ex vivo IVDs from rats lumbar IVDs was estimated and TNF- $\alpha$  and  $\alpha 2M$  were given for seven days after which the gene expression of MMP-13, Sox9, ACAN and Col II in the CEP area was measured by qRT-PCR.

**Results:** Compared to normal CEP, level of  $\alpha 2M$  was slightly increased in the CEP from degenerative patients, whereas MMP-13 levels were sharply elevated. In comparison with IL-1 $\beta$ , TNF- $\alpha$  more strongly stimulated the gene expression of MMPs and inhibited gene expression of Sox9, ACAN and Col II in rat CEP cells, which demonstrated that TNF- $\alpha$  was the more vital factor in inducing CEP degeneration. In vitro,  $\alpha 2M$  inhibited the gene and protein expression and activity of MMP-13 in a dose-dependent manner in rat CEP cells stimulated by TNF- $\alpha$ . The  $\alpha 2M$  refrained the phosphorylation of I $\kappa$ B $\alpha$  and inhibited the nuclear translocation of p65 stimulated by TNF- $\alpha$ . Finally, supplemental  $\alpha 2M$  reduced the gene expression of MMP-13, and promoted the gene expression of Sox9, ACAN and Col II in the CEP area of ex vivo IVDs cultured with TNF- $\alpha$ .

**Discussion:** The  $\alpha 2M$  was not sufficiently produced to inactivate the higher concentrations of catabolic factor MMP-13 found in the CEP of degenerated discs. Our findings suggest that supplemental  $\alpha 2M$  protects against the progression of IVD degeneration by inhibiting the effects of pro-inflammatory cytokines such as TNF- $\alpha$ .

## RELIABILITY OF A CONTINUOUS SPINAL STIFFNESS MEASURING DEVICE

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### Introduction

Few, if any, objective measures of spine function have been shown to be related to patient-reported symptoms. Recently, we have shown in repeated publications that spinal stiffness obtained by instrumented L3 indentation is positively associated with patient-reported measures of disability (1). Given this novel relation, we anticipate that stiffness measures obtained from locations in addition to L3 might yield valuable clinical information. The goal of this project was to evaluate the reliability of a new device (Vertetrack) having the ability to collect stiffness measures throughout the lumbar spine using a weighted roller then compare these results with published reliability data from the current indentation device (2).

### Methods

Continuous stiffness testing employs a weighted roller that moves uninterrupted over the spine while measuring the resulting spinal deflection along a subject-specific, laser-defined trajectory (Fig 1). A total of 13 asymptomatic participants (7 female and 6 male) were recruited and data collected from S1 to T12. Each subject was assessed in 2 sessions occurring 1 to 4 days apart. Each session consisted of 3 trials each of 15N as a baseline load and then three trials of a maximally tolerable load (~70N) as defined from pre-test familiarization trials. Intraclass correlation coefficients (ICC) with 95% confidence intervals were computed.

### Results

Overall, the within and between-day reliability of lumbar spine stiffness measures was excellent (0.99) and good to excellent (0.89-0.99), respectively (3). Specifically, the between-day ICCs of spinal stiffness measurements for the minimum load (15N) from L5 to L1 were as following: 0.89, 0.94, 0.95, 0.98, and 0.89. The between-day ICCs for the maximum tolerable load were 0.97, 0.98, 0.96, 0.91, and 0.99, respectively.

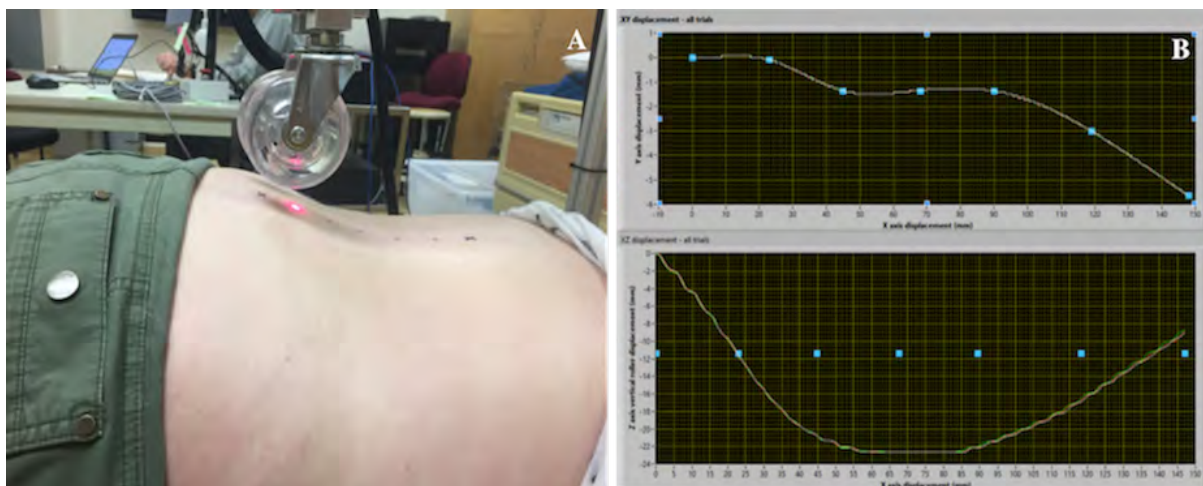
### Discussion

Vertetrack is the first device to collect stiffness data continuously throughout the lumbar spine. The within-day reliability values are similar to those of the current indentation device (2), however, between-day reliability estimates at L3 (0.95 and 0.96) are lower than those reported from the current indentation device (0.98) (2) although the significance of this difference is unknown. Further investigation is needed to determine if similarities and differences in the rolling device versus the indentation device have clinical meaning.

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**Figure 1** Spinal stiffness (A) and output (B): The top graph displays the XY trajectory and the bottom graph the vertical Z axis displacement of the roller. Blue points represent spinous process locations (S1 to T12).



## Midterm clinical results of temporary short-segment fixation without augmentation for thoracolumbar burst fractures

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### [Introduction]

Short-segment posterior instrumentation for thoracolumbar burst fractures provides superior correction of kyphosis by indirect reduction technique, but a high failure rate had been frequently reported in 1990's. We have reported the clinical results of temporary short-segment fixation without augmentation. In the report, fractured vertebra was well reduced and maintained regardless of load-sharing score during the period. Meanwhile, correction loss was observed at adjacent disc level mainly after implant removal. However, midterm results with these patients are not clear. The aim of this study is to investigate midterm clinical results of temporary short-segment fixation.

### [Methods]

Subjects comprised 35 patients with thoracolumbar burst fracture (T11-L2) who underwent surgery by ligamentotaxis procedure using Schanz screws without augmentation between 2006 and 2012 in our institution. Of these 35 patients, 12 patients who had been followed at least 5 years were included in the study. There were 8 males and 4 females and their mean age at surgery was 41.2 years (range 20-66). Implants were removed approximately 1 year after surgery after confirming union of the fracture. Mean follow up period was 7.1 years (range 5-9). We have measured local vertebral body angle (VBA) and kyphotic angle (KA), which was measured between the superior endplate of the intact vertebra cephalad to the fracture and the inferior endplate of the intact vertebra caudad to the fracture before surgery, just after surgery, approximately 1 year after initial surgery, around 2 months after implant removal, 1 year after removal, and at the final follow-up examination in lateral roentgenograms at standing position except before surgery. In addition, range of motion (ROM) at KA was measured by lateral dynamic roentgenograms at the final follow-up examination. Fracture severity and back pain were also evaluated according to load-sharing classification and Denis pain scale, respectively.

### [Results]

The mean load-sharing score was 7.4 points. VBA was corrected 9.9° after initial surgery and the maintenance of the reduced vertebra was successful during the follow-up period. Therefore, we had no patients with instrumentation failure by vertebral collapse. In contrast, KA was corrected 11° after initial surgery and 10° loss of correction was observed only two months after implant removal. However, no deterioration in KA was found after that. Although segment of motion was preserved (mean ROM at KA: 6.7°), 7 patients (58%) had fusion with cranial adjacent intact vertebra and their ROM at KA was restricted. Three patients had increase of back pain at the final follow-up examination, but none had back pain deterioration because of implant removal.

### [Conclusion]

Kyphosis recurrence was observed at disc adjacent to the injured vertebra in the early period after implant removal in temporary short-segment fixation for thoracolumbar burst fractures. However, the kyphotic change didn't progress further after that and caused no deterioration of back pain. Motion segment was preserved after implant removal, but nearly 60% of the patients had fusion with cranial adjacent intact vertebra.

## EVALUATION OF THE PRESENCE AND DISTRIBUTION OF AIR ON ABDOMINAL COMPUTED TOMOGRAPHY AFTER THORACOLUMBAR LIF AND CONVENTIONAL ANTEROLATERAL SURGERIES.

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### Introduction:

Bowel injuries are a rare complication of anterolateral thoracolumbar surgeries. However, there are some reports of bowel injury with lateral interbody fusion (LIF). The authors experienced a case in which the patient complained of abdominal pain after LIF, and a large amount of air was found on abdominal computed tomography (CT). Finally, it was not free air from a bowel injury, but we had difficulty in diagnosing the etiology. The purpose of this study was to evaluate the presence of air on CT after retroperitoneal-approach thoracolumbar surgeries.

### Methods:

From July 2016 to October 2017, ten cases were evaluated retrospectively: LIF, n=7; conventional anterolateral surgeries (ABF), n=4; and LIF+ABF, n=1. The patients were seven females and four males, The average age was 72.2 years old (range 45-82). From 2 to 7 days postoperatively, the presence and distribution of air on abdominal CT, the presence of surgical drains, and the difference by approach were evaluated.

### Results:

Air was found in the retroperitoneal cavity on the approach side in all cases. In 6 of 8 LIF cases, air existed on the contralateral side: 2 of the 8 cases were without drains. In four cases with conventional anterolateral surgery, the air was only in approach side.

### Discussion:

Bowel perforation is a serious, life-threatening complication and recognizing acute abdominal symptoms quickly is important in avoiding a cascade of negative events. A CT scan should be performed to assess for the presence of air in a suspected intestinal lesion postoperatively.

In this study, the air existed on the contralateral side only in the LIF cases. The reason might be LIF needs smaller incision than conventional surgeries, and air might spread when we released contralateral annulus fibrosis.

There were some reports that the peritoneal irritation symptoms are not so severe when the perforation happened in descending colon because it is located in retroperitoneal space. Spine surgeons who perform LIF surgeries should be familiar with those findings.

The authors declare that there is no conflict of interest regarding the publication of this article.





## **PATHOLOGY AND ANATOMICAL FEATURES OF LUMBAR DISCAL CYST TO IMPROVE THE SUCCESS OF SURGERY**

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**INTRODUCTION:** A lumbar discal cyst (LDC) is a relatively rare disease that communicates with the intervertebral disc and can cause radicular symptoms. Although LDC formation is likely related to disc lesions, the pathogenesis and the optimum management are not well understood. The purpose of this study was to clarify the anatomical features of a LDC to improve the success of surgery based on our microsurgical experience and a review of the literature on LDC and the anatomy of the anterior extradural space.

**METHODS:** The LDC diagnosis was based on MRI findings of cystic lesions with almost homogenous T1 low and T2 high signal intensity adjacent to the intervertebral disc. This study included 13 cases that underwent microsurgery. Three cases were reoperation, one had the initial surgery at another hospital and the others at our institution. The average age at surgery was 44 years; there were nine men and four women. One case involved L1/2, four cases L3/4, two cases L4/5, and six cases L5/S. Histological examination was performed in five cases.

**RESULTS:** The LDC content was xanthochromatic in six cases and light bloody or bloody in seven cases. Discectomy was performed in seven cases. The LDC was continuous with the disc in all cases, and involved the surrounding venous plexus and small vessels in five cases. In two cases with a brownish LDC, aspiration reduced the size before resection, but both cysts began to expand gradually right after. In an early reoperation case, the location of the LDC changed from the lateral side of the affected nerve root initially to the medial side at the reoperation. In another reoperation case, firm adhesion between the dura and LDC resulted in incomplete resection. Histologically, the LDC wall consisted mainly of collagen fibers with granulation tissue. Fibrocartilaginous tissues were observed in three cases and several small arteries in and around the wall in one case.

**DISCUSSION:** In the development of a LDC, mechanical stress to the intervertebral disc damages the outer annulus with or without disc herniation. This can also damage the peridural membrane (PM) and the superficial/deep layers of the posterior longitudinal ligament (PLL) because both structures firmly attach to the outer layer of the annulus fibrosus. This causes hemorrhage from the venous plexus or vessels around the PM and PLL, forming an epidural hematoma which can be wrapped with fibrovascular tissues coming from PM, PLL, or other fibrous tissues such as Hofmann's ligament. This process can lead to a LDC irritating and adhered to the nerve root in varying degrees. Thus, during surgery, it is important to observe the following: involvement of the epidural venous plexuses and small arteries, which can act as blood feeders for the LDC; firm adherence to the dural sac and/or the nerve root that can prevent complete resection; daughter cysts around the principal LDC; and recurrences such as disc herniation.

## Impacts of gluteus medius muscle weakness on risk of falling and activities of daily living in patients with lumbar spinal canal stenosis

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**Introduction:** The gluteus medius (GM) muscle, which is mainly dominated by L5 nerve root, has an important role in stabilizing the pelvis during walking. Patients with lumbar spinal canal stenosis (LSS) sometimes exhibit Trendelenburg's sign with GM weakness. However, there is no clinical report about the impact of GM weakness on the risk of falling and activities of daily living in patients with LSS. This study aimed to clarify the functional mobility and health-related quality of life (HRQOL) of patients with GM weakness caused by LSS.

**Methods:** Clinical data of patients who underwent single-level decompression surgery for LSS were prospectively collected. A total of 143 patients were assessed in this study. The decompression level was L3/4 in 18 patients, L4/5 in 93, and L5/S1 in 32. The muscle strengths of GM and iliopsoas were quantitatively measured using a hand-held dynamometer. Two functional mobility tests, including timed up and go (TUG) and two-step tests, were used to evaluate the risk of falling. JOABPEQ, RDQ, ODI, and SF-36 were used to assess HRQOL. Patients with GM strength of  $\leq 10\%$  were assigned to the poor group (P group), and an equal number of age- and sex-matched subjects were assigned to the normal group (N group). Differences between the groups were analyzed using the Student's t-test and Mann-Whitney U-test ( $*p < 0.05$ ).

**Results:** There were 14 (9.7%) patients (9 men, 5 women) in the P group, of which 2 were diagnosed with canal stenosis at L3/4, 8 at L4/5, and 4 with extraforaminal stenosis at L5/S1, suggesting that GM weakness was mainly caused due to an L5 nerve root disorder (12 patients, 85.7%). The quantitative muscle strengths of the iliopsoas as well as GM were significantly lower in the P group ( $2.2 \pm 1.1$  Nm/kg) than in the N group ( $4.0 \pm 2.3$  Nm/kg) ( $p = 0.02$ ). There were no significant differences in the two-step test scores between the groups ( $0.98 \pm 0.2$  in P vs.  $1.18 \pm 0.3$  in N,  $p = 0.06$ ), whereas the TUG test score was significantly higher in the P group ( $12.3 \pm 2.4$  s) than that in the N group ( $9.6 \pm 3.0$  s) ( $p = 0.04$ ). The JOABPEQ scores for lumbar function, walking ability, and social life function were significantly lower in the P group than those in the N group ( $p < 0.05$ ). The RDQ score was significantly higher in the P group than that in the N group ( $p = 0.03$ ). The SF-36 scores for physical functioning, role physical, and bodily pain were lower in the P group than those in the N group ( $p < 0.03$ ).

**Discussion:** This is the first study to evaluate the functional mobility and HRQOL of patients with LSS with GM weakness. Because the TUG scores reflect the risk of falling, our results suggested that GM weakness worsens the risk of falling as well as the activities of daily living in patients with LSS. Therefore, LSS patients with L5 nerve root disorder should be carefully managed to prevent falling.

## A multidisciplinary approach to the treatment of metastatic spinal tumors

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**Introduction:** The recent progress of anti-cancer drugs has improved the treatment outcomes of patients. However, variation in the clinical presentation and response to cancer treatment complicates the management of metastatic spine tumors. A multidisciplinary approach to facilitate the early diagnosis and treatment, management of various symptoms and rehabilitation to maintain patients' activities of daily living (ADL) or quality of life (QOL) is therefore needed.

**Aim:** We investigated the usefulness of a multidisciplinary approach to the treatment of metastatic spinal tumors.

**Methods:** We adopted a multidisciplinary approach to facilitate diagnostic-therapeutic health care programs for patients with bone metastases in August 2016. First, radiologists identified newly diagnosed patients by imaging analyses and reported them to orthopedists. Radiologists predicted patients with metastatic spinal tumors at a high risk of skeletal-related events (SREs) and suggested they receive orthopedic consultation via digital clinical records. Orthopedists created a database of metastatic tumors and recommended the use of bone-modifying agents (BMAs) and the regular follow-up with imaging analyses for patients at a high risk of SREs on their digital medical record. Regarding the management, orthopedists optimized the rehabilitation plan by prescribing a surgical corset or giving advice on physical activities to reduce weight-bearing for the spine. Twenty-two patients underwent spine surgery for metastatic spine tumor from January 2015 to January 2017 at our institute. Fifteen were treated without the multidisciplinary approach from January 2015 to July 2016 (Group 1), and seven were treated with the multidisciplinary approach from August 2016 to July 2017 (Group 2). We investigated the status of paralysis at the operation using the modified Frankel classification and confirmed the number of emergency operations.

**Results:** Under the modified Frankel classification, the Group 1 included one grade A patient, one grade B patient and three grade C1 patients at operation. Only one patient underwent surgery before showing neurological symptoms. Two patients underwent emergency operations. All patients in the Group 2 had a grade of C2 or better. Three patients underwent surgery before showing neurological symptoms. There were no emergency operations.

**Discussion:** The number of patients with metastatic spine tumors increased due to improvements in the treatment outcome with the development of effective anti-cancer drugs. These tumors cause SREs such as bone fracture or spinal cord compression, which can compromise patients' ADL and QOL. Previous studies have reported that a multidisciplinary approach to the treatment of metastatic spinal tumors decreased the rate of SREs and the number of emergency operations. In our hospital, with the application of a multidisciplinary approach, all patients underwent surgery before showing severe neurological symptoms, and there were no emergency operations. Although, this study has several limitations, such as the heterogeneity and small size of our population and the short follow-up interval, this approach facilitates the early detection and treatment to prevent SREs. Bone metastasis and the treatment of SREs by promoting increased cooperation with more clinical departments play an important role in the future management of patients with cancer.

## Retrospective review of short to mid-term outcome in oblique lateral lumbar fusion (OLIF51) surgery

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**Introduction:** Oblique lateral interbody fusion (OLIF) restores disc height and enables indirect decompression of narrowed spinal canals in patients with the lumbar disease such as spondylolisthesis causing decreased disc height and foraminal narrowing via oblique lateral corridor in front of the psoas muscle. Recently the concept of the technique is applied to the lumbosacral junction, which is based on the concept of traditional anterior lumbar interbody fusion (ALIF) using specially-designed retractors to achieve effective indirect foraminal decompression and lumbosacral lordosis as well as a better clinical outcome. The present study aimed to evaluate the short to mid-term clinical and radiological outcomes of this OLIF51 surgery.

**Methods:** We retrospectively enrolled 15 patients with lower back pain and radicular leg pain due to L5-S1 foraminal stenosis who underwent OLIF51 surgery (ave. 64.2 yo, 7 males, 8 females). The control subjects were those who were case-matched cases who underwent traditional posterior L5-S1 TLIF surgery. The OLIF51 surgery was performed via a 7-cm length incision in the left anterolateral abdominal wall in the complete decubitus position, and 6° lordotic titanium cage was inserted and fused through the bifurcation of great vessels followed by posterior percutaneous pedicle screw fixation with indirect decompression in the prone position. Perioperative data such as operative time and blood loss were investigated. Postoperative outcomes were also evaluated by using the Japanese Orthopaedic Association (JOA) score at baseline, just after, 3, 6, and 12 months. Radiological evaluation using the computed tomography (CT) scan was performed to measure and evaluate the section area of the L5-S1 foramen at the sagittal plane as well as L5-S1 lordotic angle in OLIF51 group subjects. A P value < 0.05 was considered as statistically significant.

**Results:** OLIF51 patients showed significantly shorter operative time in practical operative duration (excluding the preparation time of position change from decubitus to prone) compared with the traditional TLIF patients (162 min vs. 198 min), and significantly less intraoperative blood loss (65g vs. 257g). The height of Intervertebral cage used for the lumbosacral junction was 10.8mm in average. Acquired lumbosacral lordosis was 4.2° just after the surgery, with correction loss of 1.2° at final observation. Recovery of the foraminal area was increased by 41.1% just after the surgery, with a significant gradual decrease of 37.2% 6 months, then 35.1% at the final observation. JOA score showed significant improvement just after the surgery and the improvement remained until the final observation. Compared with the TLIF group the improvement was significantly better after the surgery. One of the OLIF51 cases showed increased postoperative leg pain due to severe L5 spondylolytic spondylosis. There were no operation-related complications.

**Discussion and Conclusion:** OLIF51 surgery provided considerable outcome as traditional TLIF surgery with significantly improved outcomes. Acquired recovery of foraminal stenosis showed clinical improvement, while lumbosacral lordotic angle showed slight correction loss. The mini-open OLIF51 surgery can efficiently and less invasively expose the lumbosacral IVD to achieve efficient L5-S1 ALIF.

## **BONY HEALING RATE OF STRESS FRACTURE OCCURRED IN DISCONTINUOUS LAMINA DUE TO PARS DEFECT OR SPINA BIFIDA OCCULTA**

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### **INTRODUCTION**

Lumbar spondylolysis (LS) has been considered as a stress fracture of the pars interarticularis. In virtue of advancement of diagnostic tools including MRI or CT scan and therapeutics, outcomes of the conservative treatment have been dramatically improved. Several factors affecting the bony healing have been identified. Sairyō et al. reported unilateral pars defect could be at risk of stress fracture at the contralateral pedicle as well as pars interarticularis. Also, there have been several reports on the association with spina bifida occulta (SBO). The purpose of this study was to investigate outcomes of the current conservative treatment for patients with stress fracture occurred in discontinuous lamina due to pars defect at the contralateral side or spina bifida occulta (SBO), and analyze how much they impact upon the bony healing.

### **METHODS**

From the database of all 103 consecutive pediatric patients (83 boys and 20 girls) with LS in a single outpatient clinic from January 2012 to September 2017, medical records of the patients with stress fracture of the pars interarticularis at the first presentation, accompanied with terminal-stage LS at the contralateral side or SBO at the affected lamina were retrospectively analyzed.

### **RESULTS AND DISCUSSION**

There were 12 (11 male and 1 female) patients who was diagnosed with stress fracture of the pars interarticularis at the first presentation, accompanied with terminal-stage LS at the contralateral side or SBO at the affected lamina. Mean age was 12.3 (range: 8-16) years old. All stress fractures were occurred at L5 except one case at L4. In those 12 patients, there were six patients with terminal-stage LS, five patients with SBO, and one patient with both of them.

#### ***Patients with terminal-stage spondylolysis at the contralateral side***

Among the six patients, two with early-stage LS, three with progressive-stage LS, and one with pedicle fracture were identified. One of the two patients with early-stage LS attained bony healing (50%), while no patient in the three patients with progressive-stage LS attained (0%). A patient with the pedicle fracture attained bony healing.

#### ***Patients with spina bifida occulta at the affected lamina***

Among five patients, there were two patients with early-stage LS, three with progressive-stage LS. Bony healing rate was 100% in the two patients with early-stage LS, and 66.7% in the three patients with progressive-stage LS.

#### ***Patient with both defects***

One patient with progressive-stage LS with both of terminal-stage LS at the contralateral side and SBO at the affected lamina attained bony healing.

### **CONCLUSIONS**

Terminal-stage LS at the contralateral side is still unfavorable factor for bony healing though bony healing rate has been improved.

## Endoscopy-assisted tubular surgery improves the QOL in the patients with lumbar herniated nucleus pulposus; An analysis using JOA Back Pain Evaluation Questionnaire (JOABPEQ)

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**INTRODUCTION:** Microendoscopic discectomy (MED) is a minimally invasive decompressive surgical technique using tubular retractor and spinal endoscopy for patients with lumbar herniated nucleus pulposus through unilateral paramedian approach. Although its advantage over conventional open discectomy has been reported in the literature, few studies were published in terms of the superiority on disease-specific QOL measure. The purpose of the current study was to evaluate the clinical results of the MED by using an established patient-oriented QOL scoring system, Japanese Orthopaedic Association Back Pain Evaluation Questionnaire (JOABPEQ).

**SUBJECTS AND METHODS:** This study was a retrospective review of prospectively collected surgical data. There were 41 patients with lumbar herniated nucleus pulposus treated by the MED from July 2015 through June 2016. Among them, 31 patients with a minimum of 1-year follow-up were evaluated. There were 18 males and 13 females with a mean age of 51.6 years. The indications for the surgery were persistent neurological symptoms and failure of conservative treatment over 1 month. The patients with mechanical back pain, more than grade 2 spondylolisthesis, radiographic findings of instability, and revision cases were excluded. The following symptoms were evaluated using visual analogue pain scale (VAS) and Japanese Orthopaedic Association (JOA) scoring system; back pain, buttock and lower limb pain, numbness of buttocks and lower limb. The QOL was evaluated with the disease-specific QOL measure, JOABPEQ. BSPOP (Brief Scale for evaluation of Psychiatric Problems in Orthopaedic Patients) is also utilized to evaluate psychiatric problems in the subjects. The evaluation was performed preoperatively, 3months and 1 year postoperatively. Statistical analysis was performed by using Student's t-test and step wise multiple regression analysis. Values of  $p < 0.05$  were considered statistically significant.

**RESULTS:** There were no serious postoperative complications. No instability occurred at the operated segment as evaluated with dynamic lateral radiographs at the final follow-up. All scores in VAS and JOA evaluation at 1-year follow-up significantly improved compared with those before surgery ( $p < 0.001$ ). In the JOABPEQ, low back pain, lumbar function, walking ability, and social life function improved 87.5%, 79.2%, 87.5%, and 91.7%, respectively. However, the improvement of mental health was low in 29.2%. Step wise multiple regression analysis showed that the low rate of improvement in mental health was independently correlated with BMI (odds ratio 0.58; 95%CI, 0.34-0.987;  $P=0.044$ ), preoperative BS-POP (odds ratio 2.03; 95%CI, 1.05-3.92;  $p=0.034$ ) and BS-POP postop. 3month (odds ratio 0.49; 95%CI, 0.27-0.84,  $P=0.015$ ).

**DISCUSSION:** The current study demonstrated that the MED for lumbar herniated nucleus pulposus is a safe and effective surgical technique to improve the disease-specific QOL such as the JOABPEQ. Mental health remained low even after the surgery. It was affected by the BMI and the psychiatric factors. Management for those issues should be needed to obtain the better surgical results in the domain of mental health.

## PERIOPERATIVE ADVERSE EVENTS IN SPINE, HIP, AND KNEE SURGERY: IMPACT ON HOSPITAL COST AND LENGTH OF STAY

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### Purpose

Reducing the perioperative adverse event (AE) rate is a key goal for improving quality of care and reducing health system costs. Our objective was to use the OrthoSAVES (Orthopaedic Surgical Adverse Event Severity) reporting tool to estimate the impact of AEs on hospital case cost and length of stay (LOS) in patients undergoing spine, hip, or knee procedures.

### Method

Prospective cohort study following consecutive orthopaedic/spine surgeries at an academic hospital (2011-2012). 2,654 inpatient cases were included: 693 spine, 956 hip, and 1,005 knee procedures. The OrthoSAVES tool was used to record perioperative AEs. Patient and surgery details were collected via chart review. Hospital costs for each admission were obtained from the hospital's financial department. Costs were adjusted to 2016 equivalent values. Propensity score methodology was used to assess the independent impact of adverse events on cost and length of stay. Multiple logistic regression stratified by operative site and sex was used to estimate each patient's propensity of having an AE, with consideration of: age, obesity, comorbidities, diagnosis type, primary vs. revision surgery, American Society of Anesthesiologists (ASA) score, and site-specific tertile of operating time. Each AE case was matched to two non-AE controls on site, sex, and propensity score.

### Results

The sample was 55% female and had average age 64. The majority of cases had a degenerative diagnosis type (72%). Most patients had a preoperative ASA score of two (43%) or three (50%).

785 patients (30%) suffered at least one AE: 33% of spine, 31% of hip, and 26% of knee cases. 3% of patients had any intraoperative AEs and 28% had any postoperative AEs. The most common postoperative AEs were urinary retention (11% of cases), urinary tract infection (3%), and delirium (2%). 19% of AE cases had one or more major AEs (grade three or higher out of six).

The propensity-matched analysis showed that AEs accounted for significant increases in both hospital cost and LOS: a mean of \$8,391 increase in cost (95% CI: 5470,11312) and 3.8-day increase in LOS (95% CI: 2.8,4.9) per individual experiencing an AE. This corresponded to a cumulative \$6,586,951 (14% of total cohort cost) and 3,014 bed-days (17% of all bed-days) attributable to AEs overall. AE severity also affected hospital impact, with major AEs accounting for cost/LOS increases of \$30,102/10.7 days versus \$3,763/2.4 days for minor AEs. Cumulatively, major AEs accounted for 10% of costs and 9% of bed-days; minor AEs accounted for 5% of costs but also 9% of bed-days.

Estimates varied substantially by site: among spine cases, AEs accounted for increases of \$19,560 in case cost and 7.1 days in length of stay, versus \$6,216/3.9 days in hip and \$2,103/1.3 days in knee cases.

### Discussion

Adverse events in spine, hip, and knee surgery have a significant impact on hospital resources, and their impact is larger among spine cases compared to hip and knee procedures. Changes in clinical practice to mitigate perioperative AEs may lead to significant savings to the healthcare system, while also improving quality of care and patient outcomes.

## Impact of Bicortical Purchase on Biomechanical Strength of Pedicle Screw Placement in the Thoracolumbar Spine for Adult Spinal Deformity Surgery

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**Introduction :** Although pedicle screw fixation has been one of the standard methods of instrumentation for the thoracolumbar spine, it is difficult to obtain rigid fixation especially in elderly patients owing to poor bone quality. Multiple studies have shown construct failure, which might lead to pseudoarthrosis and/or loss of deformity correction. Previous studies have reported the biomechanical advantages of bicortical over unicortical sacral pedicle screws. Thus, the present study evaluated the efficacy of a modification of the pedicle screw placement technique with bicortical purchase in the thoracolumbar spine, using insertional torque.

**Methods:** Pedicle screw placement in the thoracolumbar spine was modified with bicortical purchase under O-arm navigation in 15 patients (2 male and 13 female patients) with a mean age of 69.6 years (range, 57–79 years) who underwent posterior spinal fusion for the treatment of spinal deformity. Insertional torque was measured when the screw tip was at the midpoint and at the anterior cortex of the vertebrae. Computed tomography was performed to evaluate whether the screw penetrated or touched the anterior wall of the vertebral body and to assess the relationship between the screw tip and aorta.

**Results:** A total of 163 screws were examined, and 93 screws penetrated or touched the anterior wall of the vertebral body. The insertional torque of the 93 screws was significantly higher at the anterior cortex than at the midpoint ( $216.9 \pm 93.6$  vs.  $107.9 \pm 65.6$  inch-pounds;  $p < 0.001$ ). Additionally, 110 screws (94.8% ) did not touch the aorta and 6 screws (5.2%) touched the aorta; however, there was no deviation of the aorta or pseudoaneurysm . Additionally, no fatal event occurred.

**Discussion :** In thoracolumbar pedicle screw fixation, bicortical pedicle screw fixation provided double the biomechanical strength of conventional methods and prevented vascular injury. This method can decrease the rate of pseudoarthrosis and/or loss of deformity correction and might become an effective surgical technique for elderly patients with adult spinal deformity.



## THE INTRA-DISCAL VACUUM PHENOMENON DEVELOPED AFTER THORACOLUMBAR FRACTURES. ; THE NATURAL HISTORY AND RISK FACTORS

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### Introduction

Intra-discal vacuum (DV) is a frequently observed phenomenon in the degenerated intervertebral disc, although the etiology and clinical relevance have not been elucidated yet. DV is also found after vertebral fracture, especially in osteoporotic vertebrae. However, few attentions have been paid to the DV after traumatic thoracolumbar fracture in contrast to the intra-vertebral vacuum phenomenon. The aim of this study is to investigate the natural history of DV and its relevant factors in thoracolumbar fracture.

### Methods

We retrospectively reviewed 30 patients who had been treated successfully for thoracolumbar fracture with posterior instrumentation and fusion and underwent the implant removal surgery. Using computed tomography (CT) at the time of injury, 3-month follow-up, and just before the removal surgery (Mean: 20.7±12.2 months from the injury), the occurrence and disappearance of DV adjacent to the fractured vertebra were examined. DV was defined as the same Hounsfield unit to air within the disc space on CT image. On magnetic resonance images at injury and just before the removal surgery, endplate defect and disc degeneration were evaluated using the total endplate defect score (TEPS) and Pfirrmann grade, respectively. The relationship between DV and endplate defect was analyzed using Mantel-Haenszel Chi-square test.

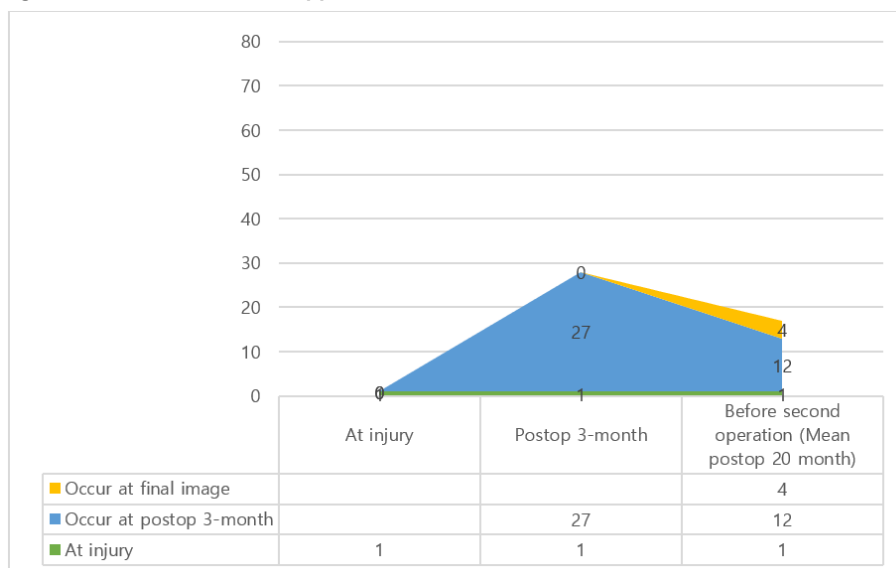
### Results

Mean age of patients was 38.3±14.4 years. Male was dominant (n=23). Eighty-two disc levels adjacent to fractured vertebra were reviewed. There were 67 (81.7%) grade II discs, 14 (17.1%) grade III discs, and 1 (1.2%) grade IV disc at injury. Twenty-six pairs of endplates (31.7%) had equal or greater than 6 TEPS at injury. DV was found in only 1 (1.2%) disc at the time of injury, which increased to 28 (34.2%) discs at 3-month follow-up. Of these, 15 (53.6%) DVs disappeared and 4 (4.9%) DVs developed newly at the time of implant removal surgery. The occurrence of DV was related with the disc degeneration (P=0.015) and total endplate defect score (P<0.001) at the time of injury. Prevalence of DV at final follow-up was related with baseline and final upper endplate defect score (P=0.034 and 0.047). There was no relationship between DV and clinical factors such as sex, age, and follow-up length.

### Discussion

About 40% of disc adjacent to fractured vertebra were combined with DV at 3-month after thoracolumbar fracture. Among them, the half of DV disappeared at mean 20-month follow-up in the circumstance of instrumentation and fusion. In short term, DV occurrence was related with baseline disc degeneration and total endplate defect score. In long term, DV occurrence was only related with the status of adjacent end plate defect. In short, the occurrence of DV was very frequent in the course of fracture healing in surgically treated thoracolumbar fracture and half of it disappeared. DV occurrence was related with disc degeneration and endplate defect at injury.

Figure 1. Occurrence and disappearance of intradiscal vacuum



## Muscular Energy Expenditure during Dynamic Balance Test in Adult Degenerative Scoliosis Patients Compared to Controls

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**Introduction:** Balance is defined as the ability of the human body to maintain its center of mass within the base of support with minimal postural sway. Maintenance of balance requires coordination between the sensorineural and musculoskeletal systems. Adult degenerative scoliosis (ADS) patients exhibit a variety of postural changes, involving the spine, pelvis and lower extremities, in their effort to compensate for the altered posture. The way those patients compensates for truncal imbalance may be variable and may depend on other constitutional factors such as age, neuromuscular condition, and BMI. In general though, the brain, through the righting reflex, will sacrifice focal alignment to optimize global balance within Dubousset's "Cone of Economy". The purpose of this study was to compare spine and lower extremity neuromuscular activity in patients with ADS prior to surgical intervention, to non-scoliotic controls, during a functional balance test.

**Outcome Measures:** Spine and lower extremity integrated electromyography (iEMG). iEMG activity is a graphic representation of the sum total EMG activity over a defined period of time.

**Methods:** Twenty-nine patients with symptomatic ADS who have been deemed appropriate surgical candidates were compared to 16 non-scoliotic controls. Each patient performed a series of functional balance tests. The functional balance test was similar to a Romberg's test in which the patients are required to stand erect with feet together and eyes opened in their self-perceived balanced and natural position for a full minute. Surface EMG electrodes were placed on the skin overlying the External Oblique (EO), Multifidus (Mf) at the level of L<sub>5</sub>, Erector Spinae (ES) at the level of L<sub>1</sub>, Gluteus Maximus (GM), Rectus Femoris (RF), Semitendinosus (ST), Tibialis Anterior (TA), and Medial Gastrocnemius (MG). One-way ANOVA analysis was used to determine differences on neuromuscular control in balance in ADS patients compared to non-scoliotic controls.

**Results:** We found that these ADS patients expended statistically significantly more muscle activity to maintain static standing, as manifest by increased muscle activity in their ES (ADS: 29.29 mV vs. H: 14.41 mV;  $p=0.010$ ), GM (ADS: 18.36 mV vs. H: 10.37 mV;  $p=0.041$ ), ST (ADS: 29.58 mV vs. H: 16.02 mV;  $p=0.050$ ), and TA (ADS: 32.50 mV vs. H: 14.49 mV;  $p=0.048$ ) muscles during one minute standing in comparison to non-scoliotic controls. Although they were not statistically significant, there was a trend toward greater muscle activity in the rest of the tested muscles. With higher values integrated EMG, ADS patients seem to expend more energy during a simple standing task.

**Conclusions:** ADS patients expend more energy during a simple standing task in an effort to maintain balance when compared to healthy controls. This study quantifies the energy expenditure as reflected by muscle activity during a simple standing task. We observed that ADS patients exhibit more muscle activity particularly in the ES, GM, ST, and TA muscles, and thus expend more energy to maintain static standing or balance. This may be due to the abnormal spine curve structure and or to asymmetry in neuromuscular control, compounded by the biomechanical forces associated with progressive sagittal imbalance.

## **SURGICAL PROCEDURES AFFECT CLINICAL OUTCOMES IN PATIENTS WITH SINGLE LEVEL DEGENERATIVE LUMBAR SPONDYLOLISTHESIS – A PROSPECTIVE, MULTICENTER TRIAL**

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**INTRODUCTION:** There was no high evidence if spine fusion is effective in clinical outcomes for degenerative lumbar spondylolisthesis (DLS). The purpose of this prospective multicenter study was to compare clinical and radiological outcomes in patients with DLS treated using different surgical procedures.

**METHODS:** This prospective observational cohort study included 20 institutes. The inclusion criteria were the presence of neurogenic claudication, single-level DLS. The exclusion criteria were previous spine operation, multi-levels lumbar spinal stenosis, osteoporosis, degenerative scoliosis, or psychological disorders. Surgical indication and methods were decided based on each institute's standard practice. A total of 165 cases were registered from 10/2013 to 3/2016. Demographic data including age, gender, body mass index, smoking, bone mineral density, comorbidity, and duration of symptoms before surgery were recorded. The patient-reported outcomes (PROs) including a visual analogue scale (VAS) for low back pain, leg pain, and numbness, Zurich claudication questionnaire (ZCQ) and EuroQol 5 Dimension (EQ-5D) were measured at preoperatively and 3, 6, and 12 months postoperatively. As radiological assessments, slippage, lumbar lordosis, lumbar axis sacral distance, range of motion at each disc level, bony fusion, and disc degeneration were also evaluated. Twelve patients were excluded. Sixteen patients underwent posterior decompression only (D group), and 137 underwent decompression and fusion (DF group). In the DF group, 41, 78, and 18 patients had posterolateral fusion (PLF), lumbar interbody fusion (IF), and another procedure, respectively. Operative time, estimated blood loss (EBL), and complications were recorded. We used propensity score matching to avoid bias related to confounding preoperative variables and compared clinical and radiological outcomes between the D and DF groups and between the PLF and IF groups. A p-value < 0.05 was considered to be significant.

**RESULTS:** The 14 patients in the D and DF groups were matched. Operative time and EBL were significantly lower in the D group than those in the DF group (95.1 vs. 185.6 min, 67.3 vs. 308.6ml, P<0.05). At 3 months postoperatively, only VAS for leg numbness and ZCQ Physical function scale had improved significantly in the DF group, compared with the D group (11.8 vs. 34.5 mm, 6.9 vs. 9.6, p<0.05). At 6 and 12 months, PROs did not differ between the groups. The 28 patients in the PLF and IF groups were matched using the propensity score. The operative time, EBL, complications and PROs at 3 months did not differ between the PLF and IF groups. The VAS for low back pain, EQ-5D score, and ZCQ patient satisfaction with treatment at 6 and 12 months were better in the IF group than in the PLF group (P<0.05). Radiological outcomes did not differ between the PLF and IF groups up to 12 months.

**DISCUSSION:** Although the number of patients in each group was small after matching, the results of this prospective multicenter trial suggest that, compared with decompression only, decompression and fusion might improve clinical outcomes such as leg numbness and physical function at 3 months and that IF might result in better clinical outcomes up to 12 months postoperatively than PLF.

## **Povidone-iodine irrigation for prevention Surgical Site Infection following spinal instrumentation.**

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### **Introduction:**

Surgical site infections (SSI) following instrumented fixation of the spine pose major problem to the spinal surgeon, since removal of the implant was usually not recommended due to risk of loss of correction and stability of the spine. In particular, deep SSI after spinal instrumentation were refractory to control infection, while were often required removal of instrumentation. We attempted to reduce SSI following spinal instrumentation, using the povidone-iodine irrigation protocol. The aim of this study was to evaluate the efficacy of this protocol for preventing SSI following instrumented stabilization of the spine.

### **Methods:**

All cases of spinal instrumentation at our institution between October 2011 and September 2017 were retrospectively reviewed. The exclusion criteria were povidone-iodine allergy and prior surgical debridement for infection. The patients were subdivided into those who had received saline irrigation after 90 seconds of 1% povidone-iodine pooling and normal saline irrigation every 1.5 hours (study group) and only routine saline irrigation every 1.5 hours (control group). The study and control groups comprised 102 and 93 patients, respectively. This study compared the rate of SSI with and without the use of povidone-iodine irrigation protocol.

### **Results:**

SSI rates were 0.98% of the study group (1 for 102 patients) and 4.3% of the control group (4 for 93 patients). SSI rates were decreased, although statistically significant different ( $p=0.15$ ). Deep SSI occurred 0 cases in study group and in 3 cases in the control group. Deep SSI rates were significantly reduced in study group ( $p=0.025$ ). Coagulase-negative Staphylococci (CNS) was detected in the study group. A total three bacteria species were detected in the control group. Two cases were by methicillin-sensitive Staphylococcus aureus (MSSA) and one case was methicillin-resistant Staphylococcus aureus (MRSA). No adverse events were occurred in study group.

### **Discussion:**

In this small preliminary study, our findings underscored the clinical benefits of our treatment strategy using the povidone-iodine irrigation protocol. Several limitations of our study must be acknowledged. Firstly, the present study was based on retrospective observational study. Thus, the patient allocation was non-randomized. Secondly, we could not detect the late onset SSI patients. Future prospective randomized controlled series in larger populations with a long term follow-up duration are needed to corroborate these results.

## DEVELOPMENT OF NEURO-MONITORING PEDICLE SCREW: RESULTS OF ELECTRICAL RESISTANCE AND NEUROPHYSIOLOGIC TEST IN PIG MODEL

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**INTRODUCTION** The conventional pedicle screw has a high electrical resistance, which can result in false-negative readings during triggered electromyography (t-EMG). The International Annealed Copper Standard (IACS) percentage is used to measure the electrical conductivity of metal. Most industries make pedicle screws from titanium alloy, which is mostly Ti-6Al-4V and has an IACS percentage of 1.01% (means the 1.01% compared to copper<sup>1)</sup>). This physical property of titanium alloy makes it challenging to find the proper current thresholds for detecting pedicle breaches. We designed two types of neuro-monitoring pedicle screws (Neuro-PS). In this study, we analyzed the electrical properties of these screws, and verified the neurophysiologic results of the screws using a pig animal model.

**METHODS** We designed two types of neuro-monitoring pedicle screws (Neuro-PS, Figure 1). In the type I screw, a gold wire is imbedded in the center of the titanium alloy pedicle screw. In the type II screw, the gold wire was placed in a trench on the surface of the screw. We measured the electrical resistance of the two pedicle screws and a conventional pedicle screw in air and within bone. To verify the electro-physiologic characteristics, we performed a triggered electromyography (t-EMG) test in a pig model.

**RESULTS** The electrical resistances of the type I and II screws were remarkably lower than the conventional pedicle screw in all screw size groups and conditions (air and bone, Figure 2). The type II screw showed lower electrical resistances than Type I screws in all size groups. Furthermore, the type II screw showed an even greater decrease in electrical resistance in bone versus air. In the electro-physiologic test using pig model, only the type II screw, whose external lead directly contacted the neural component, showed a significantly lower stimulation threshold, compared to a conventional pedicle screw.

**DISCUSSION** We proved that our Neuro-PS have lower electrical resistance compared to the conventional pedicle screw in electro-simulation analysis. In the neurophysiologic test, type II screws under the lead-nerve contact condition showed significantly lower mean stimulation thresholds than other screws, including type II screws the under lead-nerve non-contact condition. On the other hand, type II screws under the lead-nerve non-contact condition did not show a significant difference compared to control screws and type I screws. This means that although the electrical resistance of type II screws was remarkably lower than that of control screws, there was no significant difference of stimulation threshold between type II screws and control screws in the t-EMG test when the external gold lead lacked contact with the nerve root. Compared to a conventional pedicle screw, our Neuro-PS demonstrated lower electrical resistances and stimulation thresholds in t-EMG tests. These screws may provide a more accurate t-EMG result during pedicle screw placement.

Figure 1. Manufactured pedicle screws which incorporating a gold wire in the conventional pedicle screw. The gold lead with 0.5 mm diameter is placed at the center of Type I screw (A),(B) and along the surface of Type II screw (C),(D). White arrow indicate the gold lead placed at center of Type I screw.

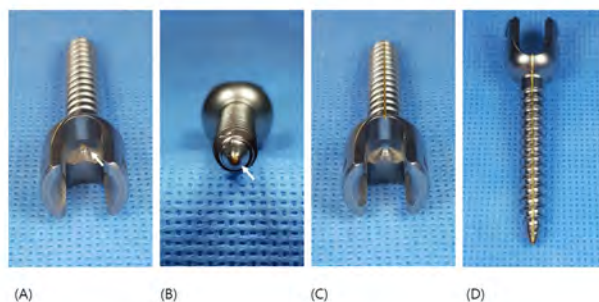
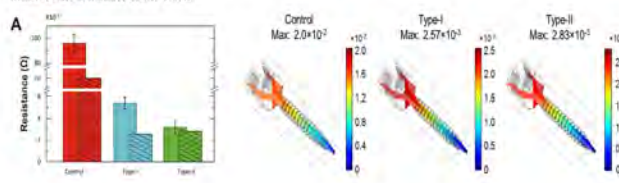


Figure 2. (A) Resistance comparison of the control, type-I, and type-II pedicle screws for the size of  $\phi 6.5-40\text{mm}$  in air condition (The bars without fill pattern). The bars with fill pattern represent the resistance calculated by COMSOL simulation. (B) Simulated voltage distribution across the control, type-I and type-II pedicle screws when a 1A current is applied to one end (head) of gold wire while the other end (tip) is connected to the ground. The maximum voltage indicates the resistance of the screw.



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## SERIAL CHANGES IN DIMENSION AND HARDNESS OF THTRANSVERSUS ABDOMINIS MUSCLE DURING AN ABDOMINAL DRAWING-IN MANEUVER IN HEALTHY SUBJECTS

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**Introduction:** The abdominal drawing-in maneuver (ADIM) is one of the common exercises for low back pain, prescribed to preferentially recruit the transversus abdominis muscle (TrA). The TrA has both anterior and posterior musculo-fascial junctions. Studies showed that performing an ADIM increased TrA thickness, and shifted both anterior and posterior musculo-fascial junction of TrA. But, these changes in dimension at both anterior and posterior junctions have not been measured simultaneously, and only assessed at two points, a resting and a contracted phase. On the other had, the use of strain elastography to assess muscle hardness has been increasing in recent years. Strain elastography assesses muscle hardness by strain ratio that is calculated by comparing strain of a muscle and that of a reference material. The aim of this study was to confirm detailed serial changes in dimension (thickness and length at both anterior and posterior sides) and hardness of the TrA during an ADIM, using two ultra sonographies (strain elastography and usual one).

**Methods:** Seven healthy female subjects (mean age: 33 years old) without a history of low back pain performed an ADIM in a supine hook-lying position. Two transducers were placed on the antero-lateral and postero-lateral side of abdomen to simultaneously record the morphologic changes of the TrA at both sides. During an ADIM, serial images of the two ultra sonographies were captured together, and the thickness and length changes of the TrA were measured frame by frame at a rate of 5 images per second. For assessing hardness of the TrA, the strain ratio between the TrA and an acoustic coupler (elastic modulus 22.6 kPa) placed over the skin was calculated (muscle/coupler) at the anterior side. To determine the relationship among changes in thickness, sliding length and strain ratio of the TrA, the Pearson correlation was calculated in each subject.

**Results:** The relationship among anterior and posterior thickness, anterior and posterior sliding length, and strain ratio of the TrA was summarized in the table below. All subjects demonstrated a significant relationship among dimensional changes in thickness and sliding length of TrA irrespective of the antero-posterior side ( $p < 0.01$ ). There was also significant relationship between strain ratio and dimensional changes of TaA in all subjects ( $p < 0.01$ ).

**Discussion:** During an ADIM, TrA increased in its thickness and decreased in its length, resulting in shifted both anterior and posterior musculo-fascial junctions. These changes were significantly linearly related each other. The results also showed a significant linear relationship between muscle hardness and morphological changes of TrA at all levels of contraction. Further studies are needed in larger sample sizes and to examine whether characteristic contraction patterns exist between individuals with or without low back pain.

	Ant. Thickness	Post. Slide	Post. Thickness	Strain Ratio
Ant. Slide	$r = 0.827 \sim 0.982$	$r = 0.859 \sim 0.951$	$r = 0.868 \sim 0.992$	$r = -0.58 \sim -0.811$
Ant. Thickness		$r = 0.907 \sim 0.969$	$r = 0.922 \sim 0.977$	$r = -0.519 \sim -0.821$
Post. Slide			$r = 0.952 \sim 0.987$	

## CELL POPULATIONS OF THE ADULT NUCLEUS PULPOSUS

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### INTRODUCTION

The nucleus pulposus of the adult human intervertebral disc appears to be comprised of several sub-populations<sup>1</sup> which currently are poorly characterised. How these subpopulations relate to the long-term stability and health of the tissue remains to be determined. Here we aimed to improve characterisation of the cells of the nucleus pulposus through transcriptional analysis.

### METHODS

We used adult bovine discs as a model system, and separated the cells of the nucleus pulposus into two populations in relation to their ability to form clusters. We also isolated cells from the bovine outer annulus fibrosus and bovine articular cartilage. We compared gene expression of these different cell types using microarray analysis.

### RESULTS

We found that, while all cells comprising the 'small chondrocyte-like cell population of the adult nucleus pulposus' were of similar size and morphology, there were distinct differences in gene expression between the relatively small proportion of cluster-forming cells (c. 10% of cells) and those from the single cell population with over 400 genes highly upregulated in the cluster-forming relative to the single-cell populations, but few upregulated in the single cell relative to the clustering cells. We also found that most of the gene markers previously described for distinguishing nucleus pulposus cells from those of articular chondrocytes or annulus pulposus cells, such as the notochordal markers brachury and cytokeratins 8,18,19, were highly expressed by the clustering population relative to the single cell population. Of previously suggested nucleus pulposus markers<sup>2</sup>, only SNAP25 was similarly expressed by both populations whereas FOXF1 was more highly expressed by the single cell population. Nevertheless, a cluster dendrogram and principal components analysis both indicate close biological similarities between all nucleus pulposus cell populations and revealed large biological differences between all nucleus pulposus cells on one hand and articular cartilage and outer annulus cells on the other hand.

### DISCUSSION

Here we identified two cellular subpopulations of the adult bovine nucleus pulposus, differing distinctly in marker gene expression. The functional role of each population is unclear, but markers of the small clustering cell population have been identified even in cells of the elderly human nucleus<sup>2</sup>. Understanding the functional role of the different sub-populations of the nucleus pulposus in disc biology is important for understanding degenerative processes. It is also necessary for defining which cell types should be targeted for appropriate cellular repair of the nucleus pulposus. The large biological differences between nucleus pulposus cell populations and those from articular cartilage and annulus fibrosus, both of mesenchymal origin, suggest that mesenchymal stem cells may not be the optimal cell source for the nucleus pulposus cell populations.

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## TRUNK SWAY RESPONSE TO CONSECUTIVE SLIP PERTURBATIONS BETWEEN SUBJECTS WITH AND WITHOUT LOW BACK PAIN.

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**Introduction:** Trunk sway responses following perturbations are critical to develop adequate prevention strategies. It is unclear how postural responses with a handheld task can validly be transferred to treadmill-induced slip perturbations in subjects with recurrent low back pain (LBP). The purpose of this study was to compare trunk sway angle, velocity, and reaction time following treadmill-induced perturbations while subjects with and without LBP held a tray.

**Methods:** There were 30 subjects with LBP and 50 control subjects who participated in the study. Each participant stood on the treadmill while he/she held a tray to produce a functional task. The consecutive three levels of treadmill-induced slips were introduced at level 1 (duration: 0.10 sec, velocity: 0.24 degree/sec, displacement: 1.20 cm), level 2 (0.12 sec, 0.72 degree/sec, 4.32 cm), and level 3 (0.12 sec, 1.37 degree/sec, 8.22 cm). The reaction time (seconds) was determined as the time between onset of the treadmill motion and recovery after toe-off. The peak trunk angle and velocity were measured following the perturbations as well.

**Results:** The trunk extension angle was significantly different ( $F = 4.22$ ,  $p = 0.04$ ) and demonstrated a significant interaction with groups and levels of perturbation ( $F = 6.83$ ,  $p = 0.01$ ). However, the reaction time was not significantly different based on the levels of perturbation ( $F = 0.43$ ,  $p = 0.51$ ). The LBP group increased trunk extension only at level 1 slip perturbation ( $t = 2.86$ ,  $p = 0.005$ ).

**Discussion:** The increased trunk extension following the first perturbation indicated a delay in adjusting trunk stability in the LBP group. However, there was no group difference following the higher magnitudes of perturbations due to possible motor learning and/or compensatory reactions. The reaction time and trunk sway velocity were not sensitive enough to demonstrate a group difference. These results indicated that the LBP group was able to minimize trunk sway with higher perturbations following the first perturbation.

**Key words:** kinematic; slip; perturbations; low back pain; motor learning.

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## PREVALENCE OF BACK PAIN IN CHINESE: PRELIMINARY DATA FROM THE POPULATION-BASED HANGZHOU LUMBAR SPINE STUDY

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**Introduction:** Little information on back health is available in the developing country of China, even though Chinese constitutes a quarter of world's population. To complement knowledge in this area, we initiated the Hangzhou Lumbar Spine Study, which is a population-based cross-sectional study of adults focusing on spinal phenotypes, lifetime environmental and occupational exposures of interests, and back pain. Here we report the study methodology, measurement reliability, cohort profile and back pain prevalence.

**Methods:** Subjects in the Hangzhou Lumbar Spine Study were randomly selected from a typical community in Hangzhou Eastern China. The study comprises a structured questionnaire, magnetic resonance imaging of the lumbar spine, dual energy X-ray absorptiometry to measure bone mineral density of the spine and hip, and DNA sample analysis. The structured questionnaire was proposed to measure lifetime environmental exposures of interests and other suspected risk factors for lumbar spinal phenotypes, and back pain. Questionnaire data were collected in a face to face interview. To measure back pain, the subject was asked "Do you have low back pain today?", and then "Have you had pain in your lower back in the past 4 weeks?". If yes, the subject was then asked if the pain limited usual activities or changed daily routine for  $\geq 1$  day to exclude minor back pain episodes. Further, the subject was asked "Over the past 12 months, about how often have you experienced low back aches/pains?" to measure back pain over the past 12 months. In addition, lifetime back pain history was assessed as back pain lasting for  $>1$  day. Finally, disabling back pain was assessed by asking "Were you ever unable to work (or do your normal activities) for at least a month due to back pain or back injury?". Response test-retest reliability was evaluated using data from the first 40 subjects who agreed to repeat the interview with the time interval of 1 month.

**Results:** To date, 478 subjects (mean age  $53.4 \pm 14.4$  years, range 20 to 88 years) met inclusion criteria and completed all the examinations. There are 205 men (42.9%) and 273 (57.1%) women. The interview items on demographic characteristics, general lifestyle and health behaviors, occupational history and associated physical demands, and back pain history obtained good to excellent reliability (Kappa=0.60-0.86). In this sample, 74 (15.5%) subjects reported having back pain today, 34 (7.1%) had back pain lasting  $\geq 1$  day over the past 4 weeks, 204 (42.7%) had back pain in the past 12 months, and 162 (33.9%) recalled having had back pain lasting  $\geq 1$  day during their lifetime. Moreover, 8.2% of subjects experienced disabling back pain for  $\geq 1$  month in their lifetime.

**Discussion:** As in many developed countries, back pain is a common health problem in Chinese adults, with approximately a third subjects studied had back pain lasting  $>1$  day in their lifetime. The structured questionnaire developed was reliable. Epidemiological information obtained from the Hangzhou Lumbar Spine Study may serve as a valuable reference for future studies on back health, particularly for mainland Chinese.

### The characteristics of low back pain, muscle mass and bone quality in glucocorticoid-induced osteoporosis patients.

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**BACKGROUND:** We previously reported that, despite recently developed potent medications including teriparatide and denosumab, the efficacy of treatment for glucocorticoid-induced osteoporosis (GIO) is inferior to that for primary osteoporosis. To better understand the characteristics of GIO and to improve treatment of GIO patients, we focused on low back pain (LBP), lean mass, and bone quality. The aim of the current study was to compare GIO patients and patients with primary osteoporosis for LBP, muscle mass, bone mineral density, and bone turnover markers.

**METHODS:** Eighty-six osteoporosis patients (27 men and 59 women) without evidence of new vertebral body fractures were included in the study. Twenty-five subjects with a mean age of 71.3 years were in the GIO group (G group); 61 patients with a mean age of 74.6 years composed the primary osteoporosis group (P group). We reviewed BMD of the lumbar spine (LS), femoral neck (FN), and total hip (TH). We calculated lean muscle mass and limb muscle mass (corrected by the square of height:lean mass index (LMI) and skeletal muscle mass index (SMI)) using the bio-impedance method (TANITA MC - 780A). Bone turnover markers were used to assess bone formation (BAP) and bone resorption (TRACP5b). Bone quality was assessed by evaluating pentosidine, and homocysteine. LBP was evaluated using the Japanese Orthopaedic Association back pain evaluation questionnaire (JOABPEQ). These factors were compared between the two patient groups. Group comparisons for lean mass were made in men and women separately.

**RESULTS:** BAP in the G group (9.7) was significantly lower than that in the P group (13.0). Pentosidine and homocysteine were significantly higher in the G group than in the P group (G group: 0.12, 15.2, P group: 0.06, 10.7, respectively). LMI and SMI in women in the G group (13.7 and 5.8) were significantly lower than those in women of the P group (14.4 and 6.1). There were no significant changes of BMD, LMI or SMI in men between the two osteoporosis groups. The JOABPEQ score in the G group (275) was significantly lower than that in the P group (319), primarily because of the lumbar spine dysfunction score and the psychological disability score.

**DISCUSSION:** GIO patients had poorer bone quality and lower bone formation than patients in the primary osteoporosis group. GIO patients have been reported at high risk for fragility fractures, even though BMD is maintained, as compared with primary osteoporosis patients. Poor bone quality is considered one risk factor for osteoporotic fragility fractures in GIO patients. In addition, GIO patients had low muscle mass and high LBP independent of BMD. The present study was a small cross-sectional study, and we could not identify the relationship between the mechanisms for osteoporosis and the outcomes. However exercise therapy and intervention for LBP might help to improve treatment efficacy in GIO patients.

## HIGH PREVALENCE OF OSTEOPOROTIC VERTEBRAL FRACTURE IN PATIENTS WITH PROXIMAL FEMORAL FRACTURE

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### Introduction

Osteoporosis and associated fragility fractures are one of the most common causes of disability and a major contributor to medical care costs around the world. Proximal femoral fracture is common and one of the most serious fractures because of associated high morbidity and mortality. It is well recognized that a previous fracture increases the risk of subsequent fractures, even after adjusting for bone mineral density. The aim of this study was to determine whether the presence of vertebral fracture predicts subsequent proximal femoral fracture.

### Materials and methods

This study was conducted with 1220 patients consecutively, aged fifty years and older who admitted with proximal femoral fracture and underwent lumbar spine radiographs at our hospital from 2009 to 2017. Two hundred ninety three patients were male, and 927 were female. The mean age was 81 years (50-104 years), and the mean body mass index was 20.5±3.6 kg/m<sup>2</sup>. As for the types of hip fracture, 683 patients had femoral neck fractures, and 537 patients had trochanteric fractures. We evaluated the prevalence of vertebral fracture in lateral lumbar spine radiographs (Th11-L5), and the total number of fractures were calculated. In addition, these findings were compared with data randomly selected from the same number of age and sex- matched control patients almost all of who had low back pain but no previous history of proximal femoral fracture.

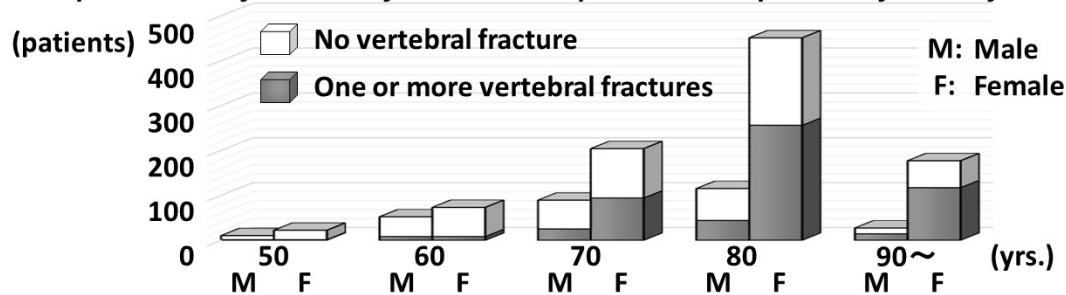
### Results

One or more osteoporotic vertebral fractures were detected in 568 patients with proximal femoral fracture (46.6%; mean age, 84 years), which were more frequent in females (92 males; 31.4%, 476 females; 51.3%). The prevalence of vertebral fracture increased with age in both genders. The incidence of vertebral fracture was significantly higher in the patients with proximal femoral fracture than in the control group (46.6% vs. 33.9%). The mean number of vertebral fractures in the group with proximal femoral fracture (2.02±1.3) was also higher than the value recorded for the control group (1.67±1.0).

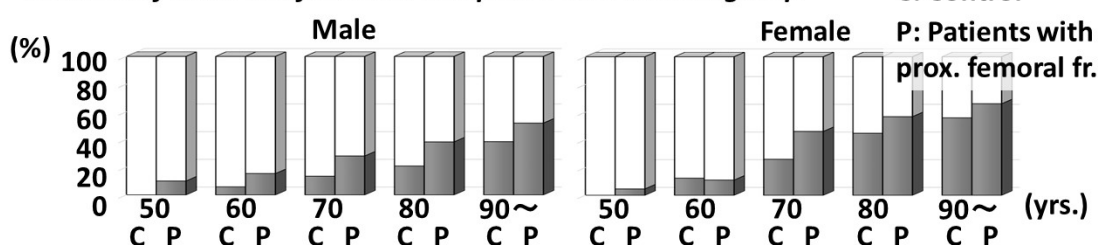
### Conclusion

We found a higher prevalence of osteoporotic vertebral fractures in patients with proximal femoral fracture than age and sex-matched control. These results suggest that a previous osteoporotic vertebral fracture is associated with the risk of a subsequent proximal femoral fracture. The clinical implication is that patients older than 50 years presenting with a vertebral fracture require immediate attention to reduce reversible risk factors of a subsequent fracture.

### •The prevalence of vertebral fracture in the patients with proximal femoral fracture



### •The rate of vertebral fractures compared with control group



## **Spinal cord stimulation therapy improves pain and walking ability, but the improvement in psychological disability according to JOABPEQ score is poor**

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### Introduction:

Spinal cord stimulation therapy (SCS) is a treatment option for severe chronic pain. In recent years, the clinical application has been expanding owing to improvement of the device used. To examine its adaptation and effects, we established the Chiba SCS Working Group in April 2014 and performed SCS therapy led by spinal surgeons.

### Methods:

SCS therapy was performed by our group from April 2014 to December 2016, and a retrospective survey was conducted for all patients who underwent SCS therapy over 6 months before. We evaluated the target disease and changes in visual analogue scale (VAS) and Japanese Orthopedic Association Back Pain Evaluation Questionnaire (JOABPEQ) scores before and after SCS therapy. In addition, we objectively investigated the percentage of landing time in 1 day by using the posture behavior monitoring device of the SCS machine, which was attached to the patient's body.

### Results:

Twenty-four patients underwent SCS therapy. In all the cases, the pain was intense and difficult to control even with strong opioids and the like. Twelve cases had failed back surgery syndrome; 5, lower back pain due to back scoliosis; 3, obstructive arteriosclerosis; 1, below-level pain after cervical spine surgery; 1, inguinal pain due to rheumatoid arthritis; 1, nerve-related pain compressed by the tumor; and 1, donor site pain after bone harvest. The VAS (mm) score (for low back and leg pains) improved significantly after SCS therapy initiation (from 80.6 and 6.63 to 42.8 and 3.82, respectively). In addition, the lying time was slightly decreased from 70.9% to 65.2%, and the hours of non-lying time activity increased. The JOABPEQ score trends for each item were as follows: pain-related disorder, from 26.2 to 38.9; lumbago dysfunction, from 19.7 to 28.6; walking dysfunction; from 14.3 to 27.0; social life disorder, from 24.4 to 22.1; and psychological disorder, from 36.7 to 36.3. The items with significant improvements in scores were pain and walking ability. Psychological disturbances showed little change.

### Discussion:

In this study, SCS therapy significantly improved pain and walking ability. However, it did not improve psychological disorder, suggesting that SCS therapy is not necessarily directly related to patient satisfaction. To obtain further therapeutic effects from SCS therapy, the approach to psychological aspects such as psychotherapy should be actively incorporated.

## Risk predictors of perioperative complications for the palliative surgical treatment of spinal metastasis

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**Introduction:** The aim of palliative surgery for spinal metastasis is to improve quality of life (QOL). Several scoring systems have been reported to guide the indication for the surgery based on the prognosis. The surgical treatment for spinal metastasis is invasive and the complication rate is considerable high. Although major complications impair patient QOL, the risk predictors had not been thoroughly studied. Therefore, the aim of this study was to identify the risk predictors of perioperative complications for the palliative surgery.

**Methods:** Multi-centered retrospective review of 140 consecutive patients with spinal metastasis who underwent palliative surgeries from 2001 to 2016 was performed. We evaluated the type and the incidence of the perioperative complication within 14 days after surgery. Clavien-Dindo classification was used to categorize the perioperative complications and grade 2 or higher were considered as perioperative complications and incorporated in this study. Patients were categorized as either complication group (C) or non-complication group (NC). Age, gender, Charlson Comorbidity Index (CCI), ambulatory, emergency operation, preoperative radiotherapy and chemotherapy, surgical approach, vertebral level of spinal metastasis, estimated blood loss (EBL), and surgical time were recorded. Univariate analysis was used to identify potential predictors of perioperative complications with the Chi-square test and student t-test. P variables less than 0.20 were included in multiple logistic regression.

**Results:** Sixteen patients (11%) experienced one or more complication within 14 days of surgery. The frequent complications were motor weakness (5 patients, 4%), surgical site infection (4 patients, 3%) and postoperative hematoma (3 patients, 2%) in turn. Diabetes (C; 38%, NC; 6%:  $p < 0.01$ ), age over 60 years old (C; 75%, NC; 41%:  $p < 0.05$ ) and metastasis of liver cancer (C; 25%, NC; 6%:  $p < 0.05$ ) were significantly associated with having complications by univariate analysis. EBL (C;  $1.3 \pm 1.3L$ , NC;  $0.7 \pm 0.7L$ :  $p = 0.08$ ), surgical time (C;  $264 \pm 189$  min, NC;  $227 \pm 121$  min:  $p = 0.46$ ), treatment with preoperative radiotherapy (C; 20%, NC; 30%:  $p = 0.32$ ) and chemotherapy (C; 25%, NC; 19%:  $p = 0.33$ ), ambulatory (C; 56%, NC; 49%:  $p = 0.40$ ), emergency operation (C; 44%, NC; 59%:  $p = 0.19$ ), CCI of 2 or more (C; 13%, NC; 11%:  $p = 0.58$ ), gender, surgical approach, and vertebral level of spinal metastasis were not the significant risk predictors of complication. A multivariate logistic regression revealed that diabetes (OR: 5.7, 95%CI: 1.5-22.1), age over 60 years old (OR: 7.4, 95%CI: 1.6-33.3) and metastasis of liver cancer (OR: 6.6, 95%CI: 1.4-30.4) were the significant predictors of perioperative complications.

**Conclusion:** The perioperative complication rate for the palliative surgical treatment was 11%. Diabetes, age over 60 years old, and metastasis of liver cancer were robust predictors of perioperative complications. These predictors should be used to risk-stratify the candidates for the palliative surgery.

## MODIC CHANGES IN THE LUMBAR SPINE ARE COMMON AGING RELATED DEGENERATIVE FINDINGS THAT PARALLEL WITH DISC DEGENERATION

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**INTRODUCTION:** Previous studies reported that the prevalence of Modic changes (MCs) in Hong Kong Chinese was much lower than in other populations. Using a sample of general population, the objectives of the current study were to determine the prevalence and distribution patterns of MCs in the lumbar spine and their associations with disc degeneration in mainland Chinese.

**METHODS:** The study sample consisted of 442 subjects (53.6±14.9 years, range 20-88 years) randomly selected from a typical Chinese community. Lumbar spines were imaged using a 3.0T magnetic resonance scanner. Eleven endplates (L1-S1) in the lumbar spine were evaluated for the presence of MCs using all T1W and T2W sagittal images. If present, MCs were classified into Type I, II, III, or mixed. The T2W sagittal image with the largest MCs was used to acquire area, anteroposterior diameter, and height measurements for MCs. Size of the involved vertebral body was also measured from the mid-sagittal image and taken as a reference. The transverse diameter of MCs was calculated as the percentage of the number of sagittal images presenting MCs to the total number of sagittal MR images (15 images for each lumbar spine). Disc degeneration was graded using a Pfirrmann scale, and rates the degree of disc degeneration into five grades.

**RESULTS:** MCs were present in 209 (47.3%) subjects and 593 (12.2%) endplates. Among these endplates, 84.1% (499) were Type II, 9.1% (54) were Type I, and 6.4% (38) were mixed MCs. Approximately 2/3 MCs were present in the lower lumbar spine and 44.9% of MCs were at the L5/S1 disc level. Most MCs (73.9%) involved both endplates of a disc. Greater age (OR=2.44 for each 10-year increase, P<0.001) and BMI (OR=1.07, P=0.016) were associated with the presence of MCs, as was adjacent disc degeneration (OR=6.00, P<0.001), controlling for age and other covariates. Greater age, BMI and adjacent disc degeneration were also associated with greater MCs size.

**DISCUSSION:** Using a randomly selected sample, epidemiological features and distribution patterns of MCs were characterized in mainland Chinese. MCs were common findings on lumbar spine MR images, with approximately half of the subjects studied having some type of MCs. Type II MCs were most common, and Type III and mixed type MCs were rare. MCs mainly presented in the lower lumbar region, particularly at the L5/S1 disc level, and tended to affect both cranial and caudal endplates of a disc simultaneously. Age and BMI were associated with the presence and size of MCs. In addition, MCs were closely associated with adjacent disc degeneration, with greater size of MCs associated with greater degree of disc degeneration. The study findings suggest that MCs may be aging related degenerative findings in the lumbar spine that parallel to disc degeneration.

### **Percutaneous endoscopic discectomy for lumbar disc herniation in athletes**

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**Introduction:** Percutaneous endoscopic discectomy (PED) has been reported to be less invasive and effective procedure for lumbar disc herniation (LDH). Damage to the back muscle is considered minimal, which is particularly important for athletes. The purpose of this study was to evaluate the clinical outcomes of PED for LDH in athletes.

**Methods:** We retrospectively analyzed 21 patients of LDH in athletes who underwent PED. There were 18 men and 3 women, and the mean age at the time of surgery was 24.9 years (range, 15-43 years). The outcomes were evaluated using visual analogue scale (VAS; 0-100mm) for leg pain and low back pain (LBP), Oswestry Disability Index (ODI), complications and hospital stay. The mean follow-up periods were 3.9 months (range, 1-12 months). Endoscopic surgery was conducted with the patients under local anesthesia. A cannula was placed posterior to the disc through an 8mm skin incision using by the transforaminal approach. Degenerated nucleus pulposus at the site was removed percutaneously. The patients received the athletic rehabilitation immediately after the surgery and sports activity started 6 weeks after the surgery.

**Results:** The mean score of VAS for leg pain before and after the surgery were 64mm and 12mm, respectively. The mean score of VAS for LBP before and after the surgery were 62mm and 11mm, respectively. The mean score of ODI before and after the surgery were 31% and 14.6%, respectively. VAS for leg pain and LBP and ODI significantly improved after the surgery. There were no complications related to the surgery such as root injury, dural tear and infection. The mean hospital stay was 7.7 days. After the post-surgical athletic rehabilitation with a physical trainer or physical therapist, all patients returned to their sports activity.

**Discussion:** PED is a minimally invasive and effective procedure for the patients with LDH, especially in athletes. The patients improved not only sciatica but discogenic low back pain. PED has the benefits of surgery under local anesthesia, preservation of normal posterior structures, less postoperative pain and faster return to sports.

## Morphological changes of the lumbar spine following extreme lateral interbody fusion: three-dimensional computerized tomography evaluation

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**INTRODUCTION:** Extreme Lateral Interbody Fusion (XLIF) is an alternative to traditional posterior lumbar interbody fusion (PLIF). Minimally invasive and with decreased morbidity, the XLIF procedure provides lumbar disc fusions while increasing IVD height and foramen height and size to improve canal and foraminal stenosis by indirect decompression. Two-dimensional analyses of IVD height and foramen measurements after XLIF have been reported. Due to the difficulty of gathering precise 2D measurement, three-dimensional (3D) quantification of pre- and post-operation IVD and foramen measurements provides increased precision for measuring morphological changes. The purpose of this study was to analyze changes in IVD height and foramen size while following XLIF patients, and to further determine the effects of varying cage heights on these morphometric analyses in XLIF surgeries.

**METHODS:** Institutional IRB approval was obtained for the study. A total of 42 discs and 84 foramina were analyzed. Patients were CT-scanned preoperatively and postoperatively within 7 days in a SOMATOM Definition Flash CT scanner. 3D reconstruction of the vertebrae at the operated levels and isolation of the endplates were completed in Mimics software, and the endplates were exported as point-cloud data. Zonal Disc height distance (DHD) was calculated as the mean distance between the point cloud data of the endplates adjacent to an IVD, which was separated into 5 zones (posterior, left-lateral, right-lateral, anterior, nucleus pulposus) and measured by a custom written C++ program. Maximum and minimum diameters of the foramen were quantified from point-cloud data of the reconstructed vertebrae using a custom written C++ program as previously reported (Fig. 1B)<sup>5</sup>. Statistical analysis was done by IBM-SPSS statistics version 24.

**RESULTS:** Following XLIF, the whole-disc mean DHD increased by an average of 2.89 mm ( $p < 0.01$ ). Zonal DHD in all five zones of the discs significantly increased by an average increase of +2.86 mm ( $p < 0.01$ , Fig. A). Post-OP measurements of both maximum and minimum diameters of the foramen were significantly higher than pre-OP: the minimum diameter increased by 1.04 mm and the maximum diameter increased by 1.92 mm ( $p < 0.01$ , Fig. B). There were no significant differences between cage height and minimum foramen diameter change, cage height and maximum foramen diameter change, and cage height and changes in whole-disc DHD. The average increase per millimeter of cage height affects: the whole-disc DHD by an average increase of +0.30 mm ( $p < 0.01$ ); the minimum foramen diameter by an average increase of +0.11 mm ( $p < 0.01$ ); and the maximum foramen diameter by an average increase of +0.20 mm ( $p < 0.01$ ).

**DISCUSSION:** The XLIF procedure does not provide any statistically significant difference in changes in DHD in the five zones of the IVD. Minimum and maximum foramen diameters were increased following XLIF because of the indirect decompression from increased DHD. The study revealed that implementation of the appropriate cage height produces similar morphological increases in the operated discs despite the varying cage heights employed in the XLIF procedure. This study indicates that with the use of appropriate cages in XLIF surgery, patients will experience similar increases in DHD and maximum/minimum foramen diameters.



## Pain and function in adult patients with scoliosis attending a rehabilitation center

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### Background

Scoliosis is a very frequent problem during adulthood. Surgery is a very common option for these patients, but there are relevant risks and side effects and not all patients are willing for such treatment. For these reasons many patients seek for a conservative treatment in rehabilitation centers. For the assessment of quality of life in these patients the SRS-22 questionnaire was first developed, and more recently the SRS-7, a shorter unidimensional questionnaire based on the Rasch analysis, was created. No comparison of these tools is available in a rehabilitation setting for adult with scoliosis.

The aim of the present study is to provide an overview of the clinical characteristics of adult patients seeking for a clinical evaluation at a rehabilitation center specialized in scoliosis conservative treatment based on the SRS-22 and the SRS-7 questionnaires.

### Methods

We retrospectively review the record of all the adult patients included in our prospective database running between 2003 and 2017. The inclusion criteria were: diagnosis of idiopathic scoliosis with a curve of 30° Cobb or more, no surgical treatment, availability of the SRS-22 and SRS-7 questionnaires. The SRS-22 is based on 5 items (Function, Psychological wellbeing, Pain, Aesthetics and Satisfaction for treatment), with scores ranging from 5 (no impairment) to 0 (high impairment). The SRS-7 gives a comprehensive score of quality of life. Patients were divided by sex. We separately analyzed the 5 items of the SRS-22 and we looked for correlation with the clinical features including Cobb angle, BMI, Angle of Trunk Rotation, age.

### Results

244 patients (37 males) respected the inclusion criteria. The mean Cobb angle was 48±14°, Age 37±15.

All the items the SRS-22 showed reduced values of: Function 3.8±0.6, Psychological wellbeing 3.5±0.8, Pain 3.6±0.8, Aesthetics 3.1±0.6 with respect to normative values for healthy adults (ranging from 4.1 to 4.6). There were no differences for sex. The global score for the SRS-22 was 3.5±0.5 (range 0-5) while for the SRS-7 was 36±13 (range 0-100). The correlation was moderate (0.53). No relevant ceiling effect was noted. The Cobb angle correlated with the SRS-22 and SRS-7 global value and with pain, but the strength was very low (0.17 and 0.18 respectively). A slightly higher correlation was found between Cobb and Aesthetics (0.26). 28% reported to use drugs for pain control, 4.5% on a weekly base, 2% on a daily base.

### Discussion

This is the first study reporting the general characteristics of patients affected by scoliosis attending a specialized rehabilitation center based on the SRS-22 and SRS-7 questionnaires. Both questionnaire can describe the population of adult with scoliosis, being the SRS-7 shorter to fill. Adult scoliosis patients poorly performed globally and in all the analyzed items. The clinical characteristics of patients are not good predictors of pain, disability and aesthetics.

## The change of radiographic spinal alignment after using high angle cage in posterior lumbar interbody fusion surgery

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### Introduction:

The spinal sagittal alignment plays important role for the body balance and prevention of back pain. During spinal correction surgery, we should avoid iatrogenic flat back as much as possible. Currently, posterior lumbar interbody fusion (PLIF) are widely used for unstable lumbar spinal disorders. Although we believe that PLIF with high angle cage can create local and whole lumbar lordosis, it is not clear whether the high angle cage can help to make adequate lumbar lordosis or not.

The purpose of this study was to clarify the effect of PLIF with high angle cage in segmental and whole lumbar lordosis.

### Methods:

Twenty four patients ( 11men and 13 women; mean age 67.9 years [30 - 84] ). All patients underwent single- or two- level PLIF using high angle peek cage (12°23mm × 2 ) for lumbar degenerative spondylolisthesis or canal stenosis with instability. We measured Segmental lordosis and lumbar lordosis (from L1 to S1) at preoperative, 1week postoperatively, and final follow up. Clinical results were assessed by Japanese Orthopedic Association Score (JOA). For comparison, fifteen patients underwent PLIF with low angle peek cage (0°, 4°).were measured same parameter.

### Results:

Pre-operative segmental lordosis was 9.5±6.6° (mean±SD) with the 12° cage. Postoperative segmental lordosis was 13.2 ±5.3( after 1week) 13.3±5.4( final follow up). Segmental lordosis increased significantly between preoperative and postoperative, and could be maintained until final follow up. Lumbar lordosis angle with the 12° cage was 28.1±16.5° (pre-op), 34.2±10.1° (after 1week), 34.2 ±11.6 (final follow up). No statistical increase in lumbar lordosis was achieved with PLIF using high angle cage between pre- and post-operation. JOA score was improved from 13.7/27 preoperatively and 24.1 /27 postoperatively (P<0.01). In the group of PLIF using low angle cage, Segmental lordosis was 11.7±5° (pre-op), 11.2±6.8 (post-op).and lumbar lordosis was 24.9±6.9° (pre-op), 24.9±10.5 (post-op). There were no significant differences in findings between pre- and post-operation using low angle cage.

### Discussion:

This study aims to assess the differences in the radiological results depending on the lordotic angles of the different angle cage in PLIF. We found that PLIF with high angle cage gave significant advantages to improve in segmental lordosis. Although the clinical improvements after PLIF with high angle cage were significantly, this procedure could not improve whole lumbar lordosis after operation.

## Intervertebral disc cells' metabolic and synthetic activity under the influence of macrophage cocultivation in 3D cell culture

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**INTRODUCTION:** Increased expression of pro-inflammatory cytokines (TNF $\alpha$ , IL-1 $\beta$ , IL-6, IL-8 and IL-17) observed with IVD degeneration is associated with aging and extracellular matrix breakdown. Synthesis of extracellular matrix is an energy-dependent process, which may be affected by the shortage of nutrient supply in degenerated IVDs. However, the effect of inflammatory mediators on metabolic activity of IVD cells is unknown. Here we studied the influence of pro-inflammatory cytokines on healthy and degenerated IVD cells' lactate production, as a measure of glycolysis, under pro-inflammatory conditions in a macrophage-cocultivation 3D cell culture model.

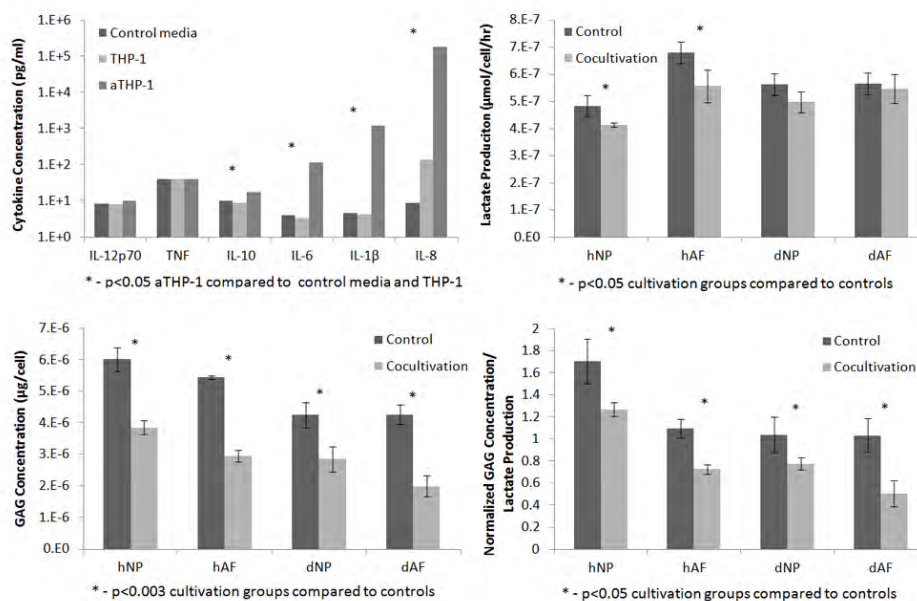
**METHODS:** Healthy primary human annulus fibrosus (AF) and nucleus pulposus (NP) cells from 24-week fetal tissue were purchased from ScienCell (Healthy group). Degenerated NP and AF cells were isolated from IVD tissue obtained during discectomy (Degenerated group, purchased from Barrow Neurological Institute BioBank). Cells were expanded in monolayer, then encapsulated in 3 mm alginate beads. The IVD cells encapsulated in alginate beads ( $2 \times 10^5$  cells/well) were cocultured with or without 100 nM phorbolmyristate acetate-activated macrophage-like THP-1 cells (aTHP-1). Viability (trypan blue in monolayer), lactate production, glucose consumption and sulfated glycosaminoglycans (GAGs, 1,9-dimethyl-methylene blue assay) were assessed. Cytokine levels were measured by cytometric bead array kit (BD Biosciences, USA). Cell morphology in 3D culture (alginate beads) was studied using immunocytochemistry: whole beads were stained with phalloidin for F-actin, DAPI for DNA, and imaged on a laser confocal microscope. All experiments were repeated in triplicate. A main effects ANOVA and post-hoc Mann-Whitney U-tests were performed to compare control, and aTHP-1 groups.

**RESULTS:** aTHP cells produced significantly more IL-10, IL-6, IL-1 $\beta$  and IL-8 ( $p < 0.05$ ) compared to control media and non-activated THP-1 cells (Figure 1A). Significant increase of IL-1 $\beta$ , IL-8 levels was observed in all coculture groups compared to controls ( $p < 0.05$ ). Proliferative activity ( $p = 0.12$ ) and viability ( $p = 0.01$ ) of both healthy and degenerated AF and NP cells decreased in aTHP-1 coculture groups. GAG production was significantly lower in degenerated NP and AF cells when compared to the healthy groups ( $p < 0.05$ ) for both cell types. Pro-inflammatory cytokines significantly decreased GAG mass/cell in all aTHP-1 coculture groups ( $p_{ANOVA} = 0.003$ ) (Figure 1B). Significant decrease ( $p < 0.05$ ) of lactate production was observed in aTHP-1 coculture groups of healthy NP and AF cells compared to control (Figure 1C). Additionally, normalized GAG divided by lactate production (Figure 1D) showed inflammatory cytokines decreased GAG production even though lactate production remained constant. The imaging study showed smaller cell size and grouping in clusters in the degenerated AF and NP cells compared to healthy IVD cells.

**DISCUSSION:** 3D IVD cell culture demonstrated morphological changes similar to those observed in human tissues with degeneration. Inflammation in the IVD causes a decrease in cell proliferation, production of key disc hydrating proteins, and rate of glycolysis.

Additionally, cells under inflammatory conditions showed a decrease in GAGs produced for the same amount of glucose consumed. Decreasing inflammation in the IVD may aid in restoring healthy ECM production without exacerbating the nutrient deprivation of the degenerated IVD.

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## Efforts toward achieving relief from refractory low back pain using Duloxetine — Experience on the use of Duloxetine—

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**Introduction** Chronic pain can continue even after tissue damage itself has healed, and can inhibit patient activity, and cause depression and anxiety which can subsequently lead to refractory responses to treatment. Orthopedic surgeons employ various techniques to deal with chronic pain treatment, but we are hardly satisfied with the current therapeutic efficacy of such measures. It is rare to encounter chronic pain that does not involve at least some degree of tissue injury, and it is actually more common to treat chronic pain in cases where some residual organic damage is present. Few reports have been published about the effect and adverse events of Duloxetine against intractable pain (spinal disease). We conducted a study aimed at investigating the effect and safety of Duloxetine and evaluating its proper use.

**Methods** Duloxetine was administered to 58 low back pain patients with insufficient response to conventional drug treatment. 45 cases (23 men, 22 women) for whom follow-up of over 6 months or more was possible were finally analyzed and reported. The average age was 72.3 (range 38-80) years old and 13 were postoperative case of lumbar spine surgery. Duloxetine started at the lowest dose and was added to a regimen that included one or more of the following: COX-2 inhibitors, Pregabalin, Tramadol and weak and strong opioids.

**Results and Discussions** The dose of Duloxetine at final follow-up observation was as follows: 20mg, 4 cases, 40mg, 22 cases and 60mg, 19 cases. The mean low back pain VAS score improved from 71 ( 38-87) before drug administration to 57 ( 22-80) at final follow-up observation. The mean lower limb pain VAS score also improved from 67 ( 0-81) to 44 (0-76), respectively. Moreover, RDQ score showed statistically significant improvement from 13.6 ( 3-21) to 11.2 (1-20;  $p < 0.05$  Wilcoxon t-test). Regarding SF-36v2 scores, statistically significant improvement of the four subscales [role physical ( $p < 0.01$ ), bodily pain ( $p < 0.05$ ), role emotional ( $p < 0.01$ ) and mental health ( $p < 0.01$ ); Wilcoxon t-test] was observed, however, significant difference was not observed in three component summary scores. These results indicate that additional administration of Duloxetine to existing analgesics was efficacious against chronic low back pain. Duloxetine can be considered a treatment option for patients with decreased QOL and anxiety due to chronic pain. In our treatment strategies against chronic pain, it is vital to first do a complete evaluation for any organic lesions that may be affecting symptoms. Having the patient thoroughly understand the pathology of the pain will likely lead to better cooperation from the patient. This also allows the patient to feel more confident about the treatment he is undergoing. With this in mind, if neuropathic pain factors seem unlikely, Tramadol HCL-acetaminophen combination formation, codeine phosphate should be administered. If a neuropathic pain component is more prominent, then pregabalin use may be considered. If nociceptive pain and neuropathic pain are mixed, it may be necessary to consider using both of the above. If adequate efficacy cannot be achieved on potent opioids, it may be an option to consider the use of Duloxetine.

## RADIOLOGICAL OUTCOMES OF LUMBAR INTERBODY FUSION USING TITANIUM-COATED PEEK CAGE

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### INTRODUCTION

Up to now, interbody cages (IBC) of titanium (Ti) or polyetheretherketone (PEEK) have been mainly used for lumbar interbody fusion (LIF). However, Each of these cages has been reported to have both advantages and disadvantages. To resolve them, Ti-coated PEEK IBC which combines both advantages has been introduced, recently. The purpose of this study was to investigate radiological outcomes following LIF surgeries using the Ti-coated PEEK IBC at 1-year minimum follow-up.

### METHODS

A total of 24 intervertebral spaces in consecutive 20 patients (6 men and 14 women, average age: 70.5 years old) who underwent posterior/transforaminal LIF using the Ti-coated PEEK IBC were evaluated. Fifteen patients with degenerative spondylolisthesis, three with *degenerative scoliosis*, and two *lumbar spinal stenosis* were treated. Three IBCs were placed at L3-4, 13 at L4-5, and eight at L5-S. Based on the CT scans at the 1-year minimum follow-up, bone union rate, screw loosening, cage subsidence, bone cyst formation around endplate, and adjacent segment disease were evaluated. All intervertebral spaces were filled with bone chips and two cages packed with local bone chips. Artificial bone was added in three patients and allogenic bone chips were used in one patient. Bony fusion was defined when partial bone continuity between vertebral bodies could be identified. Cage subsidence was defined when the cage could be seen to sink compared to the finding immediately after the surgery. Bone cyst was defined as circular low density which was newly generated postoperatively. Adjacent segment disease (ASD) was defined when an obvious progression of the intervertebral disc degeneration and/or instability.

### RESULTS AND DISCUSSION

At the 1-year follow-up, bone fusion was obtained in 23 in 24 intervertebral space, bony fusion rate was 95.8%. Non-union was observed in only one intervertebral space accompanied with screw loosening. Cage subsidence was found in 2 intervertebral spaces (8.3%, average: 2.0 mm), but bony fusion was obtained in both intervertebral spaces. Bone cyst formation was in 4 intervertebral spaces (16.7%), and screw loosening was found in 4 of 48 screws (8.3%). However, there was no association between these events. Regarding the ASD, disc herniation in one case and progression of the intervertebral instability in one case were identified. In addition, we suggest there is an advantage of the Ti-PEEK IBC on easier radiological evaluation. Although to show advantages scientifically on the Ti-PEEK IBC, more evidences will be required, we believe better clinical outcomes were obtained at 1-year minimum follow-up.

## A population-based cohort study identifies an association of *THBS2* with intervertebral disc degeneration

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**Introduction:** Intervertebral disc degeneration (IDD) contributes to several symptoms including neck and low back pain. IDD has genetic background and more than several susceptibility genes have been reported; however, none of their associations has been replicated. One of the critical problems of the genetic study of IDD that could lead to the inconsistent association is its phenotype definition. To clarify the genetic background of IDD, we examined the association of previously reported SNPs with IDD in the Wakayama Spine Study (WSS), a population-based cohort in Japan.

**Methods:** In the WSS study, 1,605 subjects participated and underwent magnetic resonance imaging (MRI) examinations of the whole spine. Discs from C2-C3 to L5-S1 were evaluated using the Pfirrmann disc scoring classification. The disc with score 4 and 5 of the classification was considered as IDD positive. Eight single-nucleotide polymorphisms (SNPs) in eight genes that were previously reported to show significant association with IDD, were examined at each disc level, consideration of non-genetic risk factors of age, sex and body mass index (BMI).

**Results:** Three SNPs, rs9406328, rs17576 and rs16924573 showed a nominal association ( $P < 0.05$ ) with WSS study. The lowest P-value was found in rs9406328 in the *THBS2* gene at disc level T12-L1 ( $P = 0.016$ ). By linear regression analyses, a significant association between rs9406328 and IDD at T12-L1 with IDD was found with no adjustment for age ( $P = 0.0031$ ). The average IDD score with 2 risk alleles of rs9406328 was significantly higher than those with 0 or 1 risk allele. The effect of rs9406328 decreased with age. The difference of the IDD score based on the risk alleles decreased with age. IDD progressed with age; however, its speed was lower in the participants with 2 risk alleles in the *THBS2*; after age 70 there was no difference in the score among the numbers of the risk allele. Also a multiple regression analysis showed significant association of the number of risk alleles of rs9406328 with IDD at C7-T1 ( $P = 0.00061$ ) and T1-T2 ( $P = 0.011$ ). No interactions were observed between the number of risk alleles and age. Genetic association was confirmed at C7-T1, T1-T2 and T12-L1, where the prevalence of IDD by disc level was lower than the other levels (Figure 1).

**Discussion:** *THBS2* is a calcium-binding protein that binds to and inactivates the matrix metalloproteinase (MMP) genes<sup>1</sup>. Mutations in the MMP-binding region of *THBS2* lead to the activation of MMPs<sup>2</sup>, which accelerates the proteolysis of proteoglycans and dehydration of the intervertebral disc, resulting in the change of MRI signal intensity. The genetic association with the lumbar levels in twin study was higher with respect to signal intensity than disc height or disc bulge<sup>3</sup>. In addition, the environmental characteristics of each disc level of lumbar spine are different, and therefore, we used the score at each intervertebral level. Considering that the gross effect of the genetic factors is the same at all levels, the effect of genetic factors is likely to be masked at the disc level by the strong influence of environmental factors.

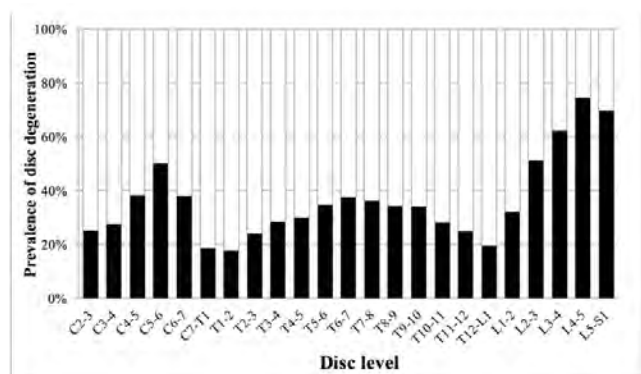


Figure 1. Prevalence of intervertebral disc degeneration at each disc level  
There are peaks in the central parts of the cervical, thoracic and lumbar spine disc sections, respectively. In contrast, the prevalence at the cervico-thoracic and thoraco-lumbar junctions is low.

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