

## A REALISTIC DISC HERNIATION MODEL EMPLOYING COMPLEX MOTION AND A MICRO-LEVEL DAMAGE ANALYSIS

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### Introduction:

To date the mechanisms of disc failure at a microstructural level have been explored in relatively simple postures. However, while lifting whilst twisting and bending is known to be a factor in the development of herniation *in vivo*, the influence of shear and rotation combined with flexion on the mechanisms of disc failure has yet to be described at a microstructural level. The objective of this study was to provide a microstructural analysis of the mechanisms of failure in healthy discs subjected to compression while held in a complex posture incorporating physiological amounts of flexion and shear limited by the facet joints.

### Methods

30 intact motion segments from 10 healthy mature ovine lumbar spines were compressed in a complex posture (7° flexion, 5° rotation and an offset compressive load producing shear displacements governed by the facet joints of approximately 2.4 mm in the anteroposterior direction and 4 mm in the lateral direction) at a displacement rate of 40 mm/min until failure occurred. 9 of the 30 samples reached the maximum displacement prior to a reduction in load and were classified as early stage failures, providing insight to initial areas of disc disruption. Both groups of damaged discs were then analysed microstructurally.

### Results

The average failure load under complex loading was 8.4kN, significantly lower statistically than previous results for a flexed posture (9.7kN)<sup>1</sup>. A circumferential mode of failure involving infiltration of nucleus material in a circuitous path to the annular periphery was present in all samples, and was the only mode of failure in 67% of the early stage tests. Microstructural analysis indicated that the mid annular region adjacent to the ridge apex and the posterior annulus were the sites of initial damage.

### Discussion

The complex posture employed in this investigation significantly reduced the load required to cause disc failure and resulted in a very different failure morphology to that observed in either simple flexion or direct compression. No instances of posterolateral damage were found without there also being damage in the posterior region, indicating that damage progresses posterolaterally with complex loading. And as in previous investigations involving flexion alone<sup>1,2</sup> the posterior and posterolateral annulus were the location of overt herniation. A key reason for these findings could be the components of shear causing one of the oblique sets of lamellar fibres in the posterior disc to be subjected to greater strain than the other as indicated by previous analytical studies but not elucidated at the microstructural level under physiologically reasonable conditions. If the disc is overloaded in this posture, these strained fibres will fail more readily than the relaxed fibres either at mid-substance, or at the annular-endplate junction.

1. Wade KR, Robertson, P.A., Thambyah, A., Broom, N.D. How healthy discs herniate: a biomechanical and microstructural study investigating the combined effects of compression rate and flexion. *Spine*. 2014;39(13):1018-28.
2. Wade KR, Robertson, P.A., Thambyah, A., Broom, N.D. 'Surprise' loading in flexion increases the risk of disc herniation due to annulus-endplate junction failure: a mechanical and microstructural investigation. *Spine*. 2015;40(12):891-901.

## COULD DISC WALL STRUCTURAL ABNORMALITIES BE RESPONSIBLE FOR HERNIATION?

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### INTRODUCTION:

The influence of disc structure on the process of lumbar disc herniation is still not fully understood. It has been shown recently<sup>1</sup> that *in vivo* herniations result from annular failure (AF, 35%) or endplate junction failure (EPJF, 65%). Both cases could be reproduced in an *in vitro* study<sup>2</sup> with complex loading. Other *in vitro* studies indicate that both posture and loading rate influence the mode of disc failure<sup>3</sup>. However, the influence of the disc structure itself on the failure process is unclear. Therefore, the goal of this study was to examine discs prior to and following complex loading in order to evaluate their structure and determine whether irregularities, if present, are responsible for the failure of the disc.

### METHODS:

Thirty ovine lumbar spinal segments were loaded under five combined loading conditions (0-12° flexion (FE), 0-9° lateral bending (LB), 0-4° axial rotation (AR), 0-800 N axial compression (AC), 1000 loading cycles, 2 Hz. Gr1: all combined, Gr2: w/o AC, Gr3: w/o AR, Gr4: w/o LB, Gr5: w/o FE) in a recently developed dynamic 6-DOF spine tester. During testing macroscopic changes of the posterior part of the disc were recorded by a video camera. The discs were scanned in an ultra-high field MRI (11.7 T) as well as with a  $\mu$ CT prior to and following testing.

### RESULTS:

Ten discs suffered annular failure, with four of these involving subligamentous herniation of inner disc material and the remaining four involving disruption of the annular wall as judged by examination of the high resolution MRI images. Of the remaining discs, seventeen suffered vertebral endplate fracture and three no apparent damage.. Most interestingly, all discs that herniated contained minor irregularities in the posterior annular wall that were visible in the pretest MRI images as can be seen in Fig. 1.

### DISCUSSION:

These results indicate that irregularities in the lamellar structure are responsible for annular failure when the disc is overloaded under the conditions used in this study. Further, if such defects are present, herniation will initiate at the site of these irregularities when the disc is overloaded, likely a consequence of the hydrostatic loading from the relatively healthy nucleus present in the tested discs. Without these defects, failure occurred via endplate fracture. We suggest that these irregularities could arise from development (for example incomplete lamellae), minor injuries and early stage degeneration. This study indicates that it is possible to use experimental MRI imaging to detect discs that are at risk of suffering annular failure, at least in the ovine samples used in the present study. It may thus be possible in the future to develop clinical imaging techniques capable of identifying patients at risk of suffering disc herniation.

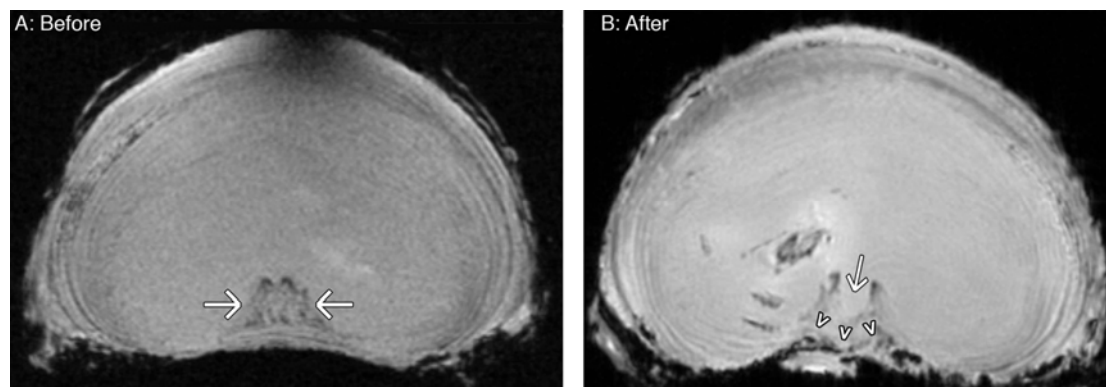


Fig. 1: Transverse 11.7T MRI section through an ovine disc prior to testing (A) irregularities indicated by arrows. Following testing (B) inner disc material herniated through this region as indicated by the arrows.

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2. Wilke, H.-J., A. Kienle, S. Maile, V. Rasche and N. Berger-Roscher (2016). "A new dynamic six degrees of freedom disc-loading simulator allows to provoke disc damage and herniation." *European Spine Journal* 25(5): 1363-1372.
3. Wade KR, Robertson, P.A., Thambyah, A., Broom, N.D. How healthy discs herniate: a biomechanical and microstructural study investigating the combined effects of compression rate and flexion. *Spine*. 2014;39(13):1018-28.

## THE EFFECT OF AN ANTI-NERVE GROWTH FACTOR (NGF) TREATMENT BY NERVE ROOT INFILTRATION FOR LUMBAR DISC HERNIATION

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### INFORMATION

Nerve growth factor (NGF) has been shown to play a key role in the generation of acute and chronic pain. However, the contribution to pain-related behavior of NGF is unclear. The aim of this study was to investigate the relationship between pain-related behavior and the change of NGF expression in dorsal root ganglion (DRG), and the effect of anti NGF antibody (anti-NGF) for the neuropathic pain using an application of nucleus pulposus (NP) rat model.

### METHODS

<Examination 1>: Adult female Sprague-Dawley rats (n=92) were used and divided into two groups; NP and sham. NP harvested from the tail was applied to the left L5 DRG of rats in the NP group. In the sham group, the same procedure was performed without NP application on the DRG. Behavioral testing was performed to investigate the mechanical withdrawal threshold using von Frey hairs. Immunohistochemical localization of NGF in the DRG was assessed. The numbers of their immune-reactive (IR) cells and all DRG neurons were counted. The mean values were expressed as a ratio of the IR cells of immunohistochemistry against all neurons. <Examination 2>: Animals in the NP group were divided into four sub-groups (n=12 in each group): LD group (low dose anti-NGF; 0.05µg/ml), MD group (middle dose anti-NGF; 0.1µg/ml), HD group (high dose anti-NGF; 1.0µg/ml) and control group (0.1M PBS). When NP was applied to the DRG, in addition, each dose of antibody (0.1ml) or PBS (0.1ml) was injected into the underlayer of the epineurium just distal to the NP. Behavioral testing was performed in the same way as Examination 1.

### RESULTS

<Examination 1>: The mechanical withdrawal threshold was significantly decreased from 7 to 35 days after surgery ( $p < 0.05$ ). Immunohistochemical examinations revealed that NGF was co-localized in both neurons and activated satellite glial cells in DRGs. Percentage of NGF-IR neurons in the NP group was significantly higher than those in the sham group at 2, 7, 14 and 21 days after surgery ( $p < 0.05$ ). <Examination 2>: Mechanical withdrawal thresholds in the MD and HD groups were significantly increased compared with the control group ( $p < 0.05$ ). The threshold in the HD group was significantly higher on 7, 14, and 21 day, the threshold in the MD group was significantly higher on days 7 and 14 compared to the control group. The threshold in the LD group was shown no difference compared with the control group.

### CONCLUSIONS

Previous studies have shown that NGF is produced in inflamed tissue, taken up by peripheral nerve terminals, and retrogradely transported to the cell body in the DRG. The results in this study, NGF was expressed both neurons and activated satellite glial cells in DRG due to application of NP, but not retrogradely. Furthermore, administration of anti-NGF antibody on DRG in a rat NP applied model was reduced the decreased thresholds. Therefore, anti-NGF antibody might be targets for the development of novel analgesics.

## DEVELOPMENT OF LUMBAR DISC DEGENERATION IN CADHERIN 2 MOUSE MUTANT

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### Introduction:

Understanding the molecular components of the intervertebral disc degeneration is important to the future management of the degenerative disc disease. However, the pathogenesis of disc degeneration is still not well understood. We recently found that the amount of N-cadherin/cadherin 2 expressing cells in the nucleus pulposus (NP) is remarkably reduced in adolescent scoliotic discs and adult degenerative discs compared to fetal discs. We hypothesized that cadherin 2 has a function in disc growth and homeostasis. This study aimed to explore the consequence of a partial loss of cadherin 2 function in mouse NP using notochordal cell specific gene targeting.

### Methods:

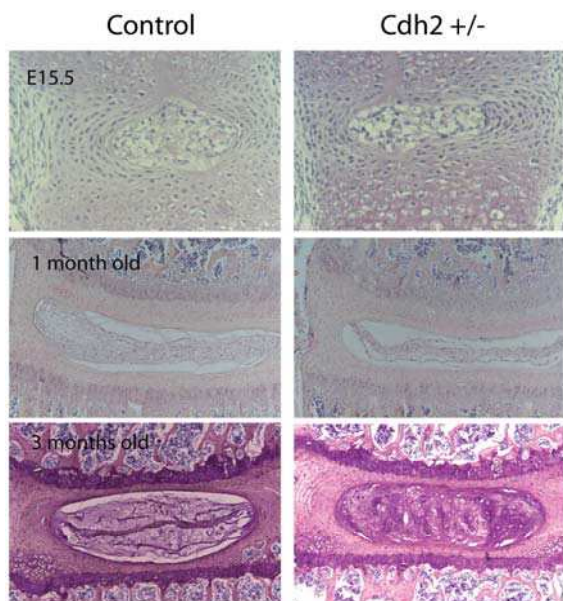
We utilized a *Foxa2* enhancer driven Cre recombination system to conditionally knockout one allele of the *Cdh2* gene in notochord and subsequently the descendent NP cells. The lumbar spine of the heterozygous mutants (*Foxa2*-Cre; *Cdh2*-*lox/+*) was harvested at E15.5, P0, 1 months and 3 months of age. H&E, FAST and Masson trichrome staining were performed to study the histologic changes. TUNEL assay was used to test cell apoptosis. Protein expression of cell proliferation marker Ki67, collagen II, fibroblastic markers FSP1 and  $\alpha$ SMA, and Wnt-signalling components was examined by immunofluorescence.

### Results:

Intervertebral disc formation and development in fetal or newborn mice was not affected in the heterozygous *Cdh2* mutants. However, loss of vacuolated notochordal cells was observed in the lumbar disc levels, but not in the tail disc levels, of 1 month old mutant mice, whereas chondrocyte-like cell clusters appeared in 3 month old mutant NP. The mutant NP shows a collagen II -rich matrix with lacuna structures. NP cells showed higher activity of both proliferation and apoptotic activity. Higher expression of fibrotic markers including FSP1 and  $\alpha$ -SMA were found in the mutant, suggesting that NP was undergoing profibrotic changes. Beta-catenin, reported as a factor of disc degeneration, showed increased translocation into nuclei in mutant NP cells.

### Discussion:

To our knowledge this study is the first to illustrate that partial loss of cadherin 2 function can lead to a transition of the NP to a fibrochondrogenic phenotype. Along with the changes in marker expression, cell clustering, and increased apoptosis found in the NP, the mutant disc thus exhibits a phenotype that resembles human disc degeneration. This suggests that cadherin 2 has a role in maintaining the function or the phenotype of notochordal NP cells and is important to disc homeostasis. The increased activity of beta-catenin also suggests that cadherin 2 function may crosstalk with Wnt signalling.



## HYPEROSMOLAR OVERLOADING INDUCES NOTOCHORDAL CELL DIFFERENTIATION WITH OSMOSENSITIVE AQUAPORIN3 UPREGULATION AND ALTERED N-CADHERIN AND CONNEXIN-43 EXPRESSION

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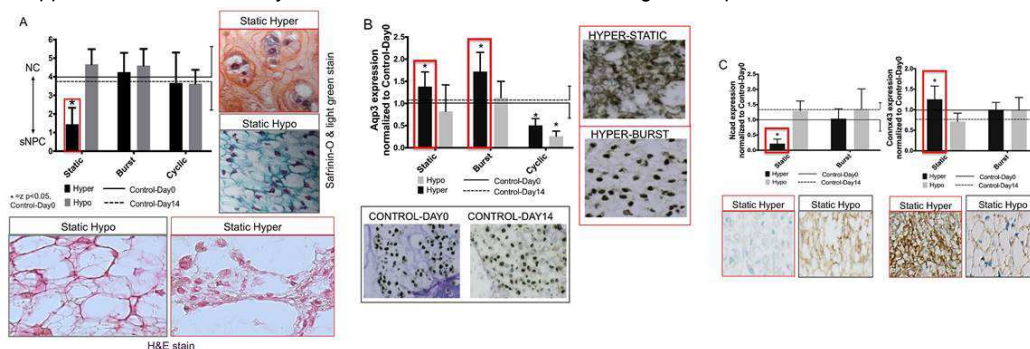
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**INTRODUCTION:** Hallmarks of intervertebral disc (IVD) aging include the maturation of nucleus pulposus (NP) cells from large, vacuolated notochordal cells (NCs) to small-chondrocyte-like NP cells (sNPCs) [1], and loss of the NP gelatinous structure. Understanding triggering mechanisms and mechanosensation changes associated with NP maturation may inform pathophysiology mechanisms. A mouse organ culture model was used to determine whether changes in osmolarity could induce NC maturation to sNPC, and whether this resulted from altered cellular osmoregulation and mechanotransduction. We hypothesized that: **1)** NC maturation is associated with hyperosmotic overloading and that this maturation is a cell differentiation process; **2)** NC maturation involves changes in osmosensitive protein expression including calcium channel transient receptor potential vanilloid-4 (TRPV4) and water channels Aquaporins 1 (Aqp1) & 3 (Aqp3); and **3)** NC maturation involves a shift in mechanotransduction from N-cadherin (N-cad) to connexin-43 (Cx43).

**METHODS:** 96 motion segments were obtained from twelve 12-week old C57BL/6 female mice tails. Segments were cultured for 14 days in isoosmolar (Control-Day14), hypoosmotic (130 mOsm) or hyperosmotic (530 mOsm) conditions with 3 durations: Cyclic (10min on and off for 1.5h/day, Hyper-Cyclic, and Hypo-Cyclic), Burst (1.5h/day, Hyper-Burst and Hypo-Burst) and Static (24h/day, Hyper-Static, and Hypo-Static). Naïve control group was non-cultured (Control-Day0). IVDs were then fixed, decalcified and embedded in paraffin. **1)** To evaluate NP maturation, sections were evaluated for cell morphology by hematoxylin and eosin (H&E), GAG content by safranin-O (Saf-O), NC phenotypic markers expression including cytokeratins 8, 19 and sonic hedgehog, and apoptosis by TUNEL. **2)** To evaluate alterations in osmoregulatory proteins, sections were stained for TRPV4, Aqp1 & Aqp3 by IHC. **3)** To evaluate mechanotransduction proteins, sections were stained for N-cad and Cx43 via IHC.

**RESULTS: 1)** H&E staining revealed presence of vacuoles and large-sized NCs in all experimental groups except the Hyper-Static group, suggesting maturation to predominantly an sNPC phenotype (Fig1.A). Saf-O staining showed high cell/matrix ratio in all groups indicative of NC phenotype, except for the Hyper-Static group which had substantial GAG accumulation indicative of maturation (Fig1.A). No differences in expression of cytokeratin 8, 19 and sonic hedgehog, or TUNEL positivity were identified in any group suggesting differentiation processes. **2)** Aqp3 expression was significantly increased in hyperosmolar conditions and remained unchanged in hypoosmolar conditions (Fig1.B) while neither TRPV4 nor Aqp1 expression were affected. **3)** N-cad expression decreased and Cx43 increased in the Hyper-Static compared to all other experimental groups (Fig1.C).

**DISCUSSION:** Hyperosmotic overloading induced NC maturation to sNPCs via differentiation since we observed maintained expression of NC-specific markers and no evidence for increased apoptosis. Expression of Aqp3 increased under Hyper-Static overloading conditions indicating its important osmoregulatory role in NC maturation. Results suggested TRPV4 and Aqp1 had little involvement in maturation but alterations in channel activity may have occurred. The loss of N-cad and GAG matrix accumulation in NC maturation is consistent with its known role modulating the juvenile NP phenotype ex-vivo [2], and the simultaneous increase in Cx43 indicated a preference towards gap junction communication in sNPCs. We conclude that the disappearance of NCs is likely to involve chronic osmotic overloading with important functional shifts in mechanotransduction.



**Figure 1: A)** Hyperosmolar conditions induced NC maturation to sNPCs as seen by lack of vacuoles, smaller cell clusters and smaller cell size, and substantial GAG accumulation. **B)** Aqp3 was upregulated by hyperosmolar conditions as compared to other groups suggesting a role for Aqp3 in intracellular osmoregulation. **C)** N-cad was down regulated in Hyper-Static conditions and Cx43 was upregulated suggesting altered intercellular communications as NCs differentiate to sNPCs. Differences were assessed by one-way ANOVA.

## TEMSIROLIMUS IS A CANDIDATE OF THE OPTIMAL MTOR INHIBITOR FOR PROTECTING HUMAN INTERVERTEBRAL DISC NUCLEUS PULPOSUS CELLS

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**INTRODUCTION:** Intervertebral disc degeneration, associated with back pain, is characterized by cell death and matrix degeneration. The mammalian target of rapamycin (mTOR) is a serine/threonine kinase that plays a central role in protein synthesis and cell growth. Rapamycin is the initially identified, first-generation mTOR inhibitor. We previously reported protective roles of rapamycin against apoptosis, senescence, and matrix degradation in disc cells. However, clinical use of rapamycin is limited due to severe adverse immunosuppression. Additional studies are thus required to identify the optimal agent for clinical application to human disc disease among other first-generation mTOR inhibitors and a natural polyphenol curcumin inhibiting mTOR.

**METHODS:** Human disc nucleus pulposus cells were isolated from 20 patient specimens undertaking lumbar surgery (68.0 ± 9.6 years; male 8, female 12; Pfirrmann degeneration grade, 3.6 ± 0.5). Cells were treated by four mTOR inhibitors (rapamycin, temsirolimus, everolimus, and curcumin) in 10% FBS-supplemented DMEM under 2% O<sub>2</sub>. Cell viability was determined by Cell Counting Kit-8 (CCK8) assay. To assess effects on mTOR signaling and autophagy, expression and phosphorylation of mTOR, its down-stream effector p70/S6K, and its up-stream regulator Akt were assessed by Western blotting. Autophagy marker LC3-II and substrate p62/SQSTM1 expression was similarly evaluated. β-Actin was used as loading control. To explore effects on cell death, aging, and matrix metabolism, cells were treated by the mTOR inhibitors in no serum-containing DMEM with 10-ng/ml interleukin-1β (IL-1β) to simulate inflammation. Apoptotic cleaved PARP, cleaved caspase-9, and senescent p16/INK4A in cell lysates and catabolic MMPs and anti-catabolic TIMPs in supernatants were assessed by Western blotting. Anabolic aggrecan and collagen types 1 and 2 gene expression was assessed by quantitative PCR.

**RESULTS:** All mTOR inhibitors showed dose-dependent decreases in CCK8 dehydrogenase activity ( $P < 0.01$  in  $>1 \mu\text{M}$ ). Based on the CCK8 findings, in every agent, 100 nM was selected as an effective but non-toxic concentration. Western blotting showed that rapamycin, temsirolimus, and everolimus decreased mTOR and p70/S6K phosphorylation but increased Akt phosphorylation ( $P < 0.05$ ). However, curcumin did not suppress mTOR and p70/S6K phosphorylation. Western blotting showed that all agents increased LC3-II and decreased p62/SQSTM1 ( $P < 0.05$ ), consistent with enhanced autophagy. The degree of autophagy induction was more prominent in rapamycin, temsirolimus, and everolimus than curcumin. Western blotting showed that all agents suppressed IL-1β-induced apoptosis and senescence ( $P < 0.05$ ), the capability of which was distinct in rapamycin, temsirolimus, and everolimus than curcumin. Further, all agents reduced IL-1β-induced MMP and TIMP releases ( $P < 0.05$ ). This trend was similar as well. Finally, gene expression of all anabolic genes was down-regulated by IL-1β but rescued by rapamycin, temsirolimus, and everolimus ( $P < 0.05$ ). Curcumin was less effective.

**DISCUSSION:** The first-generation mTOR inhibitors of rapamycin and also clinically available temsirolimus and everolimus showed protective effects against human disc cell apoptosis, senescence, and matrix catabolism. Curcumin was less toxic but less effective. In clinical use, adverse immunosuppression of mTOR inhibitors would recommend their local delivery rather than systemic administration. Therefore, intra-discal injection of temsirolimus with improved water solubility is a potential therapeutic application to inflammatory disc disease.

## LUMBAR SPINE PARASPINAL MUSCLE AND INTERVERTEBRAL DISC HEIGHT CHANGES 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 herniated IVDs, 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>. However, the lumbar paraspinal muscle (PSM) and intervertebral disc (IVD) response during prolonged spaceflight is not well described. This information could prove useful to support long space missions, such as a manned mission to Mars.

The immediate objective is to evaluate lumbar PSM cross-sectional area and IVD height 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 space missions as well as here on Earth.

*Study Design* Prospective case series *Level of Evidence* 4

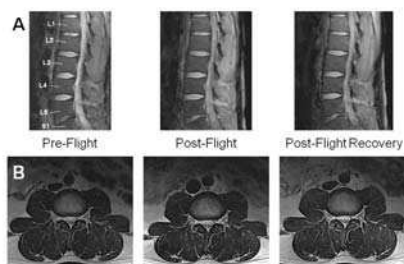


Figure 1. Characteristic pre-, post-flight and recovery lumbar spine MR images. A) L1-S1 sagittal and B) L3/4 axial T2 sequences.

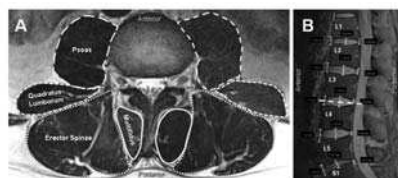


Figure 2. Characteristic location of A) lumbar paraspinal muscles identified for FCSA lean muscle area measurement on axial images at the L3-L4 level, and B) IVD height measurement on sagittal images (Anterior, Middle, and Posterior).

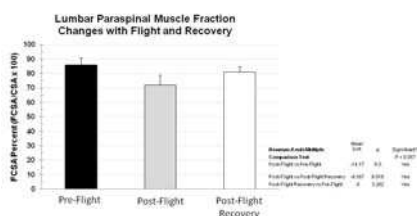


Figure 3. FCSA as a percentage of total CSA in the lumbar paraspinal muscles, n=6 crewmembers.

### METHODS

Institutional Research Board approval was obtained from NASA and the University of California, San Diego. Six NASA crewmembers (1 female and 5 males, age 46 - 55 years) were imaged supine with a 3T MRI. Imaging was conducted pre-flight, immediately post-flight and then 33 to 67 days after landing (Figure 1). 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</sup>. IVD heights were measured at the anterior, middle and posterior sections of all lumbar levels<sup>4</sup> (Figure 2). Repeated measures ANOVA was used to determine significance at  $p < 0.05$ , followed by *post-hoc* testing.

### RESULTS

Paraspinal lean muscle mass, as indicated by the FCSA, decreased from 86% of the total PSM cross-sectional area down to 72%, immediately after the mission. Recovery of 68% of the post-flight loss occurred over the next 6 weeks, still leaving a significantly lower lean muscle fractional content compared to pre-flight values (Figure 3). In contrast, lumbar IVD heights were not appreciably different at any time point.

### DISCUSSION

The data reveal lumbar spine PSM atrophy after long-duration spaceflight. Some FCSA recovery was seen with 46 days post-flight in a terrestrial environment, but it remained incomplete compared to pre-flight levels. The muscle findings suggest possible preventive steps such as core-strengthening exercises or yoga to reduce the spinal effects of 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 with available exercise equipment requires further study. The IVD findings run counter to current thinking about the effects of microgravity on disc swelling<sup>1</sup>. However our sample size is presently small for the study of IVD heights, and we have no in-flight images. Further analysis with additional crewmembers and in-flight ultrasound imaging is forthcoming.

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## HETEROGENEOUS CHANGE IN ANNULUS FIBROSUS HEIGHT AFTER NUCLEOTOMY CORRELATES WITH ANNULUS STRAINS ORTHOGONAL TO THE COMPRESSIVE LOADING AXIS

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**INTRODUCTION** Nucleotomy reduces NP pressure and decreases disc height. Disc height is a function of AF properties, NP pressurization. Measures of disc height are typically taken as the average thickness in the 2D mid-sagittal plane and therefore exclude the majority of the disc<sup>1</sup>. Regional disc height, even in the AF, may be heterogeneous after nucleotomy because of the compromised NP. This heterogeneous disc height could drive the known changes in disc mechanics after nucleotomy, including decrease in stiffness and increase in creep and range of motion. Mechanical changes after nucleotomy are first evident in the neutral zone under low compressive loading<sup>1</sup>. We aim to quantify how nucleotomy affects both regional disc height and AF internal strain under a low compressive load that represents both the neutral zone and the reference condition during *in vitro* testing<sup>1</sup>.

**METHODS Data Acquisition:** Grade II L3-L4 human cadaveric bone-disc-bone samples (n=6) were mechanically loaded and imaged intact and after partial-nucleotomy. Hydrated intact discs were compressed until a reference load of 30N was obtained, and the discs equilibrated in a bath under that displacement. After 8 hours, discs were imaged in a 7T MRI-scanner at 0.3x0.3x0.3mm voxel resolution. Discs were rehydrated before NP was partially removed (1.1±0.4g) from a left posterolateral incision. Hydration, axial loading, and imaging were repeated following partial-nucleotomy.

**Data Analysis:** In each disc, the mid-third of the AF was divided into five regions (Figure 1). Disc height was measured as bone-to-bone distance at each voxel and averaged within regions. Disc strain was computed by registering intact and partial-nucleotomy volumes<sup>2</sup> and strains were averaged within regions. Average values within each sample were pooled by region for statistical analysis.

**Statistics:** Multiple one-sample t-tests determined if percent change in both total and regional AF height, and each mean regional strain were significantly different than zero, significance at p<0.05. Percent change in regional AF height was linearly correlated with mean regional strains.

**RESULTS** AF height significantly decreased by 0.36mm (3%) after partial-nucleotomy, however, regional AF height varied across region and between samples (Figure 2A). All strains were indistinguishable from zero, except for radial strains in the posterolateral and posterior regions (Figure 2B-D). Axial strains ranged from -20% to 34%, while orthogonal strain ranges were narrower. Change in regional AF height did not affect axial strain (r=0.03, p>0.05), but did correlate with circumferential (r=0.34, p=0.0008) and radial (r=0.12, p=0.066) strains (Figure 3). Anterior tensile axial strains appeared through the mid-third of the AF, but compressive axial strains above and below composed the full equilibrium response. Through-thickness orthogonal strains were more diffuse (Figure 4). We speculate anterior tensile axial strains arose from disc wedging, though facet joints would mitigate wedging *in vivo*.

**DISCUSSION** AF height decreased by 3% after nucleotomy under a low compressive load that represented both the neutral zone and the reference condition during *in vitro* testing. However, changes in AF height varied across both regions and samples and may correlate to internal AF strains orthogonal to the loading direction.

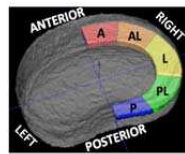


Figure 1. The right AF divided into anterior (A), anterolateral (AL), lateral (L), posterolateral (PL), and posterior (P) regions.

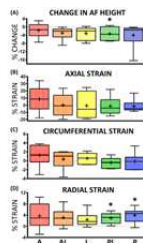


Figure 2. Regional distribution of average change in AF height, and axial, circumferential, and radial strains (n=5/disc). (A) The AF decreased in height after nucleotomy across all regions, but the amount of height decrease varied across region. Posterolateral region change in height was significantly different from zero. (B) Axial strain varied widely in anterior, anterolateral and lateral regions and varied less in posterolateral and posterior regions. The anterior region was composed of mostly tensile axial strain. (C) Circumferential strain appeared to decrease from anterior to posterior regions. (D) Radial strains were tensile across regions and were significantly different from zero in posterolateral and posterior regions. Mean values denoted by \*.

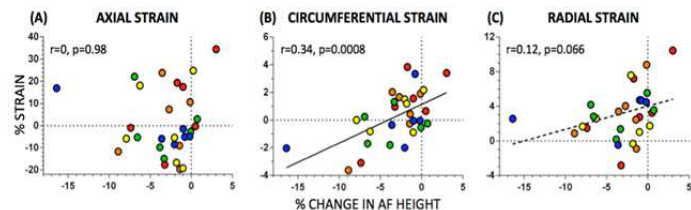


Figure 3. Change in AF height with nucleotomy correlated to AF internal strains under reference loading, but not in the direction of applied load. (A) Change in AF height was a poor predictor of axial strain. (B) Mean regional circumferential strains significantly decreased as the corresponding AF height decreased. (C) Mean regional radial strains showed a decreasing trend following decreasing AF height.

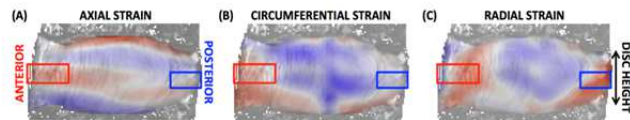


Figure 4. Internal strain in a 2D mid-sagittal plane for a representative sample. Anterior and poster AF regions are denoted in the middle third of the disc. Disc height was measured as bone-to-bone distance, but bounded within the planar AF region for analysis. (A) Axial strains in the AF showed distinct banding through the disc thickness, whereas (B) circumferential and (C) radial AF strains were more homogenous. Thus for axial strain, the full deformation response at equilibrium was not captured by the current analysis.



## TEMPORAL EVOLUTION OF EARLY DEGENERATIVE CHANGES IN STRESSED LUMBAR INTERVERTEBRAL DISCS.

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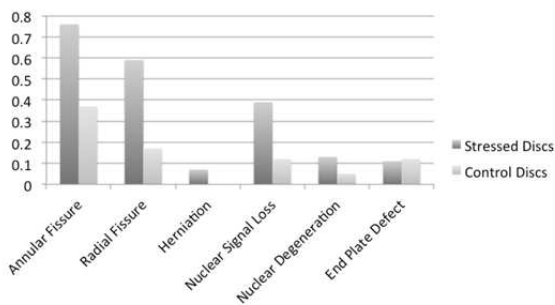
**Introduction:** In young patients presenting with low back pain due to stress-induced injury to posterior elements of lumbar vertebrae, intervertebral discs in stressed spinal segments have been shown to demonstrate higher burden of degenerative changes. Long life expectancy of these patients makes evolution of such early degenerative changes to be of obvious clinical importance; this however has not been systematically studied before. Our objective was to assess differences in temporal evolution of disc degeneration in segments of lumbar spine with and without signs of increased mechanical stresses.

**Methods:** Using two MR scans performed > 6 months apart, two radiologist evaluated intervertebral discs between T12 through S1 segments for degenerative changes in annulus fibrosus, nucleus pulposus, and end plates in 42 patients (22 males, 20 females; mean age  $16.0 \pm 3.7$  years, range 7- 25 years) with low back pain and imaging evidence of stress reaction/ fracture in lumbar spine. Data were analyzed for differences in presence and progression of disc degeneration in stressed vs. non-stressed segments.

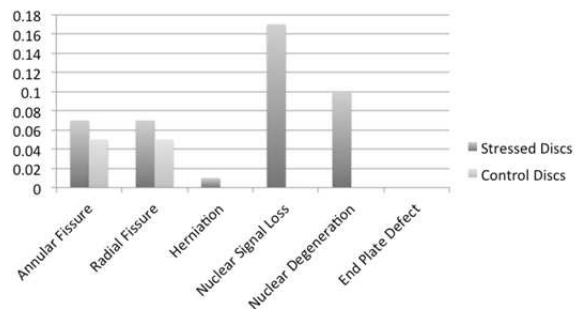
**Results:** At baseline, stressed discs had higher burden of annular fissures, radial fissures, herniation, and nuclear degeneration. End plate defect burden was comparable in stressed and control discs. At follow-up, burden of *new* annular fissures and end plate defects was comparable for stressed and control discs. However a higher proportion of stressed discs showed worsening nuclear signal intensity grade (14.3% vs. 0% control discs;  $p = 0.008$ ) and worsening nuclear Pfirrmann's degeneration grade (11.9% vs. 0% control discs;  $p = 0.017$ ). Increased risk of progressive nuclear degeneration was observed irrespective of the outcome of bony changes.

**Discussion:** Stressed discs exhibit higher burden of nuclear and annular degeneration at baseline. These discs have higher risk of *progressive* nuclear degeneration irrespective of improvement or worsening of stress-related bony changes.

### Burden of Baseline Degeneration



### Burden of Progressive Degeneration



## ANABOLIC RESPONSE OF THE INTERVERTEBRAL DISC TO EXERCISE IN HUMANS

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3. The Ottawa Hospital, Ottawa, Canada

**INTRODUCTION:** Whilst we understand which loading types are likely to injure the intervertebral disc (IVD) in humans, we have little information on whether the IVD can respond anabolically to exercise in humans and, if so, what loading protocols might facilitate this [1].

**METHODS:** We examined 25 habitual long-distance runners (>50km/wk, minimum of 5 years), 30 habitual joggers (20-40km/wk, minimum of 5 years) and 24 non-athletic individuals (no sport in last 5 years) aged 25-35 years and without a history of back pain. Lumbar IVD T2-time (spin-echo multi-echo sequence), ratio of lumbar IVD height to vertebral body height (a marker of IVD hypertrophy), and vertebral body fat fraction (VFF, via mDIXON sequence) were quantified via magnetic resonance imaging. The primary analysis evaluated the average data of all lumbar levels. To quantify physical activity patterns, participants wore a 3D accelerometer (ActiGraph) at their hip for 8d after scanning. In addition, accelerometry data were collected in 10 individuals to associate acceleration profiles with specific physical activities.

**RESULTS:** Long distance runners showed 11% higher ( $p<0.01$ ) average lumbar IVD T2-time values and joggers 9% higher ( $p<0.01$ ) than the non-sporting individuals. This effect was strongest in the central nuclear region (long-distance runners: +15% [ $p<0.01$ ], joggers: +11% [ $p<0.01$ ]). Lumbar IVD height relative to vertebral body height was 7.5% greater in the long-distance group than non-athletic individuals ( $p=0.020$ ). The positive impact of long-distance running on T2-time and IVD hypertrophy was also significant at the lower lumbar levels L3/4, L4/5, L5/S1. VFF was significantly lower in long-distance runners compared to non-athletic individuals (27.9% versus 33.5%;  $p=0.002$ ). Total physical activity, as quantified by 3D accelerometry, was not related to IVD T2-time. Rather, accelerations in the range 0.44g and 0.59g ( $g=9.81\text{m/s}^2$ ) mean amplitude deviation correlated positively with IVD T2-time. Fast walking (at 2m/s) fell within this 0.44g and 0.59g range, but walking at 1.5m/s or less fell below while running at 2.5m/s or more, jumping and sprinting were above this acceleration range.

**DISCUSSION:** The current study provides the first human data showing that a specific type of exercise is associated with positive IVD adaptations. Runners had hypertrophied and more hydrated IVD tissue (T2-time) compared to non-athletic individuals. The effect on IVD hydration was strongest in the nuclear IVD region and the impact of running was also evident at the lower lumbar spine where IVD degeneration is most prevalent clinically [2]. The same runners also had less adipose vertebral marrow which may facilitate better nutrient supply to the IVD. Accelerometry data suggested not only running but also fast walking produced accelerations in the range associated with favourable IVD hydration.

1. Belavy, Albracht, Bruggemann, Vergroesen, van Dieën (2016) *Sports Medicine* 46(4): 473-485
2. Miller, Schmatz, Schultz (1988) *Spine* 13, 173-178.

## POTENTIAL INVOLVEMENT OF UNFOLDED PROTEIN RESPONSE IN THE PATHOGENESIS OF INTERVERTEBRAL DISC DEGENERATION

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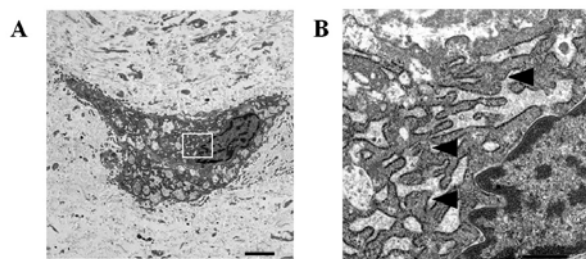
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**INTRODUCTION:** Endoplasmic reticulum (ER) is the site that synthesizes folds and modifies structural maturation of one-third of all proteins in the cell, and allows further transport of protein to the Golgi apparatus. In the process, a condition with accumulation of unfolded proteins is called ER stress. In response to ER stress, unfolded protein response (UPR) is activated in order to alleviate ER stress and sustain its function. In mammalian cells, there are three major branches of UPR: inositol-requiring protein-1 $\alpha$  (IRE1 $\alpha$ ), activating transcription factor 6 (ATF6), and pancreatic ER kinase (PERK). When the cellular stress becomes unmanageable and irreversible, UPR induces apoptosis to circumvent the ensuing damage to the surrounding milieu and cells. These events have been shown in various metabolic diseases, neurological disorders such as Alzheimer's disease and Parkinson's disease and musculoskeletal disorders including osteoarthritis, however, the interaction between intervertebral disc degeneration (IVDD) and UPR has not been well understood.

**AIM:** The main objective of this study was to clarify the involvement of UPR, especially PERK pathway, in IVDD.

**METHODS AND RESULTS:** To assess the involvement of UPR in IVDD, we first observed ER area of degenerative disc cells from surgical samples. TEM findings showed that ER of the cells was well developed and swollen, indicating that UPR was activated in the degenerative disc cells (Fig.1). Next, to investigate the activation of PERK pathway in IVDD, we evaluated the phosphorylation of PERK and the expression of PERK targeted genes, ATF4 and CHOP in human disc samples. Immunohistochemistry showed that human degenerative disc samples had higher phosphorylation status of PERK and higher expression of ATF4 and CHOP than human healthy discs. To investigate the detailed mechanisms of PERK pathway in IVDD, we silenced the expression of PERK or ATF4 in the human AF cells by lentiviral mediated shRNA system. Real-time RT-PCR analysis showed that mRNA expression of TNF- $\alpha$  and IL-6 was significantly reduced in both PERK and ATF4 silencing cells. Furthermore, we treated PERK inhibitor GSK2606414 to AF cells culturing with serum starvation and evaluated the expression of cleaved caspase-3 by Western blotting. Interestingly, treatment of GSK2606414 reduced the serum starvation mediated induction of cleaved caspase-3 expression in human degenerative disc cells, indicating that stress induced apoptosis was reduced by the inhibition of PERK pathway. Finally, to access the downstream signal of PERK pathway in AF cells, we evaluated the phosphorylation of p65 in AF cells treated with ER stress inducer Tunicamycin (TM). Western blotting clearly showed that TM induced the phosphorylation of p65.



**Fig.1 Transmission electron microscopy (TEM) findings of the human degenerative disc cells (Pfirrmann grade 4).** (A) An Example of human IVD cell. Scale bars, 2.0 $\mu$ m. (B) High magnification of IVD cell shows that the rough ER was well-developed and abnormally expanded (arrow head). Scale bars, 500nm.

**DISCUSSION:** The experiments described in this investigation demonstrate that UPR, especially PERK-ATF4-CHOP pathway regulates stress induced apoptosis as well as the expression of inflammatory cytokines through NF- $\kappa$ B signalling in AF cells. These findings lend a strong support to the hypothesis that PERK pathway is a critical mediator in the pathogenesis of degenerative disc conditions. Further studies of PERK-ATF4-CHOP pathway in IVDD may lead to the identification of new therapeutic targets relevant to disc degeneration.

## INVOLVEMENT OF AUTOPHAGY IN INTERVERTEBRAL DISC DEGENERATION AND ITS POSSIBLE CONTRIBUTION TO THE MAINTENANCE OF NOTOCHORDAL CELL HOMEOSTASIS

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**INTRODUCTION:** The intervertebral disc is the largest avascular, low-nutrient organ. Autophagy, the intracellular process by self-digestion and recycling damaged components, is an important cell survival mechanism under stress, primarily nutrient deprivation. Therefore, resident disc cells may utilize autophagy to cope with the harsh environment (low nutrition, pH, and oxygen concentration). However, clinical relevance of disc cellular autophagy is unknown. Our objective was to elucidate the involvement and roles of autophagy in human clinical and rat experimental disc degeneration.

**METHODS:** *In vitro*, human and rat disc nucleus pulposus (NP) and annulus fibrosus (AF) cells were cultured in DMEM with and without 10% FBS under 2% O<sub>2</sub> to simulate limited nutrition. Autophagic flux was assessed by Western blotting for autophagy marker LC3-II and substrate p62/SQSTM1. *In vivo*, LC3-II and p62/SQSTM1 expression was assessed by Western blotting and immunohistochemistry in human disc surgical specimens (n=20) and rat discs with sustained static compression-induced degeneration (n=24). Human discs were collected from lumbar interbody fusion surgery for spinal canal stenosis (62.0±16.2 [26–82] years; male 10, female 10; Pfirrmann degeneration grade, 3.5 ± 0.5 [3–4]). 12-week-old male Sprague-Dawley rat tails were instrumented with an Ilizarov-type device with springs and loaded at 1.3 MPa statically for up to 56 days. Further, to clarify autophagy in NP notochordal cells, immunofluorescence for notochordal brachyury, autophagic LC3, and apoptotic TUNEL was performed in discs with temporary static compression-induced milder degeneration (n=18). To observe earlier disc degeneration events, rat tails were loaded temporarily for 0, 1, or 7 days and then sacrificed at 56 days.

**RESULTS:** (1) *In vitro*, 24-h serum starvation induced increased LC3-II and decreased p62/SQSTM1 (p<0.05), consistent with enhanced autophagy. These findings were common between human and rat NP and AF cells, but more prominent in NP than AF cells (p<0.05). (2) *In vivo*, autophagy marker LC3-II and substrate p62/SQSTM1 in human NP and AF samples transiently increased in middle ages of 40–70 but subsequently decreased in older ages of >70 (p<0.05). (3) Meanwhile, LC3-II and p62/SQSTM1 expression in rat NP and AF tissues consistently decreased in response to the duration of sustained compression (p<0.05) (4) Notably, basal autophagy was remarkably higher in the rat NP than AF (p<0.05). This trend was validated by notochordal cell markers brachyury and CD24. Immunohistochemistry also demonstrated abundant autophagy-related proteins in NP notochordal cells. Moreover, four-color immunofluorescence showed (5) accelerated decreases in brachyury-positive notochordal cells relative to those in DAPI-positive total NP cells (p<0.05), (6) marked coincidence of notochordal brachyury and autophagic LC3 (p<0.05), and (7) increases in TUNEL-positive apoptotic death in brachyury-non-positive non-notochordal cells with reduced LC3 expression (p<0.05).

**DISCUSSION:** Autophagy is substantially involved in intervertebral disc degeneration. Autophagy transiently increased potentially by stress response in human middle-aged discs, but subsequently decreased in human older-aged and rat severely degenerated discs. Autophagy could be protective against apoptosis and notochordal cell disappearance, possibly contributing to the maintenance of disc health including notochordal cell homeostasis. Autophagy modulation is suggested to be a more physiological, future molecular treatment strategy for degenerative disc disease.

## STEM CELL SEEDED INJECTABLE HYDROGELS FOR INTERVERTEBRAL DISC REGENERATION IN A PRECLINICAL ANIMAL MODEL

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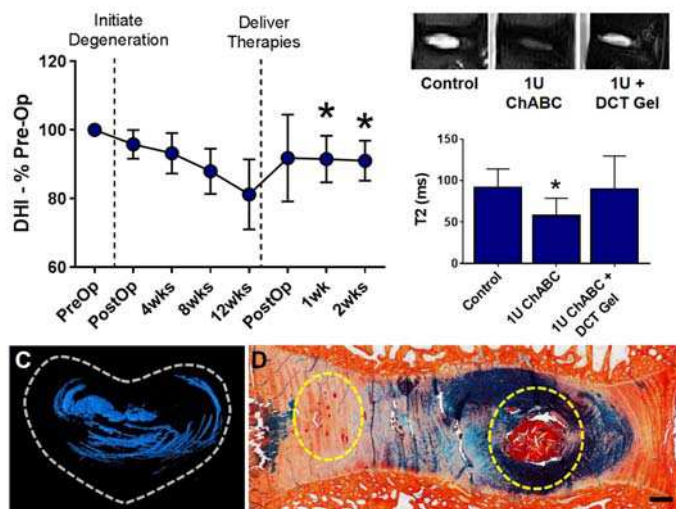
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**Introduction:** There is considerable interest in developing injectable therapeutics, including stem cells, hydrogels, and/or growth factors, to treat patients with mild to moderate, symptomatic intervertebral disc degeneration.<sup>1,2</sup> We previously developed 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>4,5</sup> The purpose of this study was to undertake a preclinical investigation establishing the feasibility and efficacy of a combined stem cell and DCT hydrogel intradiscal injection to regenerate the disc in a large animal model.

**Methods:** Surgery was performed on 3 male castrated Nubian-cross bred 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 the combined cell and hydrogel therapeutic. Four groups were randomized to the 12 degenerated lumbar discs (n=3 discs/group): DCT hydrogel alone, allogeneic MSCs + hydrogel, allogeneic MSCs preconditioned in hypoxia (2% O<sub>2</sub> for 1 week in monolayer culture) + hydrogel, allogeneic NP cells + hydrogel. Cells were transfected with GFP-actin (10 million cells/mL gel delivered) to facilitate postmortem localization, and the hydrogel was labeled with radiopaque zirconia nanoparticles to enable non-invasive imaging.<sup>6</sup> Longitudinal changes in disc height index (DHI) were quantified from lateral *in vivo* radiographs and normalized to pre-operative values. Two weeks following therapeutic delivery, animals were euthanized and motion segments assessed via MRI T2 and T1 $\rho$  mapping,  $\mu$ CT and histology (Alcian blue and picrosirius red staining of mid-sagittal sections).<sup>3</sup>



**Figure 1.** (A) Average DHI for all treated levels over time [\* =  $p < 0.05$  compared to 12 weeks]. (B) Representative T2 MRI images from each group with quantitative T2 measurements [\* =  $p < 0.05$  compared control and DCT gel injected]. DCT hydrogel visualization within the degenerative disc via 3D  $\mu$ CT reconstruction (C) and Alcian blue/picrosirius red staining (D, scale bar = 1 mm, hydrogel stained red and circled).

**Results:** Two-way ANOVA indicated no significant contribution of cell treatment to MRI or DHI outcome measures at this early time point, thus, data were pooled for analysis. A partial recovery of DHI occurred immediately following cell and hydrogel delivery, which was maintained at 89.9% of pre-operative DHI 2 weeks following treatment (Fig. 1A). The mean NP MRI T2 and T1 $\rho$  values of cell and hydrogel treated discs were not different from healthy control discs, and were significantly higher than 1U ChABC degenerated, untreated discs at 12 weeks (Fig. 1B).  $\mu$ CT illustrated that the radiopaque hydrogel was well-distributed throughout the disc, was present in both the NP and between layers of the annulus fibrosus, and had not extruded from the disc (Fig. 1C); this was confirmed by histology (Fig. 1D).

**Discussion:** Results from this study illustrate the feasibility of stem cell and hydrogel delivery as a regenerative approach using a pre-clinical animal model. These data illustrate that the hydrogel remains within the disc space over a 2 week period following delivery, and suggest that this therapeutic approach may acutely restore disc height and MRI signal of degenerate discs to near control levels.

Future work will explore the regenerative potential of combined cell and hydrogel therapies over longer durations in this preclinical model

- [1] Sakai+2015, [2] Mizuno+2006 [3] Gullbrand+2016 [4] Smith+2014 [5] Malhotra+2012 [6] Martin+2015
- Acknowledgments: This study was supported by the Department of Veteran's Affairs and the Penn Center for Musculoskeletal Disorders. The authors acknowledge Dr. Weilliam Chen for providing hydrogel components.

## COMBINED BIOMATERIALS APPROACH TO REPAIR THE INTERVERTEBRAL DISC

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**Introduction** In today's society an increasing number of people is suffering from low back pain. Possible reasons for this can be disc herniation or disc degeneration. Current treatment options are often merely combating symptoms by removal and spinal fusion for disc degeneration or for disc herniation removing extruded tissue that causes pain. Thereby, re-operation might become necessary as the nucleus pulposus is extruded again. Here we aim to reduce the risk of re-operation by investigation an approach for successful AF-injury sealing that can withstand physiological loading. Further, we aim on repairing the IVD using an inside-out approach.

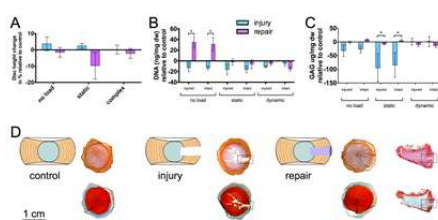
**Methods** Fresh bovine IVDs were isolated from 10 to 14 month old animals [1]. An injury was induced by a 2mm biopsy punch and the cavity formed was filled with genipin-enhanced fibrin hydrogel (Baxter) [2]. To close and seal the injury a precisely fitting silk fleece-membrane composite (Spintec Engineering inc.) was placed on the injury. Directly after this treatment control, injured and repaired IVDs were subjected to one of the following culture conditions for 14 days: 1) no loading, 2) static load of 0.2 MPa of 8 hours per day and 3) complex load consisting of 0.2 MPa load and  $0\pm 2^\circ$  of torsion at 0.2 Hz for 8 hours per day. Data to assess repair were disc height, mitochondrial activity, DNA, collagen and glycosaminoglycan (GAG) content. Further, qPCR and histology was performed.

In a second experiment different silk fleece-membrane composites were tested for cell compatibility and differentiation potential compared to unaltered silk and exogenous growth factor addition. All were made of *Bombyx mori* silk. Silk worms were engineered to incorporate growth factors i.e. GDF6 and TGF $\beta$ 3 in their silk [3, 4]. 120'000 human mesenchymal stem cells were seeded per 5x5mm<sup>2</sup> silk scaffold on the fleece side and cultured for three weeks, Fig 2D. Cell cytocompatibility was assessed by mitochondrial activity, live/dead stain and DNA content. GAG content and qPCR was performed to evaluate differentiation towards a disc-like phenotype.

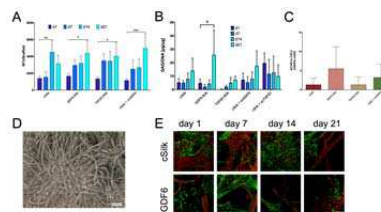
**Results** Height could not be restored but DNA and glycosaminoglycan (GAG) content is stabilized in the range of healthy control discs during loaded culture. Histology shows a big defect in injured discs that could be filled in the repaired discs. Cells on all silk types were active and proliferating, Fig 2A, E. GAG/DNA ratio is increasing over culture period except in group with exogenous TGF $\beta$ 3, Fig 2B. qPCR analysis of aggrecan (ACAN) and collagen 2 (Col2) indicates differentiation of hMSC towards a nucleus pulposus (NP)-like phenotype, Fig 2C.

**Discussion** The AF injury could be successfully closed with the genipin-enhanced fibrin hydrogel and the silk and withstand 14 days of physiological loading. Further, biochemical assays and histology indicate that injury and repair influence the whole discs. The silk fleece-membrane composite with GDF6 was able to induce an NP-like phenotype. Combining these two biomaterials might lead to a new treatment approach.

**Acknowledgements** This project is supported by the Gebert Rűf Stiftung project # GRS-028/13.



**Figure 1:** Results of organ culture experiments. **A** Disc height, **B** DNA content and **C** GAG content, all relative to control disc and comparing a sample near the injury/repair site (injured) and opposite untouched IVD side (intact). (*p*-value  $\leq 0.0284$ ) **D** Histology of discs: top row=H&E, bottom row=Safranin-O/Fast Green.



**Figure 2:** Analysis of in vitro experiments on silk fleece-membrane composites. **A** Mitochondrial activity (*p*-value: \* $0.0184$ , \*\* $0.0026$ , \*\*\* $0.0003$ ) and **B** GAG/DNA ratio (*p*-value= $0.037$ ; all *n*=5, mean  $\pm$ SEM. **C** ACAN/Col2 gene expression ratio. **D** Overview picture of silk fleece side. **E** Live/dead stain of cells on silk scaffold living cells = green (calcein-AM), silk = autofluorescence in the red range, scale bar = 100 $\mu$ m.

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## GENERATION INTERVERTEBRAL DISC-LIKE CELLS FROM PERIPHERAL BLOOD CELLS

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**Objective:** An attempt to reprogram peripheral blood cells(PBCs) into human induced pluripotent stem cell (hiPSCs) as a new cell source for intervertebral disc repair.

**Methods :** We generated intervertebral disc(IVD)-like cells from human peripheral blood via iPSCs using integration-free method. Peripheral blood cells (PBCs) were either obtained from human blood bank or freshly collected from volunteers. After transforming PBCs into iPSCs, the newly derived iPSCs were further characterized through karyotype analysis, pluripotency gene expression and cell differentiation ability. iPSCs were differentiated through multi-steps including embryoid body (EB) formation, hiPSCs-mesenchymal stem cells (MSCs)-like cells expansion, and transforming growth factor(TGF)-beta1 induction differentiation for 21 days. Cell phenotype was then assessed by morphological and biochemical analysis, as well as expression studies.

**Results :** hiPSC derived from peripheral blood cells were successfully generated, which were characterized by fluorescent immunostaining of pluripotent markers and teratoma formation *in vivo*. Flow cytometric analysis showed that MSCs markers *CD73* and *CD105* were present whereas hematopoietic markers *CD34* and *CD45* were absent in mono-layer cultured hiPSCs-MSC-like cells. Both Alcian blue and toluidine blue staining of TGF-beta1 induction differentiation pellets showed positive, and further confirmed by positive immunochemistry of collagen II and X stain. The glycosaminoglycans (GAG) content was significantly increased and the expression levels cell markers of *Col2*, *Col10*, *Sox9* and *Aggrecan* were significant higher .

**Conclusion :** This study indicated the PBCs may represent an attractive source to obtain IVD-like cells in a patient-specific and cost-effective approach, although modification of cultural conditions may required to approach the more likely phenotype.

**Key words:** peripheral blood cells, induced pluripotent stem cells, intervertebral disc-like cells

## TRANSFORMATION OF THE NUCLEUS PULPOSUS INTO CONNECTIVE TISSUE - A METHOD FOR BIOLOGIC FUSION OF A SPINAL SEGMENT?

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### **Introduction:**

The exact pathophysiological mechanisms of chronic low back pain are still not fully understood. It has been suggested that leakage of noxious substances from the nucleus pulposus through annular tears that trigger nociceptors on the superficial layers of the annulus fibrosus may be one mechanism. Another mechanism may be the destabilization of a vertebral segment during the ageing process. Usually, the vertebral segment is restabilized at older age when the disc has been transformed into connective tissue. At this stage, there will be less leakage of nucleus pulposus fluid. It is also well known that the incidence of discogenic pain is dramatically decreased when this stage is reached. Our hypothesis is that an induced transformation of the disc into connective tissue, by pharmacological means, would radically lower the prevalence of low back pain, since it will both reduce leakage and induce a restabilization of a vertebral segment. The natural intradiscal production of collagen is induced by increasing lactate levels due to the decreasing nutrition of the disc from the end plates. We therefore choose to mimic nature in initiating the connective tissue transfer by letting lactate increase the production of collagen following intradiscal injection.

### **Methods and results:**

**In vitro testing:** We defined a suitable composition and concentration of the formulation to be injected by exposing cultured human nucleus pulposus cells and fibroblasts. The compositions comprised lactic acid, the radiopaque agent iohexol and buffers to define the optimal combination. For end point, collagen production was measured by spectrophotometry. These results provided guidelines to the most effective dosage for the in vivo experiments.

**In vivo testing:** The active formulation was injected into a lumbar disc in the pig with only iohexol as control. Analyzes were performed after 7 days (n=2), 30 days (n=16) and 90 days (n=4). Flexural rigidity of the injected discs and the two adjacent discs was measured as distance between the lateral processes of the two vertebrae adjacent to the tested disc in lateral and contralateral flexion. There was a marked difference in flexural rigidity between the discs injected with the active formulation and the iohexol injected discs as well as between the formulation injected disc and the two adjacent discs at all durations. After the measurement, the discs were transected and the area of the intradiscal space was measured using image analysis. After 7 days the formulation injected discs had a disc space that was markedly reduced and after 30 days the disc space had almost disappeared. The ingrowing connective tissue was lamellar and resembled native annulus fibrosus. After 90 days the disc space had disappeared and the annulus was hard and difficult to incise.

### **Discussion:**

The results indicate that the nucleus pulposus will be replaced by connective tissue following intradiscal injection of lactic acid. However, only clinical studies will demonstrate if this might be of benefit in the treatment of discogenic low back pain. Nevertheless, "biologic fusion" of a spinal segment could also be useful in other conditions such as scoliosis, spondylolisthesis, vertebral fractures and coccygodynia.

## CELL CARRIER AND DISC DEGENERATIVE STATE INFLUENCE INTERVERTEBRAL DISC RESPONSE TO STEM CELL TREATMENT

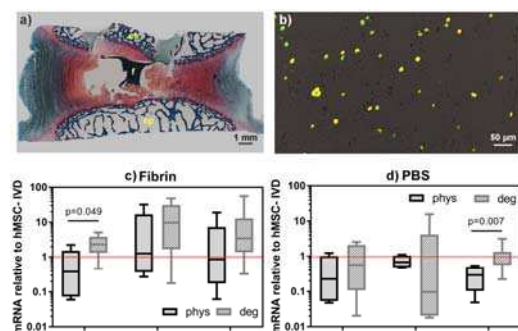
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**Introduction:** *In vitro* and *in vivo* studies have evidenced that mesenchymal stem cells (MSCs) contribute to intervertebral disc (IVD) regeneration by differentiation toward the disc phenotype and matrix synthesis and/or by paracrine signaling to endogenous cells and restoration of a healthier disc phenotype in degenerative discs. It has been suggested that the severity of disc degeneration may influence the therapeutic effect of MSCs. However, this has not been verified in a large animal model. Therefore, the goal of the present study was to analyze the effects of implanted MSCs in a bovine whole IVD organ culture model in a mechanical loaded bioreactor. We hypothesized that (i) degenerative and healthy IVDs would respond differently to implanted MSCs and (ii) the cell carrier would influence MSC effect.

**Methods:** Bovine caudal IVDs with endplates were cultured under physiological (0.1 Hz and sufficient glucose) or degenerative (10 Hz and limited glucose) conditions in a bioreactor for 7 days. A nucleotomy was performed through the endplate in order to reproduce cell delivery through the transpedicular approach. Human MSCs from 6 independent donors were applied in fibrin gel or saline solution ( $4 \times 10^6$  cells/mL) and IVDs cultured under physiological conditions for additional 7 days; fibrin and saline without MSCs were used as controls. Cell viability, histology, disc height and gene expression analyses were performed to evaluate regeneration.



**Figure 1:** a) Safranin O/Fast green stained sagittal section of a partially nucleotomized bovine intervertebral disc (IVD) restored with fibrin gel, f = fibrin, es = endplate stopper, ep = endplate; b) Calcein AM stained PKH26 labelled human mesenchymal stem cells (MSCs) in fibrin gel following 7 days of culture in whole IVDs under dynamic loading, yellow cell = live cell, red cell = dead cell; c) and d) expression of collagen type I (COL1), collagen type II (COL2) and aggrecan (ACAN) in discs with degenerative or physiological history with MSCs in fibrin or saline solution (PBS). Discs with carrier alone (fibrin or PBS) were used for normalization.

**Results:** Fibrin filled and remained in the nucleotomized space (Fig.1a), and MSC viability was maintained in nucleotomized IVDs cultured under dynamic loading (Fig.1b). IVD response to MSC treatment was conditioned by disc degenerative state and cell carrier. Degenerative IVDs showed an anabolic response to MSC delivery within fibrin gel (Fig.1c), while MSC contribution was limited when cells were applied with saline solution (Fig.1d). Moreover, MSC administration with fibrin gel induced a 2-10 fold change in aggrecan (ACAN) and collagen type II (COL2) expression of degenerative-loaded disc cells compared to IVDs receiving fibrin alone. On the other hand, physiologically-loaded IVDs showed a scarce reaction to MSCs, independent carrier type. Finally, MSCs showed significantly higher expression of ACAN and carbonic anhydrase when implanted into physiological *versus* degenerative discs.

**Discussion:** Significantly different reactions of host IVD cells and graft MSCs were found depending on the IVD degenerative state and the cell carrier. The use of a carrier capable of withstanding dynamic loading within a partially-nucleotomized IVD seems to be of key importance. It is likely that MSCs could sense dynamic loading within this carrier, which has been shown to trigger MSC chondrogenesis. In

addition, the exchange of paracrine signals between MSCs and disc cells could be facilitated by dynamic loading conditions. In our experimental setting, saline was an inefficient carrier for MSCs, possibly due less precise localization of MSCs in the IVD space and reduced sensitivity to loading. In conclusion, the response of large animal nucleotomized IVDs to MSC treatment was conditioned by both IVD degenerative state and MSC carrier. Whole organ culture bioreactors provide a useful setting for the evaluation and translation of stem cell therapies.

## HUMAN BONE MESENCHYMAL STEM CELLS PROTECT OR ACTIVATE NUCLEUS PULPOSUS CELLS BY CO-CULTURE UNDER HYPOXIA ENVIRONMENT

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**Introduction:** Numerous studies about the co-culture of bone marrow mesenchymal stem cells (BMSCs) with nucleus pulposus (NP) cells have focused on the differentiation of stem cells towards the NP cell phenotypes in various conditions. Some reports suggested that stem cells exert a multivariate influence on degenerated NP cells in animals. These studies showed that BMSCs can upregulate the viability of NP cells in a direct co-cultured system. Despite of the effectiveness of BMSCs on NP cells, there are few studies focusing on the effects of human BMSCs on NP cells especially under hypoxia. Therefore, our study aims to establish a co-cultured model of human NP cells with human BMSCs, so as to explore the biological effect of BMSCs on NP cells under hypoxic environment.

**Methods:** Human NP cells and BMSCs from patients were isolated and cultured. Then they were divided into two groups. Group A had only NP cells and the group B had NP cells co-cultured with BMSCs. The two groups were cultured for 14 days. The NP cells morphology of both groups was observed and the flow cytometry and scanning electron microscopy (SEM) were used to evaluate the cell death. We also assessed the cell proliferation with CCK8 test, and further used real-time (RT-) PCR, western blot and immunostaining to determine the expression of the extracellular matrix (ECM) and NP cells special phenotype markers.

**Results:** The expressions of proteoglycan, collagen II, sox-9, KRT19, CA12 and HIF1 $\alpha$  were increased under hypoxia and co-cultured with BMSCs. The CCK8 assay showed that compared with cultured NP cells alone, NP cells co-cultured with BMSCs group had more NP cells after 14 days ( $p < 0.05$ ). The percentage of apoptosis cells in NP cells culture group is higher than in co-culture group ( $p < 0.05$ ). RT-PCR and Western blot showed that type II collagen and elastin polysaccharide, Sox-9, krt19, CA12, HIF1 $\alpha$  synthesis secretion in NP cells co-cultured with BMSCs group were significantly higher than those of the NP cells cultured alone group. Immunofluorescence staining and Elisa also showed that NP cells co-cultured with BMSCs group increased type II collagen and protein polysaccharide, Sox-9, KRT19, CA12 and HIF expression.

**Discussion:** Our study evaluated the effect of human BMSCs on human NP cells under hypoxia by direct co-culture which is more close to the natural condition in vitro. This is the much different compared with the previous research. Our study also showed that BMSCs might protect or activate NP cell from death and degradation by regulating ECM and modulator genes. Although this study was only done in vitro, the protective effect of BMSCs was found in present study provides an essential understanding and expands our knowledge as to the utility of BMSCs therapy for intervertebral disc regeneration in the future.

## COEXISTING CERVICAL AND LUMBAR DISC DEGENERATION AND ASSOCIATED MRI PHENOTYPES: A LARGE-SCALE POPULATION-BASED STUDY

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**Introduction:** It remains unknown whether lumbar disc degeneration and patterns therein along with associated lumbar phenotypes (e.g. Modic changes, disc bulge/extrusion) are associated with coexisting cervical degenerative findings on magnetic resonance imaging (MRI). Furthermore, the risk factors attributing to such a manifestation have not been addressed. As such, the following large-scale population-based study addressed the association coexisting cervical and lumbar disc degeneration and other MRI phenotypes as well as risk factors attributed to their development.

**Methods:** Sagittal T2-weighted MRIs were obtained of the entire spine in 2,762 subjects of a population-based cohort of Southern Chinese origin. Imaging assessment was performed of the cervical and lumbar spine to assess the presence and patterns of disc degeneration and other phenotypes. Lumbar disc degeneration was assessed via the Schneiderman scoring scheme and summated to obtain a DD Score. Subjects were further stratified into two groups: Group 1 entailed individuals with normal cervical spines (n=1,847) and Group 2 consisted of individuals with cervical degenerative findings (n=915). Subject demographics were also assessed.

**Results:** Overall, 39.4% were males and 60.6 % were females with a mean age of 41.1 years. The mean age of Group 1 subjects was 38.8 years and Group 2 individuals was 45.8 years (range: 18.2 - 88.4 years) ( $p<0.001$ ). The mean age of subjects with no lumbar disc degeneration was 33.9 years and those with cervical findings was 43.9 years ( $p<0.001$ ). Of those individuals with non-degenerated lumbar discs, 18.5% presented with Group 2 findings. Alternatively, 38.9% of individuals with lumbar disc degeneration had coexisting cervical findings and higher age-adjusted lumbar DD scores ( $p<0.001$ ). A statistically significant difference was noted between lumbar age-adjusted disc bulge/extrusion, number of involved levels, region-specific disc degeneration, and Modic changes with Group 2 ( $p<0.05$ ). The most significant factor associated with Group 2 was an increase in the number of levels with lumbar disc degeneration (age & sex-adjusted: 1 level OR: 1.4; 2 levels OR: 1.5; 3 levels OR: 1.8; 4 levels OR 2.7; 5 levels OR: 3.7;  $p<0.05$ ).

**Discussion:** This is the largest MRI study to address the association of cervical to that of lumbar phenotypes on MRI. The presence and patterns of lumbar disc degeneration were significantly associated with cervical degenerative findings, suggesting that perhaps they share a common pathway of degeneration and findings may be predictive. Understanding the interplay between lumbar and cervical degenerative phenotypes and their associated clinical consequences may assist in understanding the etiology of disease and in designing preventative measures for spine degeneration.

## LACK OF SIGNIFICANT DIURNAL T2-VALUE CHANGES IN LUMBAR DISCS WITH AXIAL LOADING DURING MRI (aIMRI)

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### Introduction

The interaction between the intervertebral disc's (IVD) internal pressure and compressive forces generates a dynamic IVD behavior. With conventional MRI both reduced IVD height and IVD volume as well as reduced T2-values over the day has been reported. Recently, axial loading during MRI (aIMRI) of the spine was shown to instantaneously alter the IVD's T2-values, with for example a decrease in posterior annulus fibrosus (AF) respectively increase in nucleus pulposus (NP) induced by spinal loading<sup>1</sup>. The aim of the present study was to investigate whether there is a diurnal variation in IVD T2-values when using aIMRI. This is of importance for the planning of when to perform aIMRI investigations and for interpretations of aIMRI findings in relation to clinical symptoms.

### Methods

aIMRI with T2 mapping, of the lumbar spines of 6 healthy volunteers (30 IVD's), was performed at three different time points during a day (at 7am, 12am and 5pm). The mean age of the volunteers was 38 years (range 27-63). The IVD's had different Pfirrmann grades; 3 with grade 1, 18 grade 2, 5 grade 3, 3 grade 4 and 1 grade 5. T2-values were measured by segmentation of the IVD into 5 volumetric (10 mm width) regions of interest (ROI). Each ROI constituted 20% of the midsagittal IVD diameter with the endplates delineating each ROI craniocaudally. ROI 1 representing anterior AF, ROI 3 NP, ROI 5 posterior AF and ROI 2 respectively 4 representing the NP-AF interface.

### Results

For aIMRI, the T2-values of the entire IVD varied between 38 -138ms at 7am, 33-143ms at 12am respectively 31-147ms at 5pm (Figure 1). Large regional IVD variations were shown at all time points during the day with mean T2 values at 7am 35ms in ROI 1, 102ms in ROI 2, 128ms in ROI 3, 118ms in ROI 4 and 47ms in ROI 5, with similar values registered both at 12am and 5pm (Figure 2). There were no significant alterations of the IVD T2-values over the day, neither for the entire IVD ( $p=0.4$ ) nor for the ROI's ( $p=0.2-1.0$ ). A trend towards a decline in T2-value over the day was however seen in ROI 2-4. Individual IVD's displayed large T2-value variations, most pronounced in less degenerated IVD's, with T2-values either increasing or decreasing at 12am as compared with 7am. However, no significant T2-value variations over the day were found, neither for the entire IVD nor for the various ROI's, when correlating with Pfirrmann grades ( $p<0.3$ ).

### Discussion

With aIMRI, the diurnal effect on the IVD was neglectable in relation to the large regional IVD variances. Also, the diurnal IVD variations were statistically not significant. Since aIMRI combined with T2-mapping recently has been suggested as a promising tool to reveal functional IVD characteristics, this new knowledge is of importance. The lack of significant diurnal IVD variation with aIMRI is an advantage both for research purposes as well as in the clinical setting, giving comparable and robust data regardless of at what time-point the MRI is performed.

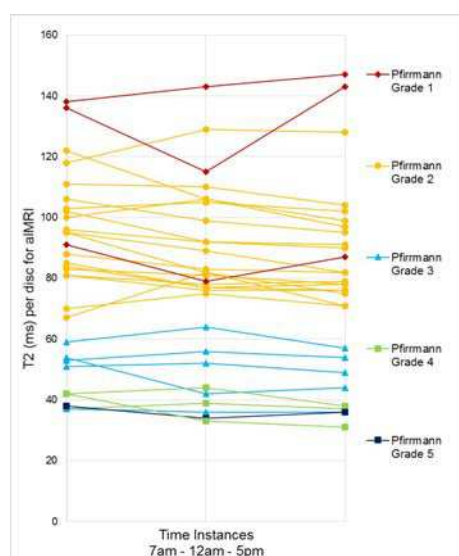


Figure 1.

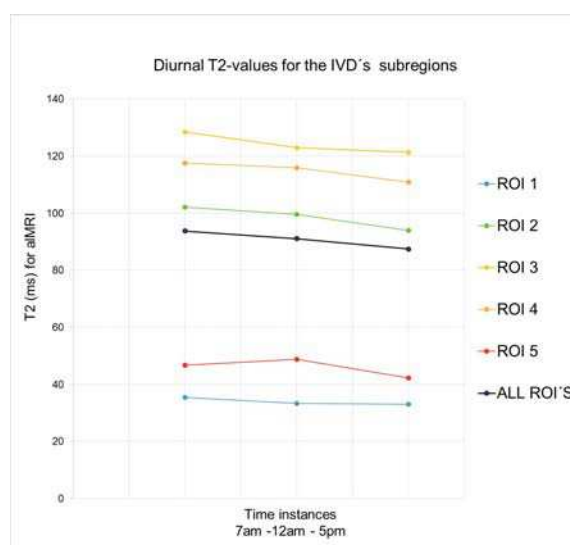


Figure 2.



## LUMBAR HIGH-INTENSITY ZONES ON MRI: IMAGING BIOMARKERS FOR SEVERE, PROLONGED LOW BACK PAIN AND SCIATICA IN A POPULATION-BASED COHORT

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**Introduction:** High-intensity zones (HIZs) of the lumbar spine can be visualized on magnetic resonance imaging (MRI). Their clinical relevance has been scrutinized and regarded as purely an incidental finding. However, previous studies largely consisted of small sample sizes, patient-based cohorts, and inadequate analysis of its association with other MRI phenotypes (e.g. disc degeneration, disc displacement, Modic changes) and the clinical profile. The purpose of this study was to assess the relationship of lumbar HIZs on MRI with LBP, sciatica, and back-related disability in a cross-sectional, population-based cohort study of Southern Chinese volunteers.

**Methods:** A total of 1,214 subjects with T2-weighted 3T sagittal MRI of L1-S1 were assessed. Presence, single level, multilevel homogeneous (HIZs of the same morphological type and location) and multilevel heterogeneous (HIZs of variable morphological types and location) HIZs based on the authors' classification scheme according to disc level, shape (round type, fissure type, vertical type, rim type, and enlarged type), and location of HIZs within the disc (posterior or anterior) as well as other MRI phenotypes were assessed at each level. Associations with prolonged/severe LBP (LBP lasting at least 30 days with the worst experience at least VAS 6), sciatica (sciatica lasting at least 30 days) and back-related disability (Oswestry Disability Index (ODI) scores  $\geq 15\%$ ) were correlated with HIZ profiles.

**Results:** There were 718 individuals with HIZs (59.1%). Of the 718 HIZ subjects, 53.3% had single HIZ (n=383), 32.5% had 2 HIZs (n=233), 11.1% had 3 HIZs (n=80) and 3.1% had 4 HIZs (n=22). For the 335 multi-level HIZs subjects, 40.0% had homogeneous HIZs (n=134) and 60.0% had heterogeneous HIZs (n=201). Disc degeneration and disc displacement were more prevalent in individuals with HIZ (p<0.001). Based on adjusted multivariable regression analyses, individuals with homogeneous or heterogeneous HIZs were significantly associated with LBP (odds ratio (OR) range: 1.53 to 1.57; p<0.05). Individuals with homogeneous HIZs had a higher risk of sciatica (OR: 1.51, p<0.05), whereas other HIZ variables were not. No significant association was observed between HIZs and back-related disability (p>0.05).

**Conclusions:** This is the first large-scale study to note that HIZs of the lumbar spine are clinically-relevant imaging biomarkers that are independently and significantly associated with prolonged/severe LBP and sciatica. Furthermore, various patterns of HIZs appear to be more related to symptoms. HIZs are important lumbar phenotypes that should be noted in the global imaging phenotype assessment of the spine, which may have immense clinical utility.

## SIGNIFICANCE OF THE DEGENERATIVE CHANGES ON LUMBAR PLAIN MAGNETIC RESONANCE IMAGING IN THE DIAGNOSIS OF LOW BACK PAIN IN THE GENERAL POPULATION—THE WAKAYAMA SPINE STUDY

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**Purpose:** The relationship between degenerative changes observed on magnetic resonance imaging (MRI) and occurrence of low back pain (LBP) is not yet completely understood. Disc degeneration, endplate changes, vertebral deformity due to osteoporotic fracture, and spinal stenosis have been reported as possible causes of LBP. However, these degenerative changes often coexist and can synergistically cause LBP. The purpose of this study was to elucidate the association between degenerative changes on observed MRI and LBP in a general population.

**Methods:** We used an established Japanese population-based cohort in this cross-sectional study. Of the 952 subjects who participated in the second survey of the Wakayama Spine Study, a total of 794 participants (men, 239; women, 555; mean age, 63.6 ± 13.1 years) underwent MRI evaluation. Lumbar disc degeneration (Pfirrmann classification: grade 1-5), endplate changes (Modic type 1, 2, and 3), and morphometric fracture in the vertebral bodies (semiquantitative method: grade 0-3) were evaluated on sagittal MRI. Percentage of fatty degeneration in the paravertebral muscle (PVM) at L1 upper endplate level and cross-sectional area (CSA) of the dural tube at L1/2-L5/S1 levels were measured on axial MRI using DICOM software. Information on the presence of LBP within 1 month and visual analog scale (VAS) scores for current LBP was obtained via patient interviews. The relationship between the degenerative changes and the presence/intensity of LBP was determined using multivariate regression analysis models, after adjusting for age, sex, and body mass index.

**Results:** LBP was present in 37% and 40% of men and women, respectively. Of these, 36% of the subjects experienced pain of intensity more than 40 mm on VAS. Factors significantly associated with the presence of LBP were disc degeneration (grades 4-5; odds ratio [OR], 2.6; 95% confidence interval [CI], 1.3-5.6), endplate change (Modic type 1; OR, 1.6; 95% CI, 1.0-2.6), and spinal stenosis (minimum CSA < 100 mm<sup>2</sup>; OR, 1.6; 95% CI, 1.2-2.2). Area under the curve in this logistic model was 0.61. Significantly associated factors with LBP on the VAS were the percent fatty degeneration of the PVM (standardized partial regression coefficient, 0.11; p=0.0106), sum of the grades of disc degeneration (0.16; p=0.0009), and the minimum CSA (-0.13; p=0.0005).

**Conclusion:** Disc degeneration, Modic type 1 endplate change, spinal stenosis, and PVM degeneration were significant associated factors of LBP although the contribution of these factors was small in the general population.

## CLASSIFICATION CRITERIA FOR NEUROGENIC CLAUDICATION CAUSED BY LUMBAR SPINAL STENOSIS

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### INTRODUCTION

Classification criteria are recommended for diseases that lack highly specific biomarkers in order to improve homogeneity in clinical research. Since imaging evidence of lumbar spinal stenosis (LSS) may not be associated with symptoms, clinical classification criteria based upon patient symptoms and physical examination findings are required.

### MATERIALS AND METHODS

Phase 1: Seventeen spine specialists (clinicians and researchers) from 8 countries participated in a Delphi process, using an internet program, to rank symptoms and signs which suggest LSS as the cause of NC or DH as the cause of RP.

Phase 2: Nineteen different spine specialists (surgeons and non-surgeons) from 5 countries recruited patients during office visits. Only patients who could be and classify with a high degree of confidence as having with either: 1) NC caused by LSS 2) RP caused by LDH or 3) non-specific low back pain (NSLBP) with non-specific leg pain radiation, were included. Patients completed survey items and specialists documented examination signs. Signs and symptoms present in  $\geq 10$  patients were analyzed by using Generalized Estimating Equations (GEE). Patients with RP caused by LHD or NSLBP served as controls. Items with  $p < 0.1$  in univariate analysis were entered in the multivariate analysis. A score to predict NC caused by LSS was developed based on the coefficient of the GEE, and used to obtain a ROC curve and the associated area under the curve (AUC).

**RESULTS** A list of 47 physician-reported findings and 28 patient-reported symptoms were selected by the group of spine specialists during the 1<sup>st</sup> phase. For the 2<sup>nd</sup> phase, 209 patients with high confidence in the diagnosis were included 63 NC caused by LSS, 89 RP caused by DH, and 57 NSLBP with non-specific leg pain radiation. Items which predicted NC with a  $p$ -value  $< 0.1$  included age  $> 60$ , bilateral leg pain, leg pain relieved by sitting, leg pain decreased by leaning or flexing, positive 30 seconds extension test, negative straight leg raise test. The N-CLASS (Neurogenic CLAudication caused by lumbar Spinal Stenosis) score was derived in order to produce an easy to use, weighted score without modifying the accuracy.

N-CLASS criteria	POINTS
Age $> 60$	4
Positive 30 seconds extension test	4
Patient report pain in both legs	3
Patient report leg pain relieved by sitting	3
Patient report leg pain decreased by leaning or flexing	3
Negative straight leg raise test (i.e. absence of leg pain at 60° elevation).	2

The patient is classified as having Neurogenic Claudication caused by LSS if the total score is 11 or more. The score has an AUC of 0.91 with a specificity of 92.1% and a sensitivity of 80.0%.

**CONCLUSION** An international collaboration of surgeon and non-surgeon spine specialists produced a set of diagnostic criteria with high specificity and sensitivity for identifying patients with NC caused by LSS. Using this set could improve the quality of basic science and clinical research in this field by improving homogeneity within groups of patients.

## RISK FACTORS FOR PEDIATRIC SPINAL PAIN

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**Introduction:** Spinal pain is very common in modern societies causing high levels of disability and increasing overall healthcare expenses. According to the evidence neck pain and low back pain (LBP) can start in early childhood and by the end of adolescence it reaches the prevalence rate of adult LBP. Pediatric spinal pain can lead to LBP in adulthood, therefore primary prevention should target children. The aim of our prospective study was the development and validity analysis of a patient's reported questionnaire (PRQ) that is capable to measure spinal pain prevalence in childhood and to evaluate the possible environmental factors leading to this condition.

**Methods** The questionnaire for children was developed by an expert group and the consensus achieved a final version including 22 items. Section 1 contains questions about the amount of physical activity and mechanical load in terms of lifestyle factors. Section 2 covers the child's health care seeking behaviour and general wellbeing. Section 3 is addressed at the parents whether spinal disorder among relatives occurred in the history. The methodological quality of the questionnaire was measured by testing the reproducibility. The test-retest cohort included 146 school children. The validity analysis was carried out in a prospective study. Second to eighth graders filled out the questionnaire. The test cohort (N=945) and the validity cohort (N=881) were generated by the random selection of the participant school-classes. Data was analysed by uni- and multivariate logistic regression models and the performance of the final multivariate model was calculated by the receiver operating characteristics (ROC) method.

**Results:** The test-retest analysis showed adequate reliability ( $Kappa > 0,7$ ) in most of the lifestyle factors and the spinal pain prevalence items.

"Spinal pain for days" prevalence was 13% in the test- and 12.4% in the validity cohort. The final predictive multivariate regression model was built up by seven risk factors: "age older than 12y old", "studying for more than 2 hours in the afternoon", "watching TV for more than 2 hours", "uncomfortable school desk", "sleeping problems", "general well-being", and "spinal disorder among relatives". A good prediction power of the model was confirmed on the validation cohort (AUC=0.76 and 0.71 respectively). Children having one factor have got a risk of 5% to suffer from spinal pain for days while the risk for that is 50% among those who have got 5 or more risk factors ( $p < 0.001$ ).

**Discussion:** The developed risk assessment tool can be used to identify the modifiable environmental and lifestyle factors causing pediatric spinal pain. These findings help to stratify the children according to their individual risk and to develop effective primary prevention actions of adult chronic low back pain.

## GLOBAL CONSENSUS OF LOW BACK PAIN OUTCOME INDICATORS FOR OLDER ADULTS

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### Introduction

Low back pain (LBP) is the most common and disabling musculoskeletal disorders among older adults. Multiple population-based studies have reported that the 1-year prevalence of LBP is between 13% and 50%. In older adults (>60 years of age), the prevalence of mild/moderate LBP decreases while the prevalence of chronic or debilitating LBP increases. Because older adults have different physical and psychosocial needs (e.g. medical comorbidity or self-care problems) as compared to younger adults, clinicians and researchers need to consider the use of age-relevant outcome measures to evaluate their clinical status and response to treatment. Unfortunately, since existing LBP assessment tools do not examine age-specific physical and psychosocial domains of function, participation and quality of life, these tools may not truly examine various factors affecting the well-being of older adults with LBP. "Crowdsourcing" is a new research approach that allows the collection of global opinions from clinicians regarding various clinical issues. As such, the objective of the current study was to use crowdsourcing to solicit global consensus from clinicians on various LBP outcome indicators for older adults.

### Methods

An online pairwise wiki survey was created to invite general practitioners, orthopedic surgeons, physiatrists, physiotherapists, chiropractors, occupational therapists around the world to vote and to prioritize various LBP outcome indicators for older adults. Seven seed outcome indicators were posted for voting while respondents were encouraged to suggest new indicators for others to vote. The survey website was promoted on social media of various healthcare professional organizations. An established algorithm calculated the mean scores of all outcome indicators. A score > 50 points implies that the indicator has > 50% chance of beating another randomly presented indicator.

### Results

At total of 128 respondents from six continents casted 2,466 votes and proposed 14 new outcome indicators over 42 days. Outcome indicators pertinent to improvements of physical (e.g. being able to perform 80% of the daily activities prior to the current episode of LBP) and age-related social functioning (i.e. being able to take care of grandkids) scored > 50 points while self-perceived reduction of LBP (i.e. minimum 2 point decreases in visual analogue scale) scored 32 points

### Discussion

Respondents generally deemed that functional improvements were more important LBP outcome indicators than symptomatic improvements. Our results stress that age-specific outcome indicators should be integrated into future LBP outcome measures for older adults, representing a paradigm shift of previous long-held beliefs on LBP assessment. Importantly, our study has demonstrated that crowdsourcing is a feasible method for soliciting opinions from clinicians worldwide to inform clinical practice and research.

## THE PREVALENCE OF LOW BACK PAIN AND ITS ASSOCIATED FACTORS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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### INTRODUCTION:

Compared to cervical lesions, thoracolumbar symptoms and lesions in patients with rheumatoid arthritis have not been fully investigated. This study aimed to identify the prevalence of low back pain (LBP) and its associated factors in patients with rheumatoid arthritis (RA).

### MATERIALS AND METHODS:

In this cross sectional study, 777 patients (153 men, 624 women) who answered Roland-Morris disability questionnaire (RMDQ), Short Form-8 (SF-8), health assessment questionnaire (HAQ) and VAS for LBP were enrolled. Parameters of coronal and sagittal spinopelvic alignment (Cobb angle, coronal shift of C7 plumb line [C7PL], PT, PI, SS, LL, TK, CL, TPA, SVA), the presence and numbers of vertebral fractures and spondylolisthesis were measured using whole spinopelvic radiographs in standing position. Dual X-ray absorptiometry of hip joint was also used to evaluate bone mineral density (BMD). Patients with previous spine surgery and/or bilateral total hip arthroplasty were excluded. The patients with VAS >30 (moderate or severe LBP) were designated as Group P; VAS ≤30, Group N. Correlations between LBP and parameters of alignment, BMD, RMDQ, SF-8, HAQ score and possible related variables (age, sex, age of onset, disease duration, surgical history, medical history [use of corticosteroid, methotrexate and biological agents]) were calculated. Logistic regression analysis was performed to determine the independent associated factors.

### RESULTS:

Mean age, mean age at onset and mean disease duration were 63.3, 51.8 and 11.5 years. The prevalence of LBP (VAS >0) was 62.7% and that of moderate or severe LBP was 22.4%. Group P patients were significantly older age ( $p < 0.001$ ), greater Cobb angle and coronal shift of C7PL ( $p < 0.001$ ), more PT, SS, LL, TPA, SVA ( $p < 0.001$ ), more CL ( $p = 0.003$ ), lower BMD ( $p = 0.025$ ), longer disease duration ( $p < 0.001$ ), lower MTX dose ( $p = 0.007$ ), more vertebral fractures ( $p < 0.001$ ), more spondylolisthesis ( $p = 0.002$ ), more ever ( $p = 0.005$ ) and current ( $p = 0.042$ ) corticosteroid users, more surgical history ( $p = 0.004$ ) and more frequent medication for osteoporosis ( $p < 0.001$ ). RMDQ and all subdomain scores in SF-8 were significantly worse in Group P than those in Group N ( $p < 0.001$ ). According to logistic regression analysis, the associated factors of patients with moderate or severe LBP were coronal shift of C7PL, TPA and disease duration (OR, 1.029 and 95%CI, 1.007-1.052; OR, 1.055 and 95%CI, 1.033-1.077; OR, 1.024 and 95%CI, 1.000-1.047, respectively).

### CONCLUSIONS:

The prevalence of LBP was 62.7%, which approximately two or three times higher than that previously reported in general population. The RA patients with LBP demonstrated spinopelvic malalignment, imbalance and poorer QOL. Moderate or severe LBP in patients with RA was associated with coronal shift of C7PL, TPA and disease duration.



## INITIAL PROMIS SCORES PREDICT SUCCESS OF THERAPEUTIC SPINAL INJECTIONS

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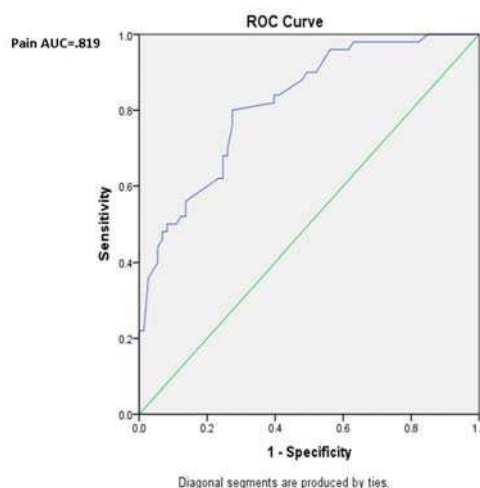
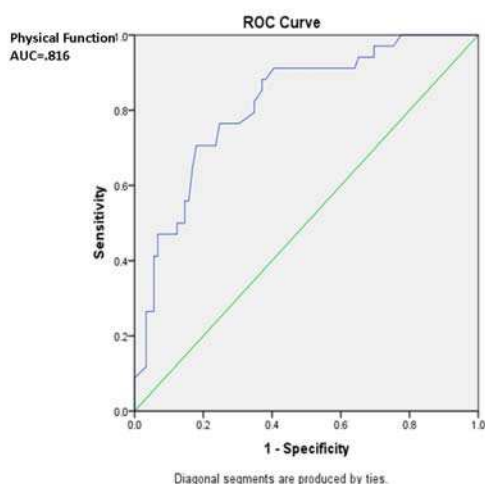
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**Introduction:** Patient-reported outcomes assessment has expanded beyond clinical research to become a real time assessment for standard of care in orthopedic practice. It is unclear how to use this information in the care of patients with spinal disorders. We examined the relationship between patient-reported outcomes (PROMIS: Physical Function, Pain Interference and Depression), and assessed if pre-procedure values were predictors of improvement after spinal epidural injections.

**Methods:** We performed prospective collection of patient reported outcomes for all consecutive patient visits to a multi-provider non-operative spinal disorders clinic between March 2015 and July 2016. There were 33,762 visits across 13,632 unique patients. Patients undergoing lumbar or sacral single level spinal injections (CPT 64483) were identified from billing records. Patients with a minimum of 30 and up to 60 days follow-up (mean 43 days) who completed all three PROMIS domains were included, resulting in 123 study patients. PROMIS physical function, pain interference, and depression t-scores were assessed at initial and follow-up visits. Minimum clinically important differences (MCIDs) were calculated using a distribution-based method. Receiver operating characteristic (ROC) curves were created to determine whether pre-procedure PROMIS scores were predictive of achieving MCID. Cutoff values for PROMIS scores that predict success or failure in achieving MCID with 95% specificity were determined. Prognostic pre- and post-test probabilities based upon these values were calculated.

**Results:** ROC curves demonstrate that pre-injection physical function scores predict post-injection improvement in physical function (area under the curve (AUC) 0.82). Pre-injection pain interference scores predict post-injection pain improvement (AUC 0.82) and pre-injection depression scores predict post-injection depression improvement (AUC 0.63). Patients with pre-injection physical function t- score below 28.2 had a 69% probability of achieving a clinically meaningful improvement in function as defined by MCID. Patients with pre-injection physical function t- score above 42.8 had a 93.1% probability of failing to achieve MCID for physical function. Patients with pre-procedure pain above 70.2 had an 85% probability of achieving MCID, whereas patients with pre-procedure pain below 60.5 had a 94% probability of failing to achieve MCID for pain. Patients with pre-procedure depression above 63.7 had a 76.8% probability achieving MCID, whereas patients with pre-procedure depression below 40.4 had a 90% probability of failing to achieve MCID for depression.

**Discussion:** Patient-reported outcomes (PROMIS) scores obtained before a single level spinal injection predicted improvement after injection. Threshold levels in physical function, pain interference, and depression can be shared with patients as they decide whether to undergo a single level lumbar or sacral spinal injection and may help guide patient expectations. Physical function scores below 28.2 and pain scores above 70.2 were likely to benefit from an injection, whereas those patients with physical function scores above 42.8 and pain scores less than 60.5 were unlikely to obtain clinical benefit. . Prognostic cutoff values can aid in shared decision-making and potentially influence resource allocation within a healthcare system.



## BIOACTIVE DIETARY POLYPHENOL PREPARATION FOR PREVENTING PAINFUL BEHAVIOR ASSOCIATED WITH LUMBAR DISC DEGENERATION – AN *IN-VIVO* RAT MODEL

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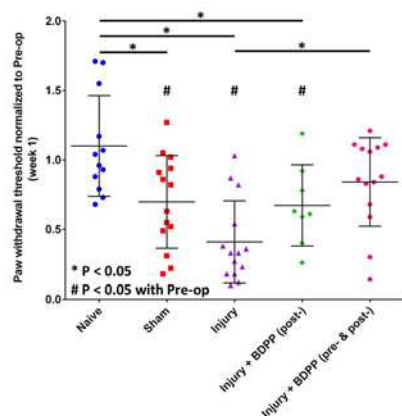
**INTRODUCTION:** Intervertebral disc (IVD) degeneration with chronic inflammation is highly associated with back pain. Polyphenols are naturally occurring compounds found in many plant-derived foods and beverages that are generally safe for dietary consumption[1]. While polyphenols can reduce pro-inflammatory cytokines and catabolism in IVD cells *in-vitro*[2, 3] with some efficacy with localized spinal applications in a radiculopathy rat *in-vivo* model[3], there are no studies on disc-related pain or oral delivery. This study determined if oral consumption of select Bioactive Dietary Polyphenol Preparation (BDPP) would effectively treat immediate and long-term painful behaviors associated with IVD degeneration induced by annular injury. The high safety of BDPP allowed us to test if pre-injury use as a dietary supplement could improve effects.

**METHODS:** For the immediate(1-week) study, thirty-eight healthy, skeletally mature SD rats were used and randomly divided into 5 groups: Naïve, Sham, Injury, Injury+BDPP (post-) or Injury+BDPP (pre- & post-). IVD injuries were induced in all rats (except Naïve and Sham) by anterior annular puncture and injection in 3 lumbar IVDs[4]. BDPP was provided for 2 weeks before injury surgery then continuously after injury (Injury+BDPP (pre- & post-)), and after injury only (Injury+BDPP (post-)) groups. BDPP was comprised of select Concord grape juice, select grape seed polyphenol extract and trans-resveratrol. For the long-term(6-week) study, pre-injury was prioritized because of larger effects with Injury and Injury+BDPP (pre- & post-) groups(n=6). Pain behaviors and IVD degeneration were assessed before surgery and weekly after surgery using hindpaw mechanical hyperalgesia and radiograph disc height. Animals were sacrificed at 1-week or 6-week post-surgery. Lumbar IVDs were harvested for morphological and IL-1 $\beta$  level analyses. DRG sensitization was quantified by immunohistochemistry for calcitonin gene related peptide (CGRP).

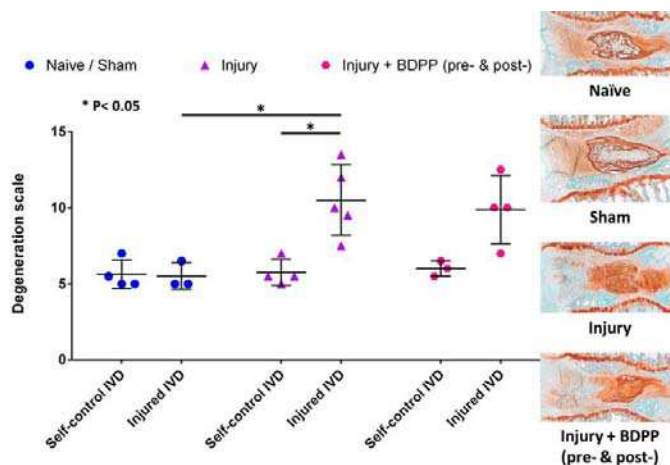
**RESULTS:** Paw withdrawal thresholds were significantly decreased in the Injury group at 1 week after surgery suggesting increased pain behaviors (Figure 1). BDPP with pre-op treatment, Injury+BDPP (pre- & post-), alleviated painful behaviors induced by annular injury with increased pain-threshold which persisted for 6 weeks. Paw withdrawal threshold was reduced for Sham at 1 week but recovered by 2 weeks(not shown), indicating specificity to annular injury. No significant beneficial effect of BDPP (post-) treatment was observed, suggesting pre-treatment was important. BDPP did not significantly affect IVD height, IVD histology (Figure 2), intradiscal IL-1 $\beta$  or DRG CGRP levels.

**DISCUSSION:** BDPP, a safe dietary supplementation, was beneficial for alleviating pain/discomfort associated with IVD injury and degeneration in rats. Results highlighted that oral treatment could be beneficial for disc-injury-related pain, but the time of starting polyphenol ingestion was critical with significant improvements in pain/discomfort only when BDPP started before injury. Pain behaviors improved with BDPP. Oral BDPP ingestion did not affect IVD repair since there were no improvements in IVD structure, degenerative grade or intradiscal pro-inflammatory cytokines. Since BDPP improved pain but not IVD inflammation, degeneration, or DRG sensitization, results suggested similarities to the human condition where pain perception is not always correlated with IVD degeneration. Future studies are required to optimize treatments and delivery methods, and identify mechanism for effects of polyphenols on relieving pain behaviors.

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**Figure 1.** Changes of normalized paw withdrawal threshold at week 1. BDPP with pre-op treatment (pre- & post-) alleviated painful behaviors induced by annular injury, i.e., reduced pain threshold, but no beneficial effect was observed when BDPP treatment started after the injury occurred (post-).



**Figure 2.** Annular injury induced disc morphological changes towards degeneration, which was not prevented by BDPP (15=severely degenerated; 5 = healthy) in long-term (6-week) study).

## MATRIX METALLOPROTEINASE-12 ACTIVITY IN A NEUROPATHIC PAIN RODENT MODEL : IMPACT ON NEUROINFLAMMATION RESPONSE

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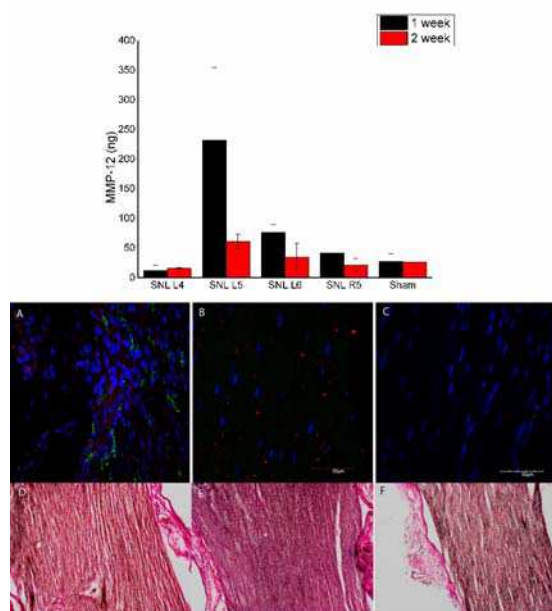
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**Introduction:** Chronic neuroinflammation mediated by activated macrophages has been implicated in the pathogenesis of neuropathic pain. Under such pathological conditions, macrophages facilitate their infiltration into affected tissues by secreting Matrix Metalloproteinases (MMPs) that degrade extracellular structural proteins, including MMP-12, which primarily degrades elastin fibers.

We have previously reported increased MMP-12 gene expression in compressed nerve roots by microarray analysis in rodents, which suggests a critical role of MMP-12 in neuropathic pain development. We hypothesize that compressed nerve roots have a higher MMP-12 activity compared to control nerve roots. Hence we sought to investigate MMP-12 activity, macrophage infiltration and elastin degradation in nerve roots of the spinal nerve ligation (SNL) rodent model.



**Methods:** All animal procedures were approved by the institutional ethics committee (R14-0009). Sixty 8-week-old male Sprague Dawley rats were divided into 2 groups, namely SNL and sham. The left side lumbar level 5 spinal nerve of the SNL group was ligated using a 5-0 suture while that of the sham group was only exposed. Pain associated behaviour was evaluated by thermal withdrawal latency (TWL) and mechanical withdrawal threshold (MWT) tests 3 days pre-operatively and 5, 7 & 13 days post-operatively. Rats were euthanized either 1 or 2 weeks post-operatively. Spinal nerves and dorsal root ganglions were harvested. Active MMP-12 in harvested nerve roots was measured using Anaspec MMP-12 activity assay. The extent of macrophage infiltration was shown by immunohistochemistry with anti-CD68, anti-MMP-12 antibodies, while the extent of extracellular elastin degradation was observed by Abcam elastic staining.

**Results:** Left hind limbs of SNL rats had lower TWL and MWT compared to their right hind limbs post-operatively, indicative of neuropathic pain development. The TWL and MWT did not differ between hind limbs for SNL rats pre-operatively and for sham rats pre- and post-operatively. Higher MMP-12 activity was observed in SNL rats (1 week: 232.2±122.5ng, 2 week: 60.8±12.4ng) compared to sham rats (1 week: 26.9±13.9ng, 2 weeks: 26.2±0.3ng). MMP-12 labelled area was higher in ligated nerve roots compared to the adjacent level, contralateral and sham nerve roots. From CD-68 staining, foamy macrophages were observed in ligated nerve root correlating with increased MMP-12 activity. There were no pathological changes observed in sham operated nerve roots as axons remained tightly packed. After 2 weeks of spinal nerve ligation, some axon drop out was observed with reduction of elastic staining intensity.

**Discussion and Conclusion:** MMP-12 activity gain correlates with increased elastin degradation and macrophage infiltration in ligated nerve roots. Time dependent reduction of MMP-12 activity may be due to abated local inflammatory response or upregulation of endogenous MMP-12 inhibitor.

## DISC HEIGHT AND TISSUE MORPHOLOGY RESTORATION BY CRYOPRESERVED HUMAN DISCOGENIC CELL TRANSPLANTATION IN A CANINE MODEL

Jordy Schol<sup>1</sup>, Daisuke Sakai<sup>1</sup>, Hiraishi Syunsuke<sup>1</sup>, Nukaga Tadashi<sup>1</sup>, Masahiko Watanabe<sup>1</sup>

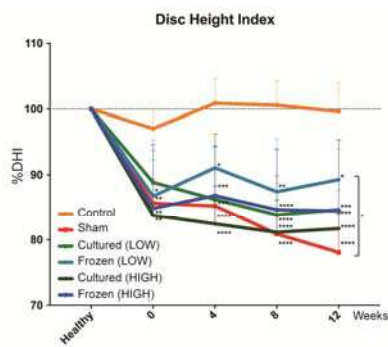
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**INTRODUCTION:** An optimal cell source towards a cell transplantation treatment against degenerative disc disease remains elusive. One promising option is discogenic cells, a therapeutic population of cells expanded and modified from adult human intervertebral disc tissue. Discogenic cells were compared for their ability to limit or improve degeneration associated disc height maintenance and restoration of histological features in a canine disc degeneration model.

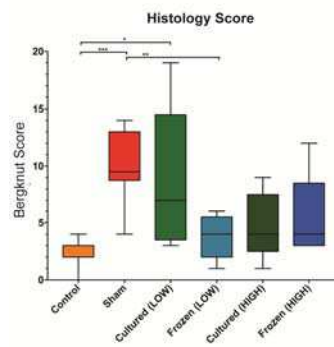
**METHODS:** This study was conducted in accordance with protocols approved by institution committee for safe animal experimentation. Ten female beagle dogs were subjected to induction of disc degeneration by aspiration of the NP (as previously described[1]) in L3/4, L4/5, and L5/6. Two weeks after NP aspiration, discogenic cells (DiscGenics, Inc) in a 1% sodium hyaluronate solution (Lurocoat®; Lifecore Biom.) were injected. Each dog received a 100  $\mu$ L injection of saline [Sham], cell suspension directly from cryopreserved state [Frozen], and 2-weeks pre-cultured cell suspension [Cultured]. Additionally, the recipients were randomly divided into a low dose ( $1 \times 10^6$  cells/mL), and high dose group ( $10 \times 10^6$  cells/mL). At day 0, 2 weeks prior, and every 4 weeks after injection, radiographic images were obtained and Disc height index (DHI) was determined [2]. After twelve weeks discs plus control disc L6/7 were explanted. IVDs were HE and Safranin-O/Fast-green stained and scored by adapted Bergknut scoring methods [3]. Significance was determined by ANOVA followed by Tukey's multiple comparison. Differences of  $p < 0.05$  were considered significant.

**RESULTS:** DHI reduction was limited by injection of both pre-cultured cell dose injection, and was improved for both frozen conditions. (Fig. 1) Histology scoring demonstrated significant improvement for low dose frozen treatment. (Fig. 2) Moreover, both high dose conditions showed an increase in score compared to the sham. Histologic images (Fig. 3) revealed a reduction in safranin-O staining for the Sham controls and a more fibrous matrix on HE staining. In contrast, the cell-treated discs exhibited retained safranin-O staining and a more clear distinction between nucleus pulposus and annulus fibrosus compared to the sham control.

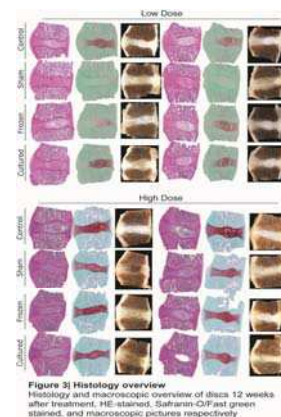
**DISCUSSION:** The present study demonstrates that, in a large canine animal model, discogenic cells are able to limit induced disc degeneration. The injection of  $0.1 \times 10^6$  cells directly from a cryopreserved state results in a significant increase in DHI and histological features. Finally, injection of cells directly from their cryopreserved state appears to be an effective approach for cell transplantation, extenuating the need for costly pre-culturing prior to dosing.



**Figure 1| Disc Height Index**  
%DHI relative to DHI 2 weeks prior to degeneration induction. Significance is indicated compared to control values unless indicated otherwise.



**Figure 2| Bergknut Scores**  
Histological scores of IVDs 12 weeks after injection. Scores from 0 - 20, signifies healthy to degenerated disc respectively.



**Figure 3| Histology overview**  
Histology and macroscopic overview of discs 12 weeks after treatment, HE stained, Safranin-O/Fast green stained, and macroscopic pictures respectively.

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## MOLECULAR MECHANISMS OF RHBMP-2 INDUCED INFLAMMATION: A RABBIT SPINAL FUSION CHAMBER STUDY

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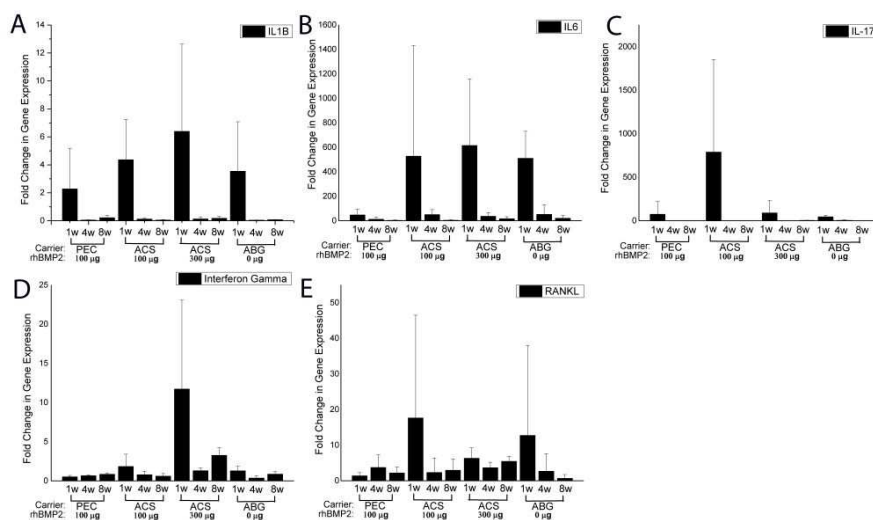
**Introduction:** Recombinant human bone morphogenetic protein-2 (rhBMP-2) has been successfully used to argment spinal fusion. However, there are safety concerns associated with rhBMP-2 usage, including heterotrophic bone formation and seroma formation. Based on previous studies, a controlled-release carrier (polyelectrolyte complex template) minimized seroma formation and heterotopic bone formation as compared to the burst-release carrier absorbable collagen sponge (ACS). The purpose of this study is to examine the inflammatory gene expression pattern of these two carriers.

**Material and Methods:** Sixty rabbits were allocated to following groups: Group 1, polyelectrolyte complex carrier (PEC) + 100 $\mu$ g rhBMP-2 (n=16); Group2, ACS carrier + 100 $\mu$ g rhBMP-2(n=16); Group 3 ACS + 300 $\mu$ g rhBMP-2(n=12) and Group 4 autologous bone graft(n=16). A retroperitoneal approach was used to expose L5/6 intervertebral disc, and the intervertebral disc defect was created by using a trephine saw. Poly-ether-ketone-ketone(PEKK) spinal fusion chambers with the respective carriers were implanted into the disc defect and secured with screws and sutures. Rabbits were sacrificed at the 1, 4 and 8 weeks. Seroma volume was quantified. Spinal fusion was assessed by manual palpation and confirmed by  $\mu$ CT scan. Tissues within the spinal fusion chamber channel were harvested for gene expression and histology.

**Results:** Manual palpation showed that Groups 1 and 3 fused completely and 50% of the samples from Group 2 achieved spinal fusion. No fusion was observed in Group 4. Expression of the inflammatory cytokines IL-1 $\beta$ , IL6 were highest in Group 3 while Group 1 was the lowest among the groups with rhBMP-2. Group 3 had higher expression of regulatory T cell cytokines such as IFN gamma and IL-10 as compared to Group 2. Group 2 had higher IL-17 and IL-4 expression levels than Group 3. The bone resorption-related marker RANKL was in the order of Group 2 >Group 3 > Group 4 >Group 1. All these inflammatory markers subsided by week 4. The upregulation of the inflammatory markers was consistent with seroma volume at week 1. Seroma volume was highest in Group 3 (2.0 $\pm$ 0.2ml), followed by Group 2 (0.90 $\pm$ 0.22ml) and Group 1 (0.18 $\pm$ 0.05ml) ( $p$ <0.05).

**Discussion:** Upregulation of IL-1 $\beta$  and IL-6 showed dose-dependent relationships with burst release rhBMP-2 in ACS group. IL-17 had higher expression in the low dose ACS +100 $\mu$ g rhBMP-2 group. Both IL-1 $\beta$  and IL-17 are inducers of RANKL osteoclastogenesis pathway. Upregulation of IFN $\gamma$  may hamper RANKL-gene upregulation in Group 3.

**Conclusion:** Suitable amounts of inflammatory cytokines could promote formation of blood vessels while excessive levels can lead to osteoclastogenesis. Slow release induced lower inflammatory cytokines expression than burst release. High inflammatory cytokines expression in burst release group was accompanied by an upregulation of the osteoclastogenic genes, which may hinder the bone formation. On the other hand, the upregulation of IL-6 and RANKL inhibitor IFN gamma may have reduced osteoclastic-related gene expression and promoted bony fusion for the Group 3. We speculate that the osteogenic activity at the interbody fusion site is dependent on the level of BMP2 which influences the balance of *in-situ* inflammation, anti-osteogenic and osteoclastogenic activities, governing the fusion outcomes.



## INHIBITION OF AUTOPHAGY THROUGH ATG5 KNOCK DOWN INDUCES APOPTOSIS AND SENEESCENCE IN HUMAN INTERVERTEBRAL DISC CELLS

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**Introduction:** The intervertebral disc is the largest avascular, low-nutrient 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 cannot 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 RNA interference (RNAi) technique.

**Methods:** Human disc tissues and cells obtained from lumbar surgery were used. *In vivo*, expression of autophagy-related gene 5 (ATG5), essential for autophagy execution, was assessed by Western blotting (WB). *In vitro*, cells were cultured in DMEM with and 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 ATG5 was assessed by WB. Next, cells after transfection of small interfering RNA against ATG5 were cultured in DMEM with and without 10% FBS for 24 hours. ATG5 knock down, autophagy inhibition, and cell viability were assessed by WB and WST-8 assay. 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 pro-apoptotic Bax, cleaved PARP, cleaved caspase-9, anti-apoptotic Bcl-2, 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) *In vivo*, LC3, p62/SQSTM1, and ATG5 expressed in both human disc NP and AF tissues. (2) *In vitro*, time-dependent increases in LC3-II and decreases in p62/SQSTM1 in response to serum starvation, consistent with autophagy induction. ATG5 also increased modestly. (3) RNAi against ATG5 induced with decreased LC3-II and increased p62/SQSTM1, clearly showing autophagy inhibition. By RNAi against ATG5, cell viability was maintained in DMEM with 10% FBS (100% vs. 96%,  $p=0.28$ ) but significantly decreased in DMEM without FBS (100% vs. 83%,  $p<0.01$ ). (4) Proinflammatory IL-1 $\beta$  induced apoptotic and senescent stimuli. Proapoptotic Bax, cleaved caspase-9, and cleaved PARP increased while anti-apoptotic Bcl-2 decreased by RNAi against ATG5. Senescent p16/INK4A also increased. (5) IL-1 $\beta$ -induced MMP-3 release was decreased by RNAi against ATG5, while TIMP expression was also reduced. In addition, RNAi against ATG5 was less sensitive to *aggrecan-1* and *collagen type 2- $\alpha$ 1* mRNA expression.

**Discussion:** This study demonstrated the involvement of autophagy including ATG expression in human degenerative disc NP and AF tissues and cells. Knock down of ATG5 led to decreased cell viability and increased cell death and aging under stressful conditions of limited nutrition and inflammation, indicating the importance of autophagy in maintaining disc cell homeostasis. However, effects of autophagy on matrix metabolism are controversial; therefore, further investigations are required. Nevertheless, autophagy modulation is a potential molecular treatment strategy for disc disease.



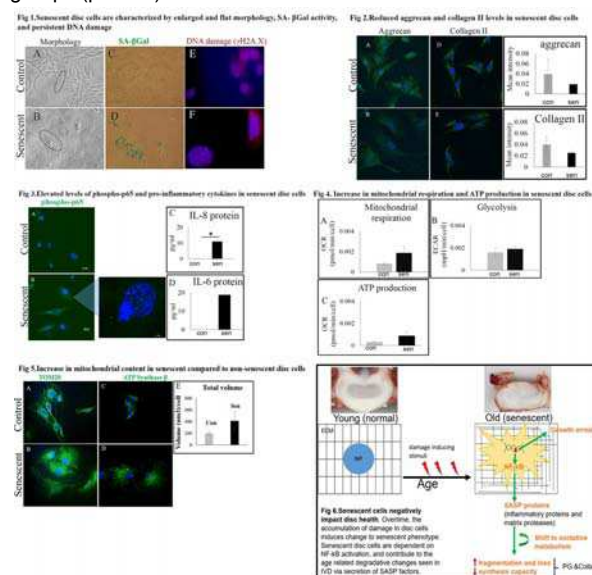
## HUMAN SENESCENT DISC CELLS EXHIBIT METABOLIC SHIFT AND IMBALANCED MATRIX HOMEOSTASIS.

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**INTRODUCTION:** The age-associated impairment in disc tissue health and structure has been attributed to the increased levels of inflammatory proteins and matrix proteases in the disc. How the resident disc cells undergo a phenotypic change and promote the age-associated degradative changes in the disc is still unknown. Previous reports from our lab had shown that cellular senescent phenotype increases with ageing in disc and that it could contribute to the age-associated disc degenerative changes [1]. Senescent cells are irreversibly growth arrested, secrete numerous pro-inflammatory cytokine and matrix proteases, a phenomenon termed as senescent associated secretory phenotype (SASP) [2]. The goal of the study was to characterize senescent disc cells in vitro and examine the metabolic changes that senescent disc cells undergo in order to support their chronic secretion of numerous SASP factors at elevated levels.

**METHODS:** Human disc nucleus pulposus (hNP) cells isolated from surgical specimens were induced to undergo senescence by oxidative stress using 500  $\mu\text{M}$  of  $\text{H}_2\text{O}_2$  in 10% FBS at 5%  $\text{O}_2$ . Untreated cells were used as controls. All outcome measures were performed 10 days post treatment to allow establishment of senescence. Level of cellular senescence was assessed by examining cell morphology, SA- $\beta$ gal activity and by immunodetection of DNA damage marker  $\gamma\text{H2A.X}$ . SASP factors (IL-6 and IL-8) levels were measured by ELISA. Activated NF- $\kappa\text{B}$  (p-p65), aggrecan, and collagen II levels were measured by immunofluorescence. Mitochondrial respiration and ATP production and glycolysis were measured using XF Extracellular Flux Analyzer (Seahorse Bioscience) [3]. Mitochondrial content (volume) was assessed by examining mitochondrial proteins TOM20 and ATP synthase  $\beta$  by confocal Z-stacks using Nikon A1. Student's independent t-test was used to test significance between groups ( $p < 0.05$ ).



**RESULTS:** Oxidative-stress-induced senescent disc cells were characterized by having an enlarged and flattened morphology, exhibiting an increase in SA- $\beta$ gal activity and number of DNA damage foci ( $\gamma\text{H2A.X}$ ), and reduced aggrecan and collagen II content (Fig 1&2). Elevated level of activated NF- $\kappa\text{B}$  and NF- $\kappa\text{B}$  target pro-inflammatory cytokines, IL-6 and 8 (Figure 1b), was present in senescent disc cells (Fig 3). Compared to control cells, senescent disc cells had higher mitochondrial respiration, ATP production, and unchanged glycolytic capacity (Fig 4). Additionally, mitochondrial volume was elevated in senescent disc cells compared to controls (Fig 5).

**DISCUSSION:** The age-related degenerative disc hallmarks - reduced aggrecan and collagen II levels, and increased inflammatory proteins and matrix proteases- are all characteristic features of senescent disc cells. Hence, the senescent disc cells could contribute to the age-associated degradative changes in the disc. Additionally, the study illustrates that senescent disc cells increase mitochondrial content, oxidative phosphorylation, and ATP production, presumably to support the energetic demand of synthesis and secretion of SASP factors. The unanticipated metabolic shift of NP cells suggests that identifying the metabolic adaptation to aging is essential in understanding the cellular and

molecular mechanisms that underlie degeneration.

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## SHARED DECISION MAKING IN ORTHOPAEDIC SPINE CARE LEADS TO BETTER HEALTH OUTCOMES: A PROSPECTIVE COHORT STUDY

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### Introduction:

Clinical guidelines recommend shared decision making (SDM) involving patients and their clinician when considering elective spine surgery. The goal is to ensure that patients are well-informed about treatment options and their respective risks and benefits, and patients receive their preferred treatment. However, few studies have examined the relationship between SDM and health outcomes. The purpose of this study was to examine whether patients with a lumbar herniated disc (LDH) or lumbar spinal stenosis (LSS) who are well-informed and receive their preferred treatment have better health outcomes.

### Methods

A prospective cohort study enrolled eligible patients consulting an orthopaedic specialist with LDH or LSS. Participants were surveyed by mail one week after an initial visit with a specialist to assess knowledge, preferred treatment, and baseline quality of life (QoL), EQ-5D and Oswestry Disability Index (ODI). A follow-up survey was sent six months after the visit or at least three months after surgery for those who had surgery. The survey assessed treatment, QoL, satisfaction and regret. Patients with a passing knowledge score ( $\geq 40\%$ ) and receiving their preferred treatment (either surgery or non-surgical) were considered to have made an informed, patient-centered (IPC) decision. Regression analyses accounted for clustering of patients within clinicians and controlled for surgery, spinal pathology, age, gender, and baseline QoL to test hypotheses that patients who made IPC decisions would have higher QoL, higher satisfaction and less decision regret at follow-up. Unadjusted outcomes with adjusted p-values are presented.

### Results

The initial survey response rate was 64.5% (200/310); 56.5% (83/147) for patients with LDH and 71.8% (117/163) for patients with LSS. Follow up survey response rates were 82% (164/200) and similar among LDH and LSS patients (78.3% vs. 84.6%). The overall sample was on average 59.9 (SD 15.2) years old (49.7 for LDH and 67.1 for LSS patients), 42% female, 87% non-Hispanic White, and 56% had a college degree. About one third had surgery (31%) within the 6 months of the visit. Overall, 27.8% met criteria for IPC decisions (39.0% for LDH and 19.8% for LSS patients), and IPC decisions were associated with significantly better overall and disease-specific quality of life at follow-up. Differences between patients who met criteria for IPC decisions and those who did not on the change in QoL scores were 0.17 increase for EQ-5D ( $p < 0.0001$ ) and 14.9 point decrease on ODI ( $p < 0.0001$ ). Participants who made IPC decisions were more likely to be extremely satisfied with their pain (73.3% vs. 40.9%,  $p = 0.009$ ), more likely to be very or extremely satisfied with treatment (65.9% vs. 26.4%,  $p = 0.0003$ ), and had less regret (22.2% vs. 55.9%  $p < 0.0001$ ). Outcomes favoring patient who met criteria for IPC decisions were greater for LDH than for LSS patients.

### Discussion

This study prospectively evaluated patient engagement in elective orthopaedic surgery decisions as part of routine care. Results suggest that well-informed patients who receive their preferred treatment have higher satisfaction and greater improvement in health outcomes. These findings support clinical guideline efforts that encourage shared decision making as part of elective spine surgery evaluations.

## INCIDENCE AND RISK FACTORS FOR EARLY POSTOPERATIVE MORTALITY AND COMPLICATIONS FOLLOWING ADULT SPINAL DEFORMITY SURGERY DATA FROM THE NATIONAL SURGICAL QUALITY IMPROVEMENT PROGRAM FROM 2011 TO 2013

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**Introduction:** Although adult spinal deformity surgery has a relatively high rate of complications, there has rarely been a large case series reported on this. Therefore, the purpose of this study was to investigate recent incidence and risk factors of mortality and complications in patients undergoing adult spinal deformity surgery using the American College of Surgeons National Surgical Quality Improvement Program database (ACS-NSQIP).

**Methods:** In the database of the 2011 to 2013 ACS-NSQIP, the cohort of patients ( $n = 1484$ ) who were older than 20 years and underwent adult spinal deformity surgery was established by primary and other Current Procedural Terminology (CPT) and International Classification of Disease, Ninth Revision (ICD-9) codes. The incidences of mortality, major complications and minor complications within 30 days post-surgery was investigated, and their risk factors were assessed using the logistic regression modeling.

**Results:** Of 1484 patients undergoing adult spinal deformity surgery, the overall complication rates were 15.8% (235 patients), with a mortality rate of 0.6% (9 patients), a major complication rate of 10.4% (154 patients), and a minor complication rate of 8.2% (121 patients). Multivariate analysis identified American Society of Anesthesiologists (ASA) 4 status ( $P = 0.009$ ; odds ratios [OR], 34.697) as a high risk factor for mortality. For major complications, male gender ( $P = 0.013$ ; OR, 1.567), osteotomy procedure ( $P = 0.008$ ; OR, 1.674) and prolonged operative time ( $> 5$  hours) ( $P < 0.001$ ; OR, 2.142) were significant risk factors. Dependent functional status ( $P = 0.003$ ; OR, 4.838), anterior or anterior + posterior approaches ( $P = 0.001$ ; OR, 2.022), and prolonged operative time ( $> 5$  hours) ( $P = 0.004$ ; OR, 1.821) were associated with high risk of minor complications.

**Discussion:** The rates of mortality, major complication, and minor complication were 0.6%, 10.4% and 8.2%, respectively. While mortality depended on patient physical status represented by ASA 4, major or minor complications were associated with male gender, dependent functional status, and surgical factors such as osteotomy procedure, prolonged operative time ( $> 5$  hours) and having an anterior surgical approach. Therefore, this information will be helpful in surgical counselling and preoperative surgical planning.

## A NOVEL USE OF THE SPINE TANGO REGISTRY TO EVALUATE SELECTION BIAS IN PATIENT RECRUITMENT INTO CLINICAL STUDIES: AN ANALYSIS OF PATIENTS PARTICIPATING IN THE LUMBAR SPINAL STENOSIS OUTCOME STUDY (LSOS).

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**Introduction:** Patients enrolled in clinical studies typically represent a sub-set of all who are eligible, and selection bias may compromise the generalizability of the findings. Using Registry data, we evaluated whether surgical patients recruited from one of the referring centres into the Lumbar Spinal Stenosis Outcome Study (LSOS; a large-scale, multicentre prospective observational study to determine the probability of clinical benefit after surgery) differed in any significant way from those who were eligible but not enrolled.

**Methods:** Data were extracted for all patients with lumbar spinal stenosis registered in our in-house database (interfaced to Eurospine's Spine Tango Registry) from 2011 to 2013. Patient records and imaging were evaluated in relation to the admission criteria for LSOS to identify those who would have been eligible for participation but were not enrolled (non-LSOS). The Tango surgery data and Core Outcome Measures Index (COMI) data at baseline and 3 and 12 months after surgery were analysed to evaluate the factors associated with LSOS-enrolment or not.

**Results:** 514 potentially eligible patients were identified, of which 94 (18%) were enrolled in LSOS (range 2-48% for the 6 spine specialists involved in recruiting patients) and 420 (82%) were not; the vast majority of the latter were due to non-referral to the study by the surgeon, with only 5% actually refusing participation. There was no significant difference in gender, age, BMI, smoking status, or ASA-score between the two groups ( $p \geq 0.18$ ). Baseline COMI was significantly ( $p=0.002$ ) worse in the non-LSOS group ( $7.4 \pm 1.9$ ) than the LSOS group ( $6.7 \pm 1.9$ ). There were no significant group differences in any Tango surgery parameters (additional spine pathologies, operation time, blood loss, complications, etc) although significantly more patients in the non-LSOS group had a fusion procedure (38%, vs 18% in LSOS;  $p=0.0004$ ). Postoperatively, neither the COMI nor its subdomain scores differed significantly between the groups ( $p > 0.05$ ). Multiple logistic regression revealed that worse baseline COMI ( $p=0.021$ ), surgeon ( $p=0.003$ ), and having fusion ( $p=0.014$ ) predicted non-enrolment in LSOS.

**Discussion:** A high proportion of eligible patients were not enrolled in the study. Non-enrolment was explained in part by the specific surgeon, worse baseline COMI status, and having a fusion. The findings may reflect a tendency of the referring surgeon not to overburden more disabled patients and those undergoing more extensive surgery with the commitments of a study. Beyond these factors, non-enrolment appeared to be somewhat arbitrary, and was likely related to surgeon forgetfulness, time constraints, and administrative errors. Researchers should be aware of potential selection bias in their clinical studies, measure it (where possible) and discuss its implications for the interpretation of the study's findings.

## THE RELATION BETWEEN DIFFUSE IDIOPATHIC SKELETAL HYPEROSTOSIS(DISH) AND LOW BACK PAIN: A POPULATION-BASED COHORT STUDY

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**Introduction:** DISH is often seen in the degenerative spine, and recent research has focused on disability in patients with DISH. At the same time, a relationship between low back pain (LBP) and disability in adult spinal deformity has been demonstrated. However, the relationship between DISH and LBP remains unclear. This study was aimed to investigate the relation between DISH and LBP using a population-based cohort.

**Methods:** This cross-sectional study was part of a large-scale population based Japanese cohort study named Research on Osteoarthritis/osteoporosis Against Disability (ROAD). This study included 1647 volunteers (573 men, 1074 women; mean age, 65.3 years) in the ROAD Study. Presence of DISH was diagnosed according to Resnick criteria using lateral whole spine radiographs. DISH type was classified to only "cervical type", "only thoracic type", "only lumbar type" and "diffuse type" (DISH was existed more than 2 region). Lower back pain was estimated by an interview.

**Results:** Prevalence of DISH was 10.8% (men 22.0%; women 4.8%). Subjects with DISH were significantly older than those without DISH (72.3 years and 64.4 years, respectively). All DISH included thoracic spine (thoracic type 88.7%, diffuse type 11.3%). Prevalence of LBP was not significantly different between subjects with and without DISH (23.2% and 20.6% respectively,  $P=0.4328$ ). In addition, Prevalence of LBP was not significantly different between subjects with thoracic type and diffuse type (22.9% and 25.0%, respectively,  $P=0.7185$ )

**Conclusion:** To the best of our knowledge, this is the first study to assess the relation between DISH and LBP in a population-based cohort. Although several studies have shown that adult spinal deformity was associated with LBP, DISH was not significantly associated with LBP.

## A PROGNOSTIC MODEL OF THE OUTCOME OF SURGERY FOR DISC HERNIATION

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### Introduction

Spine surgeons need to be able to make evidence-based predictions regarding the outcome of their surgical procedures, based on reliable prognostic information. The risks and benefits of different treatment modalities must be adequately communicated to the individual patient. This is particularly important in view of recent developments towards shared decision-making, where physicians and patients both actively participate in selecting the therapeutic intervention. There is a lack of validated prognostic tools to support the spine surgeon in daily practice. Some evidence is available regarding various predictors of surgical outcome; however, to date no studies have developed comprehensive clinical prediction models for spine surgery. We used Spine Tango registry data collected in our own clinic to develop prognostic models for patients with lumbar herniated disc to predict their outcome 12 months after spine surgery.

### Methods

Predictor variables were drawn from the Spine Tango surgery forms and patient forms of the registry. Potential predictors included patient sex and age, extent of lesion, number of previous surgeries, surgeon experience and specialty (neuro/ortho), insurance type (private/semi-private/general), morbidity state (ASA), BMI, smoking status, patient's declared main problem (back pain/leg pain/sensory disturbances/other), preoperative Core Outcome Measures Index (COMI) score, preoperative back pain, and preoperative leg pain. Outcome variables were recorded on the 12-month patient questionnaire and included COMI score and back and leg pain. Prediction models were fitted with the least absolute shrinkage and selection operator (lasso) coefficient shrinkage method using the full cohort.

### Results

A total of 1127 patients (43% female; median age 48, range 15-89) with lumbar herniated disc were identified. The median preoperative COMI score was 8 (range 1-10), median back and leg pain were 4 (0-10) and 7 (0-10). Postoperative, the median COMI score was 2.5 (0-10), back pain 2 (0-10), and leg pain 1 (0-10). Predictors of better outcomes were 1) single-level surgery, 2) no previous spine surgery, 3) leg pain as main problem (as opposed to back pain or sensory disturbance), 4) private or semi-private insurance, 5) non-smoker.

### Conclusion

The prediction models will provide reliable estimates to enable a tailored prediction of the outcome of surgery for individual patients. The statistical models form the basis of an online prognostic tool that will improve access and usability of prognostic information in clinical practice, for the purposes of joint decision-making. In the long-term, this should help improve the safety and effectiveness of spine surgical treatment and thereby reduce costs. It should also improve patients' satisfaction with surgery, since their expectations can be better managed with "bespoke" predictions of outcome in relation to their own particular condition/circumstances.

## VERTEBRAL ENDPLATE DEFECT AS INITIATING FACTOR FOR INTERVERTEBRAL DISC DEGENERATION IN THE GENERAL POPULATION

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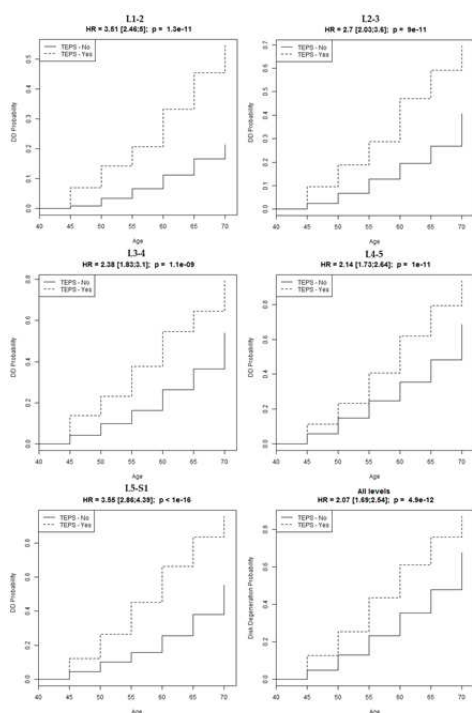
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**INTRODUCTION.** Precise understanding of the mechanisms leading to development of intervertebral disc degeneration (DD) in general population is lacking. In a degenerating disc, mechanical and structural changes lead to further worsening of disc integrity. Increasing attention has been paid to vertebral endplate defects as having a possible role in the etiopathogenesis of DD. In this investigation we aimed to determine the relationship between vertebral endplate defect and DD in general population.

**METHODS.** The study population to this cross-sectional MRI population study consisted of 831 twin volunteers from TwinsUK (mean age 54 (STD 8) years, 95.8% female). Lumbar T2-weighted magnetic resonance images were coded for endplate defects from 8310 endplates into six grades. An initial training phase was held in which an inter-rater agreement on endplate defect detection and grading of  $\geq 0.85$  was reached on at least 100 subjects and 1000 endplates. Total endplate score (TEPS) was achieved by summing both endplate defect grades from the same disc level. DD was evaluated for 4155 discs using two different classifications; Pfirmann grading, and a quantitative trait for DD based on a 4-point grading systems. Multivariable regression analysis was used to determine relationships between the traits of interest and the known risk factors for DD, age and body mass index (BMI). A receiver operator curve for TEPS predicting DD was generated, and survival analysis paired with Cox proportional hazards models analysis performed.

**RESULTS.** There was statistically significant association between DD and age and BMI. These associations lost significance when TEPS was included as predictor in multivariable model. TEPS was strongly and independently associated at every lumbar disc level with DD (Pfirmann  $p \leq 0.001$ ; 4-point grading systems  $p < 1e-16$ ). A cut-off point score of 5 for TEPS was found above which there was a higher DD prevalence. Across all age subgroups, probabilities of having DD were significantly increased in those considered TEPS positive ( $\geq 5$ ).

**CONCLUSIONS.** Our large, population-based study has shown that endplate defect was strongly and independently associated with DD at every lumbar level and in all age groups. We suggest that endplate defects can indeed be an initiating factor in the etiology of DD. These results provide a mechanism by which increasing age and BMI predispose to DD.



**Figure 1.** Survival analysis paired with Cox proportional hazards models analysis. Probabilities of having DD are significantly increased with age in TEPS positive ( $\geq 5$ ) subgroups at each disc level (denoted 'TEPS - Yes' in the Figure). The probabilities increase with age. DD = disc degeneration by Pfirmann, HR = hazard ratio, TEPS = total endplate score.



**Figure 2.** MRI scan showing endplate defect grade VI both at the L4/L5 rostral and caudal endplates, with associated Modic changes (MC) over both rostral and caudal bone marrows and disc degeneration evaluated as Pfirmann grade 5 and 4-point grading system grade 10. As the endplate is a fundamental part of the vertebral body-endplate-intervertebral disc motion segment, one could consider endplate defects to be an initiating factor not only for disc degeneration, but also for MC.

## A PROSPECTIVE, RANDOMIZED STUDY OF PATIENT CONTROLLED EPIDURAL ANALGESIA VS PATIENT CONTROLLED INTRAVENOUS ANALGESIA FOR POSTOPERATIVE PAIN CONTROL AFTER LUMBAR FUSIONS

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### Introduction

Pain control for patients in hospital after lumbar fusion can be difficult and is a common source of anxiety for patients and their family members; the optimal approach to postoperative pain control has not yet been determined.

**Methods** Patients (N=49) undergoing one- or two-level lumbar fusion were studied prospectively and randomized to postoperative pain control with patient controlled epidural analgesia (PCEA) or with a patient controlled intravenous analgesia (PCIA) delivery system. Pain levels, hospital stay, incidence of nausea, vomiting, itching, hypotension, and mobilization data were recorded and compared between groups.

### Results

The two randomized groups were demographically similar, with preoperative pain scores that were not different (PCEA, 7.13; PCIA, 7.67). Hospital stay was 4.08 days in the PCEA group, and 4.38 days in the PCIA group. Immediate postoperative pain scores immediately following surgery were not statistically different (PCEA, 2.92; PCIA, 4.96). Pain scores on Days 1, 2, and 3 postop were significantly lower in the PCEA (2.13/ 2.71/ 2.13) vs. PCIA groups: (5.00/ 4.54/ 4.75). In the PCEA and PCIA groups, the incidence of postop itching was 37% and 13% ( $p=0.05$ ), and nausea/vomiting were 56% and 74%, respectively ( $p=0.43$ ). Postoperative symptomatic hypotension was seen in 7% of PCEA patients and 13% PCIA patients ( $p=0.67$ ).

### Discussion:

Both groups did well after surgery, with similar length of stay. The epidural group had less overall pain in the first three days after surgery. The incidence of postoperative nausea and vomiting, and hypotension were similar in the two groups. The epidural catheter is a good method of achieving better postoperative pain control than the traditional IV PCA with minimal increase in minor side effects.



## ASSOCIATIONS OF NEUROPEPTIDE Y GENOTYPE AND CIRCULATING LEVELS WITH RESPONSE TO EPIDURAL STEROID INJECTION IN PATIENTS WITH AXIAL LOW BACK PAIN

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**Introduction:** Neuropeptide Y (NPY) has been shown to be elevated in painful degenerative conditions. Changes in NPY are associated with changes in pain in subjects with neck and back pain, and NPY has been localized to the annulus fibrosis in human intervertebral discs removed for back pain, underscoring its potential relevance in axial low back pain. We therefore investigated the association of circulating levels of NPY as well as NPY genotype with response to epidural steroid injections for axial low back pain.

**Methods:** Patients with axial low back pain without radiation into the lower extremities were recruited from an academic medical center who consented for epidural steroid injection (n=48) as part of their routine clinical care. Serum blood samples were taken immediately prior to the procedure and approximately 14 days post-injection and assayed for Neuropeptide Y by ELISA. DNA was extracted from whole blood samples and tested for the presence of a single nucleotide polymorphism in the promoter of the NPY gene (reference SNP cluster ID 16147) previously shown to be associated with circulating NPY levels. Responders to injection were defined as improvement in pain score by 50% on a numeric pain rating scale from pre- and post-procedure, and disability levels were measured using the Oswestry Disability Index.

**Results:** Among subjects undergoing ESI, 23 were responders and 25 non-responders. Responders had higher levels of NPY at baseline than non-responders (p=0.026). In addition, baseline levels of NPY correlated with improvement in Oswestry Disability Index (r=-0.327, p=0.035) and pain score after injection (r= -0.261, p=0.08). Subjects with the variant allele demonstrated a trend toward higher serum NPY levels and greater reduction in pain after LESI.

**Discussion:** NPY has an important role in modulating inter-individual variations in emotion and stress resiliency, which may relate to subjects reported response to treatments such as an epidural steroid injection. Higher levels of circulating NPY, consistent with the presence of the NPY promoter SNP, was associated with a greater improvement in pain and disability. Based on the observed associations with individual improvement, NPY represents a potential predictive biomarker to be explored in future prospective studies aimed at personalizing treatment plans for patients with low back pain.

## RESPONSE TO DULOXETINE IN CHRONIC LOW BACK PAIN: EXPLORATORY POST HOC ANALYSIS OF A PHASE 3, RANDOMIZED, PLACEBO-CONTROLLED TRIAL IN JAPANESE PATIENTS

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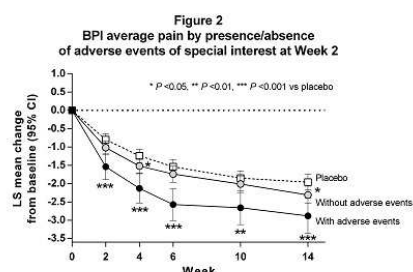
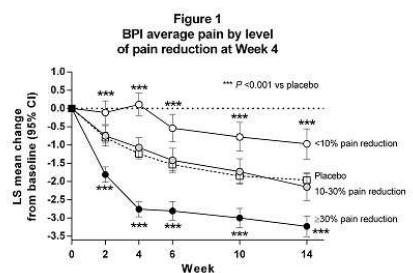
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**Introduction:** Duloxetine is a selective inhibitor of serotonin and norepinephrine reuptake with demonstrated efficacy in the treatment of chronic low back pain (CLBP). However, some patients with CLBP may respond better to duloxetine than other patients. The objective of this analysis was to assess whether duloxetine-treated patients with CLBP with early pain reduction or treatment-related adverse events gain more benefit than other patients.

**Methods:** This post hoc analysis of a Japanese randomized, placebo-controlled trial assessed whether patients with CLBP who respond to duloxetine 60 mg/day with  $\geq 30\%$  pain reduction at Week 4 or who have treatment-related adverse events of special interest (TR-AESIs; nausea, somnolence, and constipation) during Weeks 0-2 are more likely to have clinically significant improvements in pain and quality of life (QOL) than patients without early pain reduction or TR-AESIs. Adult patients with CLBP for  $\geq 6$  months who used nonsteroidal anti-inflammatory drugs for  $\geq 14$  days/month for  $\sim 3$  months, with no radiculopathy or other specific low back diseases, and Brief Pain Inventory (BPI) Severity average pain score  $\geq 4$  were eligible. Exclusion criteria included low back surgery, recent invasive CLBP treatment, crutches or walker use, and major depressive disorder. Patients (N=456) were randomized (1:1) to duloxetine 60 mg/day or placebo for 14 weeks. Primary efficacy measure was change from baseline to Week 14 in BPI Severity average pain.

Post hoc subgroup analyses of duloxetine-treated patients were early pain response (pain reduction  $\geq 30\%$ , 10%-30%, or  $< 10\%$  at Week 4) and early TR-AESIs (with or without TR-AESIs by Week 2). Outcome measures were changes from baseline in BPI Severity average pain and BPI Interference (QOL) domain scores at Weeks 2, 4, 6, 10, and 14, and proportion of patients with  $\geq 30\%$  or  $\geq 50\%$  pain reduction (response rate) at Week 14.



**Results:** Compared with placebo-treated patients (n=226), duloxetine-treated patients with  $\geq 30\%$  early pain reduction (n=108) had significantly greater decreases in BPI Severity average pain and BPI Interference scores (all domains) at most time points, whereas patients with 10%-30% (n=63) or  $< 10\%$  (n=48) early pain reduction did not (Figure 1). Significant improvements in general activity and walking ability were seen starting at Week 2. Compared with placebo-treated patients, duloxetine-treated patients with early TR-AESIs (n=50) had significantly greater decreases in BPI Severity average pain score (all time points; Figure 2), general activity, mood, walking ability, and enjoyment of life (some time points), whereas duloxetine-treated patients without early TR-AESIs (n=180) only had significantly greater decreases in BPI Severity average pain score at Weeks 4 and 14. Week 14 response rates ( $\geq 30\%$ / $\geq 50\%$  pain reduction) were 94.4%/82.4%, 66.7%/49.2%, and 25.0%/18.8% for patients with  $\geq 30\%$ , 10%-30%, and  $< 10\%$  early pain reduction, respectively, 74.0%/64.0% for patients with early TR-AESIs, and 67.2%/54.4% for patients without early TR-AESIs.

**Discussion:** This post hoc analysis suggests that efficacy (pain reduction) and/or safety (adverse events) responses in the early treatment period may predict which patients with CLBP are most likely to respond to duloxetine with a clinically significant reduction in pain and improvements in QOL.

**Trial registration:** Clinicaltrials.gov, NCT01855919

**Funding:** Shionogi & Co. Ltd

## WHAT SPACEFLIGHT TEACHES US ABOUT LUMBAR SPINE BIOMECHANICS

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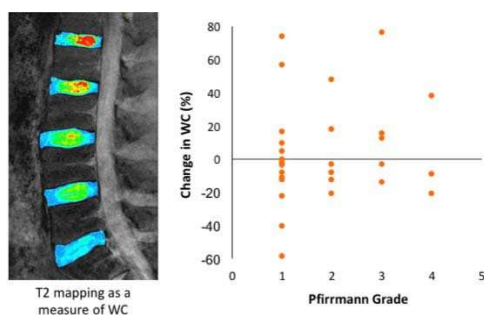
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**Introduction:** NASA crewmembers experience localized low back pain (~43% incidence) and heightened risk of lumbar disc herniation following spaceflight (4.3x). This elevated spine injury risk is thought to arise from a lack of diurnal loading in prolonged microgravity, which might lead to supraphysiologic disc swelling and an associated change in posture and spinal stiffness. To identify lumbar pain and injury mechanisms, we conducted a longitudinal study of NASA crewmember spinal anatomy and biomechanics before and after six months of microgravity exposure on the International Space Station.

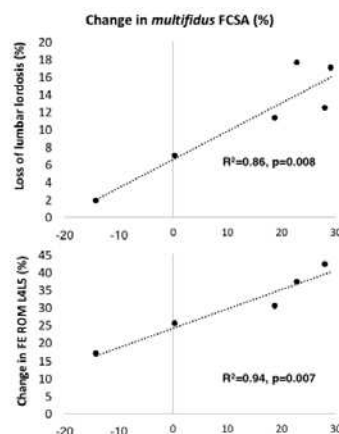
**Methods:** With IRB approval, six NASA astronauts were assessed at two time-points: before launch ("pre") and one day following six months spaceflight ("post"). We used supine 3T MRI and measured lumbar lordosis, disc water content (T2-weighted intensity), the presence/absence of vertebral endplate irregularities, and functional cross-sectional area (FCSA) of lumbar spine extensor muscles (*multifidus* and *erector spinae*) at L3/L4. We used dynamic fluoroscopy to quantify intersegmental flexion-extension range of motion (FE ROM) in both standing and lying postures. Lastly, we collected pre- and post-flight pain questionnaires and spine health reports from flight surgeons. Statistical analyses include paired t-tests and simple regression analyses.

**Results:** Lumbar lordosis decreased (flattened) by an average of -11.1% ( $p=0.019$ ). Standing FE ROM decreased for the middle three lumbar discs (L2-L3: -22.1%,  $p=0.049$ ; L3-L4: -17.3%,  $p=0.016$ ; L4-L5: -30.3%,  $p=0.004$ ). By contrast, no significant motion changes in these discs were observed during FE in a side-lying posture ( $p>0.05$ ). Surprisingly, disc water content did not differ systematically from pre- to post-flight (Figure 1). *Multifidus* and *erector spinae* FCSA changed variably between subjects, with four of six crew experiencing a 20-30% decrease in *multifidus* FCSA. Changes in *multifidus* FCSA strongly correlated with changes in lordosis ( $r^2=0.86$ ,  $p=0.008$ , Figure 2) and standing FE ROM at L4-L5 ( $r^2=0.94$ ,  $p=0.007$ , Figure 2). While *multifidus*-associated changes in lordosis and ROM were present amongst all crew, only those with severe endplate irregularities (2 of 6 crew) had post-flight lumbar symptoms (including chronic low back pain or disc herniation).

**Discussion:** This unique longitudinal study underscores the coupled role of passive and active spine stabilizers in maintaining spine health. Our data dispel the common notion that discs excessively swell in space, a finding supported by recent work reporting negligible changes in disc height following spaceflight. Rather, the increases in stature commonly observed post-flight may be due to *multifidus*-associated decreases in lumbar curvature. The primary contribution of active (muscles) compared to passive (disc, facets, ligaments) stabilizers with microgravity-induced spine stiffening is supported by the observation that ROM is decreased during standing on Earth (when muscles are active) but not during side-lying (when muscles are more relaxed). Another important finding is that pre-flight lumbar spine health may be a critical risk factor for developing post-flight symptoms. In summary, our findings shed light on mechanisms of post-flight back pain and disc injury – *multifidus* atrophy causes spinal flattening and increased stiffness, that when combined, creates the potential for injury in those subjects with pre-existing evidence of vertebral endplate insufficiency.



**Figure 1:** Change in water content (WC) is represented by the % change in T2 mean between pre and post flight. We found no relationship between prolonged microgravity and disc WC, with or without adjusting for pre-flight Pfirrmann grade.



**Figure 2:** Scatterplots showing the linear relationship between change in *multifidus* FCSA with change in lumbar lordosis (top) and FE ROM at L4-L5 (bottom).

## DOES THE ACTIVATION OF DEEP AND SUPERFICIAL LUMBAR MULTIFIDUS DIFFER DURING WALKING AT DIFFERENT SPEEDS AND INCLINATIONS BETWEEN YOUNGER AND OLDER ADULTS?

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**Introduction:** The power locus during walking shifts proximally with ageing from ankle to hip. Lower limb muscle activity patterns have been well examined, yet few studies measure lumbar paravertebral muscle activity during walking. Multifidus is a complex muscle with differential activation of deep and superficial fibres shown in young adults during sagittal-plane motion and walking. Whether this is also true for older adults, and whether activation patterns change with age was of interest. We aimed to determine and compare activation patterns for deep and superficial multifidus in young and older adults during walking at varied speed and inclination.

**Methods:** Ten volunteers in their twenties (3f,7m; 26.3±2.5yrs; mean BMI 23.5±4.5kg/m<sup>2</sup>) and nine volunteers in their sixties or seventies (3f,6m; 67.1±4.2yrs; BMI 25.0±2.9 (p=0.36)) walked on a treadmill in eight conditions; at 2km/h and 4km/h, each at 0, 1, 5, and 10° of inclination. Subjects walked continuously for 90s per condition, with a 30–45s rest between each. Intramuscular electromyography (EMG) recordings were acquired from the deep and superficial multifidus unilaterally using bipolar Teflon-coated intramuscular electrodes inserted at L5 under ultrasound guidance according to established methods. Activity for each muscle region was characterized by: amplitude of the peak of activation (normalized to the maximal activity in the slow speed and 0° inclination), position of the peak within the gait cycle (0–100%), and duration of muscle activity as a percent relative to the full gait cycle. Statistical analysis was undertaken using ANOVA.

**Results:** No difference for the amplitude of the peak of activation was shown between young (143.1± 64.1) and older (139.9±37.3) cases for deep multifidus, while superficial multifidus was significantly lower in the older than younger cases across all walking conditions (young 178.2±84.7; older 130.1±60.3; p<0.001). Where the peak of activation occurred within the gait cycle did not differ with multifidus region or age (average across both muscles and all conditions; young: 48.6±13.3%; older: 47.8±16.7%). Across all participants, the duration of activation of both the deep and superficial multifidus was longer during faster than slower walking conditions (p<0.01). Moreover, the duration of activation, relative to the full gait cycle, was significantly greater for both the deep and superficial multifidus in the older group across all conditions compared to the younger participants (p<0.01).

**Discussion:** Differential activation of deep and superficial lumbar multifidus was shown more-so in young than older adults under various walking conditions. Faster speed elicited longer duration activity, which may support the use of fast-walking for multifidus rehabilitation. Regardless of speed or inclination, more prolonged activation of both deep and superficial regions of the multifidus were observed during gait in the older group. In addition, lower peak amplitude of superficial multifidus was shown for older compared to younger adults suggesting a shift toward a more tonic role of multifidus with ageing. Examining the influence of factors such as pain or falls history on the activation within multifidus during common functional activities like walking appears warranted. Whether multifidus activity can be modified with intervention should be investigated in longitudinal studies.

## PARASPINAL MUSCLE PASSIVE STIFFNESS REMODELS IN DIRECT RESPONSE TO SPINE STIFFNESS: A STUDY USING THE ENT1 DEFICIENT MOUSE

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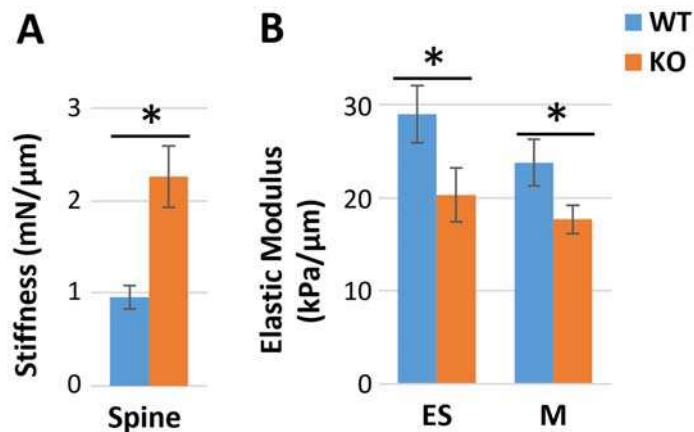
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**Introduction:** Experimentally induced intervertebral disc degeneration has been shown to cause an increase in multifidus passive stiffness [1]; this was hypothesized to compensate for a decrease in spine stiffness associated with disc degeneration. Recent work has demonstrated that mice lacking equilibrative nucleoside transporter 1 (ENT1) develop progressive ectopic calcification of the fibrous connective tissues of the spine, which affects the lumbar spine by 6 months of age [2], and likely creates a mechanically stiffer spine. This ENT1 deficient mouse thus may serve as an excellent model to test the hypothesis that a change in spine stiffness results in an inverse compensatory change in stiffness of the adjacent paraspinal muscles.

**Methods:** Experiments were conducted on 4 groups of mice (n=8 mice/group): wild-type (WT) and ENT1 knockout (KO) at 2 or 8 months of age. Lumbar spines were removed, fastened at either end leaving the intervertebral levels between L2 and L5 exposed, and tested in cyclic compression and tension at 0.33% deformation/second. The force-deformation data were used to determine neutral zone length and stiffness. Single muscle fibres and bundles of fibres were isolated from lumbar multifidus and erector spinae (combined longissimus and iliocostalis), as well as tibialis anterior (a non-spine related control), and tied to pins attached both a force transducer and a high speed motor. Sarcomere length and force were recorded as each sample was rapidly stretched every 2 minutes by increments of ~0.25  $\mu\text{m}$ . Force was normalized to the cross sectional area of the sample to give a measurement of stress which was plotted against sarcomere length. A quadratic curve was fitted to the data and passive elastic modulus (stiffness) was calculated as the tangent slope at a sarcomere length of 3.2  $\mu\text{m}$ . For both age groups, t-tests compared modulus between KO and WT for each muscle, in both fibres and bundles, as well as neutral zone length and stiffness between KO and WT spines.

**Results:** At 2 months of age, neither spine nor muscle stiffness was different between KO and WT ( $p>0.05$ ). At 8 months of age, compared to WT the lumbar spines of ENT1 KO mice had a stiffer ( $p=0.0056$ ; Figure 1A) and shorter ( $p=0.0006$ ) neutral zone, and both multifidus ( $p=0.0262$ ) and erector spinae ( $p=0.0016$ ) muscle fibres were less stiff (Figure 1B); however, fibre bundles were not different. Additionally, tibialis anterior was not different between KO and WT.

**Conclusions:** This work has confirmed that calcification of spinal connective tissues in the ENT1 KO mouse results in a stiffened spine, while the concurrent decrease in muscle fibre elastic modulus in the adjacent paraspinal muscles suggests a direct compensatory relationship between the stiffness of the spine and the muscles that are attached to it. The lack of difference in muscle fibre bundle stiffness between KO and WT suggests that the main remodeling response occurs at the cellular as opposed to the extracellular level.



**Figure 1:** Lumbar spine neutral zone stiffness (A) and muscle (ES = erector spinae; M = multifidus) fibre elastic modulus (B) of ENT1 KO and WT mice.

1. [1] Brown S et al. (2011). Spine 36 (21); 1728–36. [2] Warraich S et al. (2013). J Bone Miner Res 28(5); 1135-49.

## LUMBOSACRAL ORIENTATION IN REFERENCE TO GRAVITY LINE SHIFTS POSTERIORLY WITH AGING

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**Introduction:** Standing sagittal alignment of the spine deteriorates into stooping with aging.<sup>1)</sup> The reference line for the mal-alignment and the effect of aging are, however, not fully investigated.

**Aim:** The purpose of this study is to clarify the sagittal lumbosacral alignment in reference to gravity line (GL) with the effect of aging.

**Materials and Methods:** 136 healthy subjects (a mean 39.7 years, 20 ~ 69 years; 40 men, 96 women) were examined by a slot-scanning 3D X-ray Imager (EOS) with simultaneous force plate measurement,<sup>2)</sup> obtained sagittal spinopelvic alignment, GL, and offset of bony landmarks (centre of the head [CAM], lumbar vertebrae, base of sacrum [CBS], hip axis [HA]) from GL. GL was defined a vertical line drawn through the centre of vertical pressure measured by the force plate. Subjects were divided into 5 age groups by decade: 20s (n=27), 30s (n=46), 40s (n=35), 50s (n=20), and 60s (n=8). Differences in the parameters among age groups and the offset were analysed. Simple linear regression analyses were performed to estimate the effect of age among the radiographic parameters.

**Results:** The L4-, L5-, and CBS-offsets in the groups of subjects in their 40s, 50s, and 60s were significantly posterior to those of subjects in their 20s. The L5- and CBS-offset in subjects in their 50s and 60s were also significantly posterior to those of subjects in their 30s. The tendency was the same in HA among age groups, but the mean location of the HA was never behind the GL (Fig.1). In the global alignment, SVA was positively correlated with age ( $r^2=0.1368$ ,  $p<0.0001$ ), but no correlation was detected between CAM-offset and age. Age was positively correlated with cervical lordosis ( $r^2=0.1058$ ,  $p=0.0001$ ) and pelvic tilt ( $r^2=0.0945$ ,  $p=0.0003$ ).

**Discussion & Conclusion:** Our results suggest that aging induces trunk stooping, but the global alignment is compensated mainly by an increase in cervical lordosis and pelvic tilt with lumbosacral posterior shift to maintain the orientation of the head, probably for the purpose of horizontal gaze.

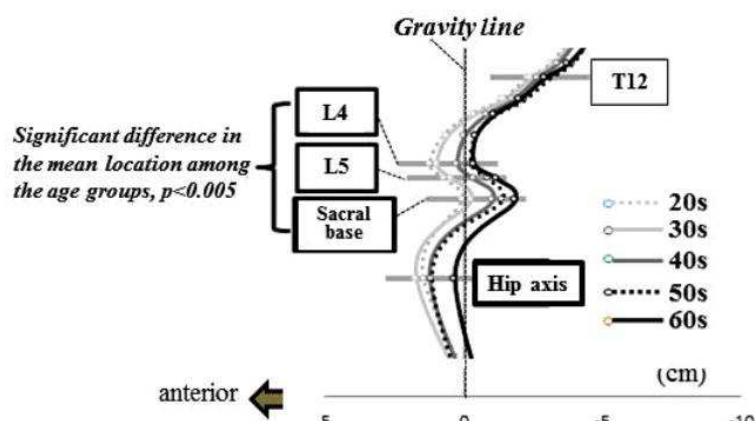


Fig.1 Relationship between sagittal spino-pelvic alignment and gravity line in reference to age groups

- 1) Glassman SD, Bridwell K, Dimar J, et al. (2005) The impact of positive sagittal balance in adult spinal deformity. *Spine* 30, 2024-2029. 2) Hasegawa K, Okamoto M, Hatsushikano S, et al. (2016) Normative values of spino-pelvic sagittal alignment, balance, and health-related quality of life in relation to age in a cohort of healthy adult subjects. *European Spine J.*; 25:3675-3686.

## VISUALIZATION AND PATHOLOGICAL CHARACTERISTICS OF CARTILAGE AND SUBCHONDRAL BONE CHANGE IN LUMBAR FACET JOINT IN OVX MOUSE MODEL USING PROPAGATION-BASED PHASE-CONTRAST COMPUTED TOMOGRAPHY

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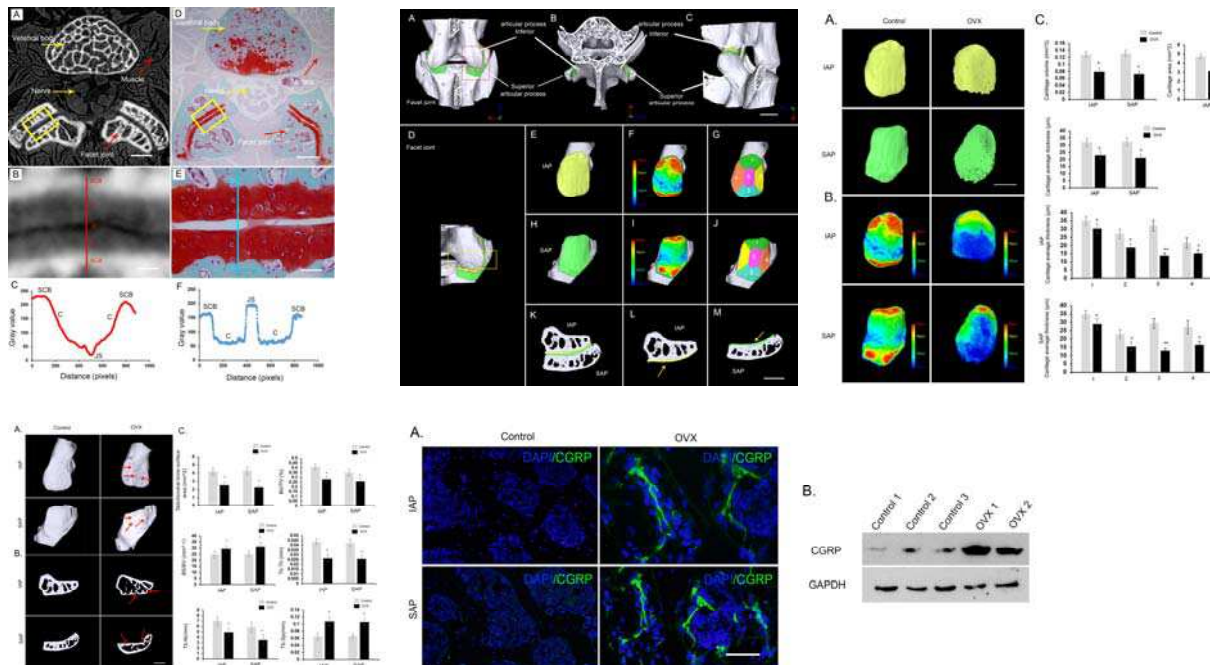
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**INTRODUCTION** There is little information regarding the morphology change of cartilage and subchondral bone in OVX-induced lumbar facet joint (LFJ) osteoarthritis. The purpose of this study was to 3D visualize and pathological characteristics of cartilage and subchondral bone change in OVX-induced lumbar facet joint osteoarthritis mouse model using propagation-based phase-contrast computed tomography (PPCT) combining with histopathological method.

**METHODS:** The mice were subdivided randomly into two groups of bilaterally OVX animals and control animals, with ten animals in each group. All animals in OVX and control groups were killed 8 week postoperatively. For a detailed qualitative and quantitative three-dimensional (3D) evaluation, structural alterations of facet joint cartilage surface and subchondral bone architecture were evaluated by a propagation-based phase-contrast computed tomography (PPCT) system. The image quality were evaluated and compared with histology.

**RESULTS SECTION:** PPCT imaging provides 3D visualization of altered cartilage with simultaneous high detail of the subchondral bone abnormalities. Quantitative analysis demonstrated that the cartilage volume, surface area and thickness were decreased in OVX groups both in the inferior articular process (IAP) and superior articular process (SAP) compared to the control group at the same ages. Meanwhile, these morphological change were accompanied by obvious destruction of the subchondral bone surface and trabecular bone in the OVX group. The delineation of 3D pathological changes in PPCT imaging is similar to histopathological finding with Saf O staining. In addition, increased CGRP ingrowth in subchondral bone were observed and confirmed by WB in OVX group compared with control group.

**DISCUSSION and SIGNIFICANCE:** These results indicated that PPCT may has great potential for in simultaneously analysis of the LFJ by providing 3D morphological change about cartilage and the subchondral bone, and their relationship in OA conditions. Degenerative FJC possess greatly increased nerve ingrowth in subchondral bone may play an important role in the progression of OVX-induced LFJ OA and caused low back pain.





## CHANGES IN COMBINED HYDROSTATIC AND OSMOTIC PRESSURE ALTER METABOLIC TURNOVER IN NUCLEUS PULPOUS CELLS IN VITRO

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**INTRODUCTION** We have focused on metabolic turnover in nucleus pulposus (NP) as a response to changes in combined physicochemical stresses: hydrostatic pressure (HP) and osmotic pressure (OP), since these stresses occur due to weight-bearing and joint-loading. We hypothesized that a specific combination of HP and OP reproduces anabolic and catabolic functions by NP cells/clusters. We measured metabolic related gene expression by bovine NP (bNP) cells/clusters in response to changes in HP ( $\Delta$ HP) and OP ( $\Delta$ OP) using a novel culture system and a semi-permeable membrane pouch.

**MATERIAL AND METHODS** bNP cells were harvested from caudal joints (2-3 weeks old cows) purchased from a local abattoir. The NP cells/clusters were enzymatically isolated, seeded on agarose-coated 6-well plates, and incubated in DMEM/Ham's F-12 (1:1) with 10% FBS and antibiotics for 4-5 days. We injected the suspended NP cells/clusters into a semi-permeable membrane tubing (500 KD MWCO). Both ends of the tubing were sealed to make a pouch. The pouches were divided to 14 groups comprising of a combined algorithm of the first 3 days with either  $\Delta$ HP (0 - 0.5 MPa, 0.5 Hz) and/or  $\Delta$ OP (310 - 450 mOsm) followed by the same algorithm for the second 3 days (Figs. 1-4). The pouches were harvested at days 4 and 7. Then, the NP cells/clusters were ejected from the pouches by flushing with PBS. mRNA was extracted using RNeasy Mini kit (Qiagen). We measured gene expression of aggrecan core protein (*Agg*), collagen type-II (*Col-2*) as an anabolic marker, cell proliferation (*PCNA*), and matrix metalloproteinase-13 (*MMP-13*) compared to *GAPDH* for normalization using TaqMan<sup>®</sup> qPCR.

**RESULTS** Comparing algorithm of  $\Delta$ OP at day 7 (Fig. 2), *Agg* was upregulated, but did not retain the level for 7 days and declined at low OP. *Col-2* was upregulated due to high OP for the first 3 days, but did not retain the level for the next 3 days. *MMP-13* was upregulated due to  $\Delta$ OP, but did not retain the level over 7 days. Overall, OP stimulates more catabolic gene expression than anabolic ones. Comparing  $\Delta$ HP at day 7 (Fig. 3), *Agg*, *Col-2*, and *PCNA* were upregulated due to  $\Delta$ HP. *MMP-13* was upregulated due to  $\Delta$ HP and retained it at high HP. Overall,  $\Delta$ HP at low OP stimulated anabolic and catabolic gene expression. Comparing  $\Delta$ HP and  $\Delta$ OP at day 7 (Fig. 4), *Agg* was upregulated due to  $\Delta$ HP at high OP. *Col-2* was upregulated due to  $\Delta$ HP and loading HP at high OP. *PCNA* was upregulated due to  $\Delta$ HP at high OP. *MMP-13* was upregulated due to  $\Delta$ HP, but not HP loading at high OP.

**DISCUSSION** We intended to reproduce  $\Delta$ OP and  $\Delta$ HP in NP and these combined algorithms *in vitro*. We profiled gene expression of metabolic molecules by NP cells/clusters in response to  $\Delta$ OP and  $\Delta$ HP. A set of profiles will be useful to study mechanisms of pathogenesis and to develop biological treatments under  $\Delta$ HP and  $\Delta$ OP physiologically. Repetitive  $\Delta$ OP and  $\Delta$ HP will reproduce NP homeostasis and/or progressive regenerative or degenerative NP.

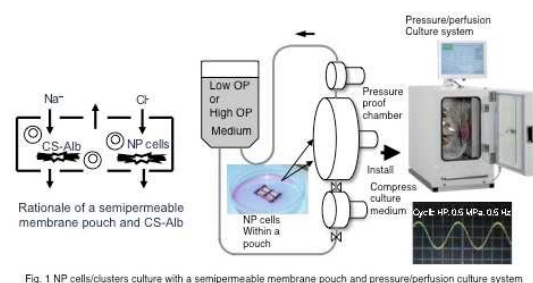


Fig. 2 Effects of Osmotic Pressure in Nucleus Pulposus Cells

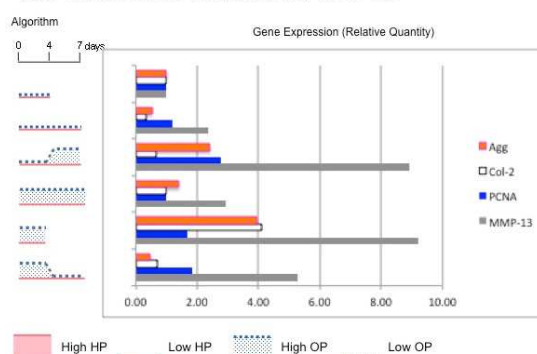


Fig. 3 Effects of Hydrostatic Pressure in Nucleus Pulposus Cells

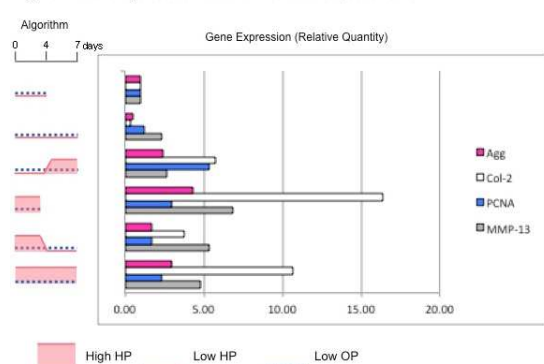
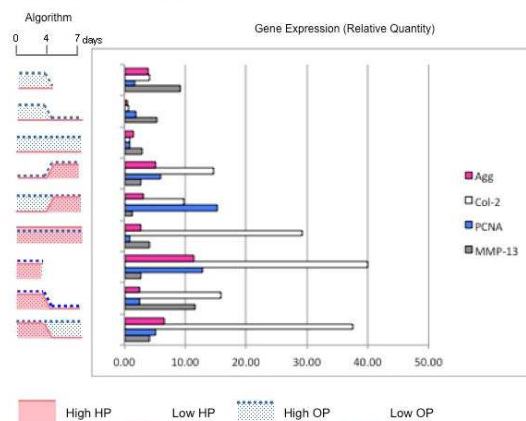


Fig. 4 Effects of Hydrostatic Pressure and High Osmotic Pressure in Nucleus Pulposus Cells





## VERTEBRAL ENDPLATE DEFECT AS INITIATING FACTOR FOR MODIC CHANGE IN THE GENERAL POPULATION

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**Introduction.** The etiology of Modic change (MC) is still unclear. MC is rarely seen in vertebrae adjacent to healthy intervertebral discs, but appear to be associated with disc degeneration (DD), disc herniation and Schmorl's nodes. Precise understanding of the role of endplate defect in the etiology MC and DD is lacking, especially in the general population. Our aim was to characterise associations between endplate defects and MC.

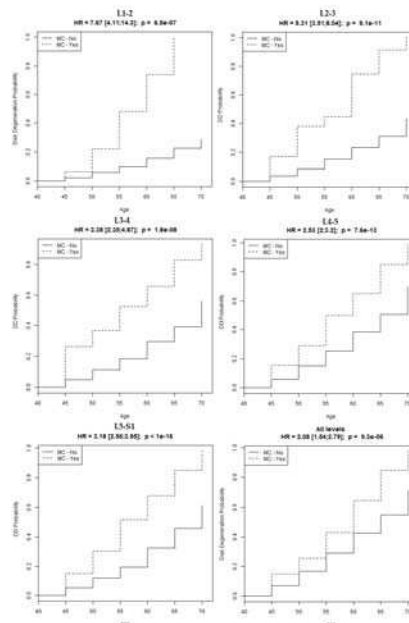
**Methods.** The study sample in this cross-sectional MRI study consisted of 831 twin volunteers from TwinsUK (mean age 54 (SD=8) years; 95.8% female). Lumbar T2-weighted MR images were used to grade endplate defects in 8310 endplates on a scale of 1-6. Total endplate score (TEPS) was achieved by summing both endplate defect scores from the same intervertebral disc level. MC had been coded as absent (grade 0) or present (grade 1) previously and, importantly, was independent of the assessment for TEPS. A survival analysis paired with Cox proportional hazards model analysis was used, with subjects subgrouped by age decade. Receiver operating curves (ROC) were calculated to define critical endplate values predictive of MC.

**Results.** MC was present in 267 (32.1%) subjects, with a higher prevalence at lower lumbar levels (3.5% at L1/2-L3/4 vs. 15.9% at L4/5-L5/S1,  $p<0.001$ , Figure 1). TEPS was strongly and independently associated with MC at each lumbar level ( $p<0.001$ , adjusting for body mass index, age and gender). The ROC showed a TEPS cut-off score of 6 after which there was a higher prevalence of MC. Probability of having MC was significantly increased in all TEPS positive ( $\geq 6$ ) age subgroups (Figure 2).

**Discussion.** This large, population based study confirmed that endplate defects are strongly and independently associated with MC at every lumbar level and in all age groups. As we have previously shown MC to be associated with DD and an independent risk factor for low back pain, we postulate the endplate defect is the initiating trigger for MC and DD.



**Figure 1.** Prevalence and distribution of Modic change (MC) in the lumbar spine. The majority of MC is found in the lower lumbar spine (L4-S1) indicating a possible role of mechanical forces acting on the adjacent intervertebral discs and endplates of this anatomical region.



**Figure 2.** Survival analysis paired with Cox proportional hazards models analysis. Probability of having Modic change (MC) is significantly increased in DD positive age subgroups at each disc level. The probability does increase with age. HR=hazard ratio.

## P.ACNES MAY BE A KEY FACTOR OF MODIC CHANGES, A CLINICAL AND IN VITRO STUDY

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**Introduction:** disc degeneration (DD) is a common disorder confusing the aging population. Modic changes (MCs) is closely correlated with DD. Recent studies demonstrated that Propionibacterium acnes (P. acnes) is associated with MCs. However, their accurate relationship remains controversial.

**Method:** 12 Discs, adjacent to lumbar MCs from the patients who underwent spine surgery, were collected, embedded and proliferated for RT-PCR and gene sequencing to identify the bacterium. Then, P. acnes was inoculated in Brain Heart Infusion Broth. The supernatants from P. acnes cultures was prepared by centrifuge and the concentration of endotoxin in the supernatants was measured. The bacterial supernatants were added to culture medium for nucleus pulposus cell (NPC), annulus fibrosus cell (AFC) and endplate cells. Then, Viability of disc and endplate cells were tested by CCK8 assays at 24, 48 and 96 h. To evaluate how P. acnes influence the disc cells, gene expression was analyzed by real-time PCR and cell lysates were analyzed using western blotting.

**Results:** P. acnes was isolated in 6/12 lumbar intervertebral discs from 9 patients. Staphylococci were detected in fluid from another 3 discs. The difference of prevalence between P. acnes and other bacterium was significant. After treated disc and endplate cells with P. acnes supernatants, CCK8 assay showed significantly reduced cell viability. RT-PCR assay and Western blotting strengthened the results.

**Conclusion:** MCs may be correlated with P. acnes, which would influence the survival and function of disc and endplate cells. Thus, the infection of P. acnes may be a key factor of MCs and accelerate the disc degeneration.

## PROPIONIBACTERIUM ACNES INCUBATION IN THE DISCS CAN RESULT IN TIME-DEPENDENT MODIC CHANGES: A LONG TERM RABBIT MODEL

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**Introduction:** Modic changes (MCs) have been widely observed, and assume to be closely associated with low back pain and Propionibacterium acnes (*P. acnes*), but there are few animal models showing how MCs are progressed. The aim of this study is to evaluate the feasibility of inducing of MCs by injection of *P. acnes* into the lumbar intervertebral discs of rabbits.

**Methods:** Ten rabbits were used for the study. The L2-3 and L3-4 discs of all rabbits were injected with 100 $\mu$ L *P. acnes* ( $1.6 \times 10^7$  CFU/mL) as *P. acnes* group, L4-5 disc were injected with 100 $\mu$ L normal saline as vehicle, and L5-6 disc was untreated (blank). MCs was investigated by magnetic resonance imaging (MRI) before operation and at 2 weeks, 1, 3, 4.5, 6 and 9 months postoperatively. Following sacrifice, histological analysis, blood test and micro-CT were performed. Cytokine expression in nucleus and endplate tissues was quantified using real-time polymerase chain reaction (RT-PCR)

**Results:** From 3-months post-operatively, the *P. acnes* group showed significantly decreased T1-weighted signal intensity, while the T2-weighted signal was significantly higher at 3 and 4.5 months, and then decreased remarkably at 6 and 9 months. 11/20 inferior endplates were identified as type I MCs at 4.5-months, and 9/20 were identified as type II MCs at 9-months. RT-PCR showed that expression of IL-1 $\beta$ , TNF- $\alpha$ , IFN- $\gamma$ , MMP-9 and ADAMTS-5 in the NP, and IL-1 $\beta$ , TNF- $\alpha$  and ADAMTS-5 in the endplates, were significantly up-regulated following injection of *P. acnes*. Histological slices of discs injected with *P. acnes* showed disc degeneration, endplate abnormalities and inflammatory response, with micro-CT confirming bone resorption.

**Discussion:** *P. acnes* incubation the disc can induce degeneration of the disc and an inflammatory response in the endplate region, presenting as time-dependent MCs type I and II. Histological examination and PCR analysis confirmed an inflammatory-like response. The BMD loss and trabecular bone quality reduction in the endplate revealed by micro-CT can also should be attributed to *P. acnes* infection.

## MULTI-DIMENSIONAL ASSESSMENT OF VERTEBRAL ENDPLATE BREAKS ON MRI: IMPLICATIONS IN SPINE DEGENERATION AND PAIN/ DISABILITY

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**Introduction:** The vertebral endplate is a critical component of the motion segment. The endplate is vulnerable to extensive wear and tear during one's life-time. Magnetic resonance imaging (MRI) is an effective tool to detect the structural endplate dimensions and changes. Previous studies have noted endplate abnormalities/defects or "breaks" to be associated with intervertebral disc degeneration. However, such endplate findings were not always synonymous with disc degeneration severity or pain and disability. Endplate breaks vary in morphology and size. However, the role of such variation in endplate dimensions upon disc integrity and other MRI phenotypes (e.g. Modic changes, facet joint degeneration) remains speculative, and their implications upon pain and disability debatable. As such, the aim of the current study was to investigate the role of endplate dimensions in disc degeneration, and their relationship with other MRI phenotypes as well as the clinical profile.

**Methods:** One hundred and eight Southern Chinese subjects were recruited (50% male; mean age: 53 years) and underwent T2W 3T MRI of the lumbar spine (n=1,080 endplates). Any structural endplate breaks were identified and their dimension was measured in terms of maximum width and depth using RadiAnat Dicom software. These measurements were then standardized with actual width of the endplate and depth of the vertebral body, respectively. Both width and depth of all endplate breaks in each subject were added separately and scores were assigned on the basis of size from 1 to 3. Combining both width and depth scores gave *cumulative endplate break scores*. Disc degenerative scores and associated disc degenerative changes based on Pfirrmann grading, posterior disc bulge, Modic changes, HIZ and facet joint profiles were also assessed. Subject demographics, low back pain (Visual Analog Scale: VAS) and disability profiles (Oswestry Disability Index: ODI) were obtained and correlated to the endplate and other MRI phenotype profiles.

**Results:** Intra-rater reliability for all measurements were found to be excellent. Endplate breaks were observed in 67.5% of the subjects (51% males; mean age: 52 years) and in 14% of the endplates (58% males; 57% upper two lumbar levels; 67% inferior endplate). Standardized width and depth of the endplate breaks were found to be increased with age ( $p=0.02$  &  $p=0.007$ , respectively), Modic changes ( $p<0.001$  &  $p=0.003$ , respectively), Pfirrmann grades ( $p<0.001$  both cases) and posterior disc bulge ( $p=0.03$  &  $p=0.005$ , respectively). Width of the endplate breaks was also seen to be increased with irregular and narrow facet joints ( $p<0.05$  &  $p=0.01$ , respectively). *Cumulative endplate break scores* showed strong positive association with ODI (ODI;  $p<0.05$ ) and VAS compared to disc degenerative scores.

**Discussion:** This is the first study to assess the multi-dimensional morphology of endplate breaks. Different sizes of endplate breaks may represent different etiologies. Large size endplate breaks were strongly associated with degenerative spine changes and other MRI phenotypes as well as more back-related disability. Findings from this study stress the need to assess endplate findings from a multi-dimensional perspective, whose role may have clinical utility

## WHO PLAYED THE IMPORTANT ROLE IN THE DEGENERATION OF RATS DISC, THE NUCLEUS PULPOSUS MESENCHYMAL STEM CELLS AGE-RELATED CHANGES?

Deli Wang

**Introduction:** The functions of mesenchymal stem cells (MSCs) appear to decline with age due to cellular senescence, which could reduce the efficacy of MSCs-based therapies. Recently, MSCs have been identified in the nucleus pulposus, which offers great potential for intervertebral disc (IVD) repair. However, this potential might be affected by the senescence of nucleus pulposus MSCs (NPMSCs), but whether or not this exists remains unknown. This study aims examining the presence of senescent NPMSCs in IVD and investigating the age-related changes in NPMSCs.

**Methods:** NPMSCs isolated from young (3-month-old) and old (14-month-old) Sprague-Dawley rats were cultured in vitro. Differences in morphology, proliferation, colony formation, multilineage differentiation, cell cycle, and expression of  $\beta$ -galactosidase (SA- $\beta$ -gal) and senescent markers (p53, p21, and p16) were compared between groups.

**Results:** The major findings of our study demonstrated that (i) both young and old NPMSCs fulfilled the requirements for MSCs definition; (ii) young NPMSCs presented a better proliferation capacity and colony-forming ability than old NPMSCs; (iii) the 3-lineage differentiation potential of NPMSCs declined with age; (iv) increased G0/G1 and G2/M phase arrest and decreased S phase entry was observed in old NPMSCs compared with young NPMSCs; and (v) NPMSCs displayed characteristic senescent features with age, including an increased in SA- $\beta$ -gal expression and significant activation of the p53-p21-pRB pathway, which were both associated with cell senescence.

**Discussion:** This is the first study proving that increased senescence of NPMSCs is present in IVD with advancing age. Considering that stem cells play a key role in maintaining the homeostasis of normal tissue, aging of stem cells in IVD may provide new insight into the mechanisms of IVD degeneration. The understanding of the mechanisms underlying these degenerative processes may be important in helping to improve the prevention and treatment of IVD degeneration. Furthermore, the age-related decline in the functional properties of NPMSCs should be taken into consideration when evaluating the potential utility of autologous NPMSCs isolated from aged donors for regenerative medical therapies.

## RESISTIN PROMOTES CCL4 EXPRESSION THROUGH TOLL-1 LIKE RECEPTOR-4 AND ACTIVATION OF THE P38-MAPK AND NF- $\kappa$ B SIGNALING PATHWAYS: IMPLICATIONS FOR INTERVERTEBRAL DISC DEGENERATION

Jianru Wang, Hui Liu, Zemin Li, Zhaomin Zheng

**Introduction:** Although the biological effects of resistin have been studied in many diseases, few studies have investigated the role of resistin in IVDD. Several chemokine genes are up-regulated by the pro-inflammatory cytokine IL-1 $\beta$  and resistin in chondrocytes. Recently, we showed that TNF- $\alpha$  and IL-1 $\beta$  induced CCL4 expression in NP cells and may play an important role in promoting the cytokine-dependent migration of macrophages into the disc through its receptor, C-C chemokine receptor 1 (CCR1). The objective of this study was to investigate whether resistin induces the expression of CCL4 during IVDD and whether Toll-like receptor-4 (TLR-4) and the NF- $\kappa$ B signaling pathway are involved in this process.

**Methods:** The expression pattern of resistin and CCL4 in different degenerated human NP tissues were measured by qPCR; Effect of resistin on the migration of macrophages was measured by cell migration assay. Resistin-induced CCL4 expression were analyzed by qPCR, ELISA and cell immunofluorescence. Involvement of TLR-4, p38-MAPK, and NF- $\kappa$ B signaling pathways were studied by siRNA or Lenti-virus mediated knockdown, co-immunoprecipitation, and chromatin immunoprecipitation (ChIP) assay.

**Results:** Expression of resistin and CCL4 was elevated in degenerated nucleus pulposus (NP) tissue. Resistin promoted macrophage migration through CCL4 and its receptor. Expression of CCL4 was significantly increased by resistin treatment. The pharmacological inhibition or siRNA knockdown of TLR-4 blocked the resistin-induced CCL4 expression. Co-immunoprecipitation data confirmed the binding of resistin to TLR4. Pharmacological inhibition of the NF- $\kappa$ B and p38-MAPK signaling pathways attenuated the resistin-induced CCL4 expression. A chromatin immunoprecipitation (ChIP) assay and lentivirus mediated knockdown showed that resistin regulate CCL4 expression through p65.

**Discussion:** The expression of resistin and CCL4 in 19 disc samples with different stages of degeneration showed that resistin and CCL4 expression were significantly induced during disc degeneration. Chemokines are a specific class of cytokines that typically mediate chemoattraction between cells. During intervertebral disc degeneration, inflammatory cells such as macrophages infiltrate into the disc and cause inflammation. Our study is the first to show that resistin could induce CCL4 expression in NP cells, which is consistent with previous reports suggesting that CCL4 expression could be induced by resistin. Furthermore, promoter studies have shown that resistin regulate CCL4 expression at the transcriptional level. Our data showed that pharmacological inhibitors of TLR4 and TLR4 siRNA application could inhibit resistin-induced CCL4 expression, which was further confirmed with co-immunoprecipitation. We further demonstrated that resistin activates the p38-MAPK and NF- $\kappa$ B signaling pathways by the phosphorylation of p38 and p65. Pharmacological data shows that MAPK signaling regulates CCL4 expression differently; p38 positively controlled resistin-dependent induction of CCL4. Our ChIP data also showed that p65 binding activity to the CCL4 promoter was increased by resistin treatment. Based on our findings, this study shows that resistin binds to TLR4 and increase the expression of CCL4 through p38-MAPK and NF- $\kappa$ B signaling pathways in NP cells, and this expression causes infiltration of macrophages. This study might provide a feasible therapeutic target for controlling the inflammatory response associated with IVDD.

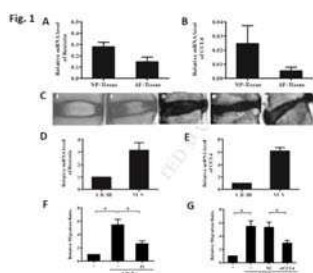


Figure 1 The expression of resistin and CCL4 in human NP tissue and the resistin-induced macrophage migration.

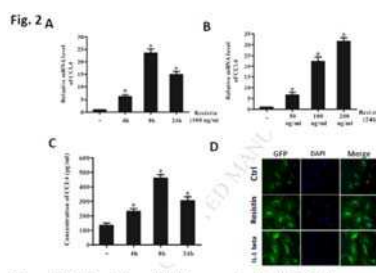


Figure 2 Resistin-induced CCL4 expression in the NP cells.

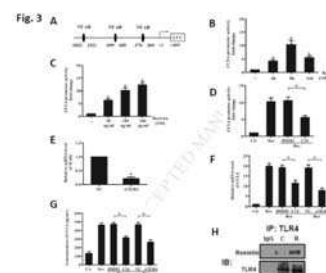


Figure 3 TLR-4 is involved in the induction of CCL4 by resistin.

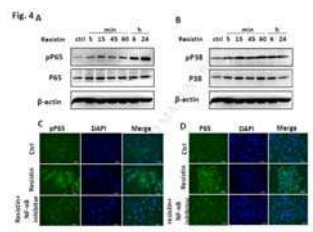


Figure 4 Resistin activates the p38-MAPK and NF- $\kappa$ B signaling pathways.

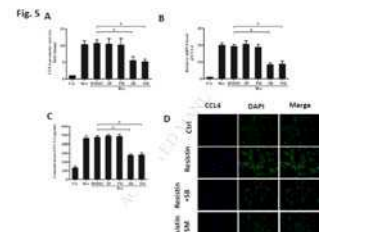


Figure 5 Inhibition of the p38-MAPK and NF- $\kappa$ B signaling pathways blocks the induction of CCL4 by resistin.

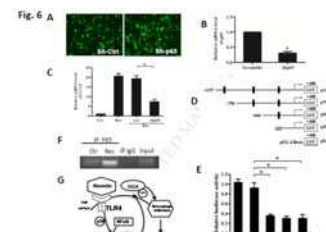


Figure 6 Lentivirus-mediated knockdown of p65 blocks the induction of CCL4 by resistin.

## INTERVERTEBRAL DISC/BONE MARROW CROSS-TALK WITH MODIC CHANGES

### (ISSLS Prize – Basic Science)

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**Study design:** Cross-sectional cohort analysis of patients with Modic Changes (MC).

**Objective:** Our goal was to characterize the molecular and cellular features of MC bone marrow and adjacent discs. We hypothesized that MC associate with biologic cross-talk between discs and bone marrow, the presence of which may have both diagnostic and therapeutic implications.

**Background Data:** MC are vertebral bone marrow lesions that can be a diagnostic indicator for discogenic low back pain. Yet, the pathobiology of MC is largely unknown.

**Methods:** Patients with Modic type 1 or 2 changes (MC1, MC2) undergoing at least 2-level lumbar interbody fusion with one surgical level having MC and one without MC (control level). Two discs (MC, control) and two bone marrow aspirates (MC, control) were collected per patient. Marrow cellularity was analyzed using flow cytometry. Myelopoietic differentiation potential of bone marrow cells was quantified to gauge marrow function, as was the relative gene expression profiles of the marrow and disc cells. Disc/bone marrow cross-talk was assessed by comparing MC disc/bone marrow features relative to unaffected levels.

**Results:** Thirteen MC1 and eleven MC2 patients were included. We observed pro-osteoclastic changes in MC2 discs, an inflammatory dysmyelopoiesis with fibrogenic changes in MC1 and MC2 marrow, and upregulation of neurotrophic receptors in MC1 and MC2 bone marrow and discs.

**Conclusion:** Our data reveal a fibrogenic and pro-inflammatory cross-talk between MC bone marrow and adjacent discs. This provides insight into the pain generator at MC levels and informs novel therapeutic targets for treatment of MC-associated LBP.

This study was supported by the Swiss National Science Foundation Grant 145961, 158792, and 164726 as well as the National Institutes of Health Grant AR063705

## AUTOMATION OF READING OF RADIOLOGICAL FEATURES FROM MAGNETIC RESONANCE IMAGES (MRI's) OF THE LUMBAR SPINE WITHOUT HUMAN INTERVENTION IS COMPARABLE WITH AN EXPERT RADIOLOGIST

(ISSLS Prize – Bioengineering Science)

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**Introduction:** Investigation of the automation of radiological features from Magnetic Resonance Images (MRIs) of the Lumbar Spine. Our objective was to automate the process of grading lumbar intervertebral discs and vertebral bodies from MRIs. MR imaging is the most common imaging technique used in investigating low back pain (LBP). Various features of degradation, based on MRIs, are commonly recorded and graded e.g. Modic change and Pfirrmann grading of intervertebral discs. Consistent scoring and grading is important for developing robust clinical systems and research. Automation facilitates this consistency and reduces the time of radiological analysis considerably and hence the expense.

**Methods:** 12,018 intervertebral discs, from 2009 patients, were graded by a radiologist and were then used to train: 1) a system to identify and label vertebrae and discs in a given scan, and 2) a Convolutional Neural Network (CNN) model that predicts several radiological gradings. The scans used in the experiments are limited only to the T2 sagittal scans. There are six main radiological features that this study has focused on are: 1) Pfirrmann Grading, 2) Disc Narrowing, 3) Spondylolisthesis, 4) Central Canal Stenosis, 5) Endplate Defects, and 6) Marrow signal variations (Modic changes). The scans were annotated with various radiological scores (global, the whole spine, and local, per disc) by a single expert experienced spinal radiologist (IMcC). The performance of the radiologist was tested using a sample of 121 scans that were rescored 6 months following the original scoring. The performance of the model, in terms of class average accuracy, was compared with the intra-observer class average accuracy of the radiologist.

**Results:** The detection system achieves 95.6% accuracy in terms of disc detection and labelling. The model is able to produce predictions of multiple pathological gradings that consistently matched those of the radiologist. The Model identifies 'Evidence Hotspots' are the voxels that most contribute to the degradation scores.

**Discussion:** Our automated system takes around 1-2 minutes to process a scan. For scans of adequate quality, the vertebral bodies and discs were detected accurately in 95.6% scans with detection failing only if scans were corrupted or of poor quality, or if transitional vertebrae were present. The entirety of the disc regions of the scans were used as the input data for classification of the radiological features scored. Automation of radiological grading is now on par with human performance. The system can be beneficial in aiding clinical diagnoses in terms of objectivity of gradings and the speed of analysis. One benefit of automated reading is to produce a numerical signal score that would provide a scale of degeneration and so avoid an arbitrary categorization into artificial grades. This is an important stepping stone in the investigation of the relationship between MRIs and clinical diagnoses of back pain in large cohorts.

**Acknowledgement:** This work was supported by the RCUK CDT in Healthcare Innovation (EP/G036861/1) and the EPSRC Programme Grant Seebibyte (EP/M013774/1). The Genodisc data were obtained during the EC FP7 project (HEALTH-F2-2008-201626).

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## IS INFECTION THE POSSIBLE INITIATOR OF DISC DISEASE? AN INSIGHT FROM PROTEOMIC ANALYSIS

(ISSLS Prize – Clinical Science)

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**Study design:** Proteomic and 16S rDNA analysis of disc tissues obtained *in-vivo*

**Objective:** To address the controversy of infection as an etiology for disc disorders through protein profiling.

**Summary of Background Data:** There is raging controversy over the presence of bacteria in human lumbar discs *in-vivo*, and if they represent contamination or infection. Proteomics can provide valuable insight by identifying proteins signifying bacterial presence and, also host defense response proteins (HDRPs) which will confirm infection.

**Methods:** 22 discs (15-disc herniations (DH), 5-degenerate (DD), 2-normal in MRI (NM)) were harvested intraoperatively and immediately snap frozen. Samples were pooled into three groups and proteins extracted were analysed with liquid chromatography-tandem mass spectrometry (LC-MS/MS). Post identification, data analysis was performed using Uniprot, Pantherdb, Proteome discoverer and STRING network. Authentication for bacterial presence was performed by PCR amplification of 16S rDNA.

**Results:** LC-MS/MS analysis using Orbitrap showed 1103 proteins in DH group, compared to 394 in NM and 564 in DD. 73 bacterial specific proteins were identified (56 specific for *Propionibacterium acnes*; 17 for *Staphylococcus epidermidis*). In addition, 67 infection specific HDRPs; unique or upregulated such as *Defensin*, *Lysozyme*, *Dermcidin*, *Cathepsin-G*, *Prolactin-Induced Protein*, *Phospholipase-A2* etc., were identified confirming presence of infection. Species specific primers for *P. acnes* exhibited amplicons at 946bp (16s rDNA) and 515bp (Lipase) confirming presence of *P. acnes* in both NM discs, 11 of 15 DH discs and all five DD discs. Bioinformatic search for protein-protein interactions (STRING) documented 169 proteins with close interactions (protein clustering co-efficient 0.7) between host-response and degenerative proteins implying that infection may initiate degradation through *Ubiquitin C*.

**Conclusion:** Our study demonstrates bacterial specific proteins and host defense proteins to infection which strengthen the hypothesis of infection as initiator of disc disease. These results can lead to a paradigm shift in our understanding and management of disc disorders.

## **SURGICAL OUTCOMES OF POSTERIOR LUMBAR INTERBODY FUSION IN PATIENTS OVER 80 YEARS OF AGE**

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### **Introduction:**

The number of elderly people is increasing. Therefore, spinal surgery for patients over 80 years of age is becoming more common. However, there are few reports assessing the outcomes of posterior lumbar interbody fusion (PLIF) for patients over 80 years of age. The purpose of this study was to investigate the surgical outcomes for patients over 80 years of age who underwent PLIF.

### **Methods:**

Subjects comprised 55 patients over 80 years of age who underwent single segment PLIF, single segment PLIF with another segment decompression or double segment PLIF between 2007 and 2014 in our institution. Of these 55 patients, 47 patients who had been followed at least 2 years were included in the study. There were 18 males and 29 females and their mean age at surgery was  $81.8 \pm 1.8$  years (range 80-86). Mean follow up period was 40 months and follow up rate was 85.4%. Clinical outcomes were evaluated according to the Japanese Orthopaedic Association scoring system (JOA score). We also evaluated recovery rate of the JOA scores, according to the formula: recovery rate (%) = [(postoperative score – preoperative score) × 100] / (maximum possible score – preoperative score). Plain radiographs and CT scan were used to assess the status of union. Intra and post-operative complication was noted from medical records.

### **Results:**

Early surgery-related neurological complication did not occur. Dural tear was observed in 4 patients. Superficial SSI was observed in 1 patient and hematoma evacuation due to neurological deterioration was performed in 1 patient. No general complications such as brain or heart stroke occurred in any patients during admission. Two patients died of pneumonia after discharge. The mean JOA score had improved from 12.7 (5-20) to 22.8 (8-29) at the time of peak recovery and declined to 18.7 (7-29) at the final follow up. The mean recovery rate was 62.9% at the time of peak recovery and 35.1% at the final follow-up. Successful bone union was obtained in 42 patients at the final follow-up (union rate 89%). Eleven patients had neurological deterioration and 6 patients required additional surgery 6-42 months after initial operation. Except for these 11 patients with neurological deterioration, 24 patients (51.1%) could keep the around score (declination within 3 points). Meanwhile, remaining 12 patients (25.5%) had declination of the score 4 points or more without neurological deterioration due to physical hypofunction by aging.

### **Conclusion:**

In this study, the recovery rate after PLIF in patients over 80 years of age at peak was comparable to that in the past reports and nearly half of the patients could keep the status of recovery. However, 23.4% of the patients had neurological deterioration and another 25.5% of the patients had declination of the score due to physical hypofunction at the final follow-up.

## TIME TO REMOVE OUR ROSE-TINTED GLASSES: A CANDID APPRAISAL OF THE RELATIVE SUCCESS OF SURGERY IN OVER 4'500 PATIENTS WITH DEGENERATIVE DISORDERS OF THE LUMBAR SPINE, HIP OR KNEE

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### Introduction

Anecdotally, lumbar spine surgery is believed to deliver poorer patient outcomes than total hip (THR) and knee (TKR) replacement surgery; however, the formal studies hitherto conducted in small, select groups of spine patients do not always substantiate this. Notably, these studies have predominantly employed generic health-related quality of life (HRQL) outcome measures, such as the Short Form 36 (SF-36), which do not always adequately reflect the benefit of specific types of surgery and may be less able to discriminate between the successes and failures of treatment. The allocation of limited resources for both the treatment of and research into degenerative musculoskeletal disorders requires evaluation of effectiveness using sensitive patient-reported outcome measures (PROMs). This study sought to compare the surgical outcomes of a large number of patients with degenerative disorders of the lumbar spine, hip or knee, using a brief joint-specific PROM that includes the "Core Outcome Measures Index" (COMI).

### Methods

Preoperatively and 12-months postoperatively, 4'594 patients (3'937 lumbar spine, 368 hip, 269 knee) undergoing first-time surgery completed a PROM that included the Core Outcome Measures Index (COMI) for the affected joint. The latter comprises a set of single items on pain, function, symptom-specific well-being, quality of life, and disability — all in relation to the specified joint problem. Other global ratings of treatment "success" were reported 12 months postoperatively.

### Results

In multiple regression analyses, controlling for confounders, the mean improvement in COMI score at 12 months was greatest for the hip patients and lowest for those with degenerative spinal deformity (the statistical reference group). Compared with spinal deformity, the odds of achieving "success" were: higher for hip (OR 4.6;95%CI,2.5-8.5) and knee (OR 4.0;95%CI,2.1-7.7) (no difference between spine subgroups) for "satisfaction with care"; higher for hip (OR 16.9;95%CI,7.3-39.6), knee (OR 6.3;95%CI,3.4-11.6), degenerative spondylolisthesis (OR 1.6;95%CI,1.2-2.2), and herniated disc (OR 1.7;95%CI,1.2-2.4) for "global treatment outcome"; and higher for hip (OR 13.8;95%CI,8.8-21.6), knee (OR 5.3;95%CI,3.6-7.8), degenerative spondylolisthesis (OR 1.6;95%CI,1.3-2.1), and herniated disc (1.5;95%CI,1.1-2.0) for "patient acceptable symptom state". Patient-rated complications were greatest in degenerative spinal deformity (29%) and lowest in hip (18%).

### Discussion

The current study is the largest of its kind and the first to use a common but joint-specific instrument to report patient-reported outcomes in those undergoing surgery for degenerative disorders of the spine, hip or knee. The findings provide a sobering account of the significantly poorer outcomes after spine surgery compared with large-joint replacement. Further work is required to hone the indications and patient selection criteria for spine surgery. The data should be used to lobby research funding-bodies, governmental agencies, industry, and charitable foundations to invest more in spine research/registries, in the hope of ultimately improving spine outcomes.

## ADJACENT SEGMENT DEGENERATION AFTER LUMBAR TOTAL DISC REPLACEMENT: 5-YEAR RESULTS OF A MULTICENTER, PROSPECTIVE, RANDOMIZED STUDY WITH INDEPENDENT RADIOGRAPHIC ASSESSMENT

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**Introduction:** One of the potential benefits of lumbar total disc replacement (TDR) over fusion for the treatment of painful disc degeneration is the possibility of reducing adjacent segment degeneration (ASD). There has been little investigation into this area in large prospective studies. The purpose of this study was to analyze pre- to post-operative changes of the disc adjacent to the level receiving a TDR at 5 year follow-up.

**Methods:** Patients from 14 sites were enrolled in the study, 218 assigned to the investigational group, activL<sup>®</sup> and 106 assigned to the control group, ProDisc-L. All patients were treated for single-level symptomatic disc degeneration non-responsive to non-operative care. Flexion/extension, neutral lateral and anteroposterior radiographs were made at each study visit. Pre- and 5-year post-operative radiographs were available for 135 patients in the investigational group and 63 patients in the control group. All radiographs were evaluated by an independent lab specializing in image assessment. Measurements made from the radiographs included adjacent segment degeneration based in the Kellgren-Lawrence scale and the scale described by Zigler et al. (JNS 2012), range of motion, disc height, and translation.

**Results:** When compared to pre-operative images, 8.8% of the investigational group and 19.0% of the control group had increased ASD scores at 5-year follow-up ( $p < 0.05$ ). Results were the same using either the Kellgren-Lawrence or the Zigler ASD scale. Figure 1 provides the percentage of patients in the investigational group with increased ASD scores from pre-operative to 5 year post-operative for each degree of range of motion at the TDR level at 5 years. For each additional degree of range of motion, there was a consistent decrease in the percentage of patients with ASD.

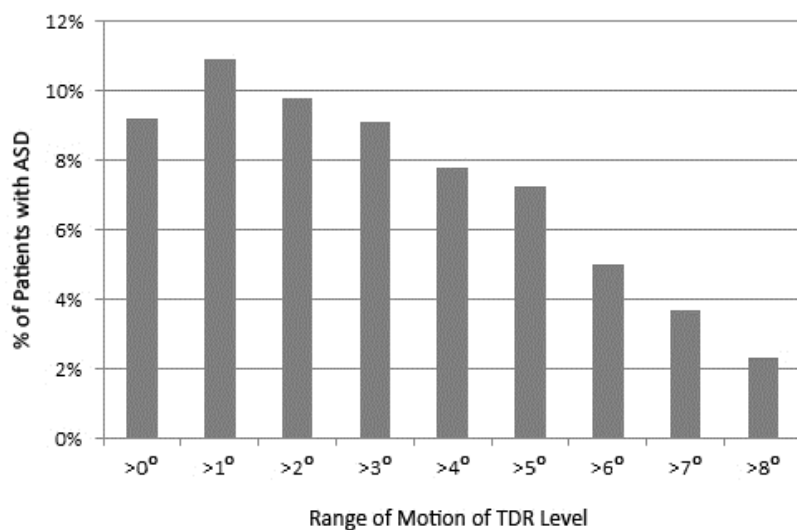


Figure 1. The percentage of patients with ASD decreased as the range of motion of the TDR level increased.

The rate of ASD was significantly greater in patients more than 40 years of age than those aged 40 years or less (19.6% vs. 5.0%;  $p < 0.01$ ; data pooled for investigational and control groups).

**Discussion:** The results of this prospective, 5-year follow-up study found that the rate of adjacent segment degeneration was 8.8% for the activL<sup>®</sup> device. This is similar to the rate of 9.2% reported in another TDR study with 5-year follow-up (Zigler et al, JNS, 2012). That study found ASD to be significantly less with TDR than with fusion. The rate of ASD declined with increasing range of motion at the TDR level, possibly suggesting a protective effect of motion. The higher rate of ASD among older patients may suggest that some changes in adjacent level discs may be attributable to the aging process. The current study adds further support that increased motion reduces the occurrence of adjacent segment degeneration.

## PREVIOUS SURGERY SIGNIFICANTLY INCREASES THE RISK OF BOTH SURGICAL AND GENERAL COMPLICATIONS DURING SURGERY FOR DEGENERATIVE DISORDERS OF THE LUMBAR SPINE

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**Introduction:** It is well known that previous surgery increases the risk of complications during spine surgery, but few studies have quantified the dose-response effect of multiple surgeries using multivariate models that account for possible confounders.

**Aim:** This study sought to quantify the effect of the number of prior spine surgeries on perioperative complications (general and surgical) in patients undergoing surgery for different degenerative disorders of the lumbar spine.

**Methods:** The study included 4'940 patients with lumbar degenerative disease documented in the Spine Tango Registry of Eurospine, the Spine Society of Europe, from 2004 to 2015. The patients' medical history and surgical details were documented on the Spine Tango Surgery form, as were general-medical complications and surgical complications arising between admission and discharge (multiple choice options). Multiple logistic regression models were built to investigate the relationship between the number of any previous surgeries and the presence of a perioperative complication, controlling for other potential confounders (age, sex, smoking, BMI, comorbidity, number of vertebral levels affected).

**Results:** There were 9.4% surgical complications (most commonly dural tear, neurological, haematoma, infection) and 6.5 % general complications (most commonly cardiovascular, urinary, pulmonary, liver/GI). In the multivariable models (adjusting for confounders), previous surgery significantly increased the odds of incurring a general medical complication (OR 1.185, 95%CI 1.074 – 1.307; p=0.001) and a surgical complication (OR 1.148, 95%CI 1.051 – 1.253; p=0.002). In other words, for each previous surgery, the odds of incurring a medical complication increased by 19% and a surgical complication, by 15%.

**Discussion:** We were able to demonstrate a significant effect of any previous spine surgery on the risk of incurring a complication during surgery. The greater the number of any prior spine surgeries, the higher the risk of a complication. The results of this study can be used when considering or consenting a patient for further surgery, to better inform the patient of the risk of complications associated with the surgery.

## RISK FACTORS FOR POOR PATIENT-REPORTED QOL OUTCOMES AFTER PLIF: AN ANALYSIS OF TWO-YEAR FOLLOW-UP

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### Introduction

The Japanese Orthopaedic Association Back Pain Evaluation Questionnaire (JOABPEQ) allows a multidimensional and independent evaluation of five categories of health-related quality of life (QOL) outcomes (*Pain-related disorders* [PrD], *Lumbar spine dysfunction* [LSD], *Gait disturbance* [GD], *Social life dysfunction* [SLD], and *Psychological disorders* [PsD]). This study aimed to identify risk factors for poor QOL outcomes of each category in the JOABPEQ after posterior lumbar interbody fusion (PLIF) at the two-year follow-up.

### Methods

One hundred patients (39 men and 61 women; mean age, 69.6 years [44–84]) who underwent single- or two-level PLIF between January 2011 and October 2014 for lumbar degenerative spondylolisthesis or foraminal stenosis with a two-year follow-up were reviewed. The effectiveness of surgery was assessed by preoperative and two-year postoperative scores of the JOABPEQ and the effectiveness rate was calculated in each category. The following demographic and clinical data and radiographic parameters were compared between the patients with effectiveness of PLIF and those without in each category: age, sex, body mass index, number of PLIF segments, fusion level, total number of decompression segments, radiographic adjacent segment degeneration (ASD), fusion status, lumbar lordosis (LL), sacral slope (SS), fusion angle, and range of motion ([LL at extension] - [LL at flexion]). Multivariate logistic regression analysis was performed to detect the risk factors for ineffectiveness of PLIF in each category of the JOABPEQ using variables of  $p < 0.2$  in univariate analysis.

### Results

Sixty-nine patients underwent single-level PLIF; 31 patients, two-level PLIF. The effectiveness rate in each category were 73.8% in PrD, 45.7% in LSD, 78.4% in GD, 58.0% in SLD, and 31.0% in PsD, respectively. In PrD, the risk factors for ineffectiveness of PLIF were age (odds ratio [OR], 1.09; 95% confidence interval [CI], 1.01–1.18;  $p = 0.03$ ), preoperative SS (OR, 0.92; 95% CI, 0.85–0.99;  $p = 0.02$ ), and  $\Delta$ LL ([2y postoperative value] - [preoperative value]; OR, 0.90; 95% CI, 0.82–0.98;  $p = 0.02$ ). In LSD, the risk factors were number of PLIF segments (OR, 3.36; 95% CI, 1.27–8.87;  $p = 0.02$ ) and non-union (OR, 4.63; 95% CI, 1.19–18.08;  $p = 0.03$ ). In GD, the risk factors were age (OR, 1.13; 95% CI, 1.03–1.24;  $p = 0.01$ ), preoperative LL (OR, 0.94; 95% CI, 0.90–0.98;  $p = 0.004$ ), and radiographic ASD (OR, 4.39; 95% CI, 1.20–16.04;  $p = 0.03$ ). In SLD, the risk factors were age (OR, 1.08; 95% CI, 1.02–1.15;  $p = 0.007$ ) and  $\Delta$ LL (OR, 0.93; 95% CI, 0.87–1.00;  $p = 0.049$ ). In PsD, the risk factors were age (OR, 1.11; 95% CI, 1.04–1.17;  $p = 0.001$ ) and  $\Delta$ LL (OR, 0.91; 95% CI, 0.84–0.98;  $p = 0.01$ ).

### Discussion

Our study showed that PLIF was effective especially for improvement of PrD and GD by the detailed QOL assessment using the JOABPEQ. However, different risk factors existed for postoperative poor QOL outcomes among five categories of the JOABPEQ. Particularly, the surgery-related factors (increase in number of PLIF segments, non-union, and radiographic ASD) had a negative impact on improvement of LSD and GD.

## LOCAL APPLICATION OF VANCOMYCIN POWDER DECREASES THE AMOUNT OF BACTERIA IN THE OPERATIVE FIELD AND LEADS TO LESS INCIDENCE OF SURGICAL SITE INFECTION

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### Introduction

Surgical site infection (SSI) is one of the most difficult complications in spinal instrumentation surgery. Recently, local application of vancomycin (VCM) powder is widely used to prevent SSI, however, efficacy of VCM powder is still controversial. The purpose of this study was to evaluate the effects of intra-wound VCM powder on drainage tube culture and SSI in spinal instrumentation surgery.

### Materials and Methods

Since January 2015 to July 2016, 314 patients underwent posterior spinal instrumentation surgeries with local application of VCM (VCM group). They were compared with 354 patients who underwent posterior spinal instrumentation surgeries without VCM between January 2013 and December 2014 (Control group). Statistical differences in age, gender, primary disease, and comorbidities were not found between these groups. In both groups, tip of wound drainage tube was cut at the time of removal and underwent bacterial culture in all cases. Number of positive culture cases, types of bacteria, and clinical course including SSI were investigated in both groups.

### Results

Drainage tube culture was positive in 1.6% (5/314 cases) in VCM group and 7.3% (26/354 cases) in Control group ( $p=0.004$ ). Detected bacteria in VCM group were as follows; *MSSE* in 2 cases, *Acinetobacter baumannii* and *Pseudomonas aeruginosa* and *Enterococcus faecalis* in 1 case each. In control group, *MSSE* in 12 cases, *MRSE* in 7 cases, *Acinetobacter baumannii* in 3 cases, *Serratia marcescens* in 1 case, and others in 3 cases. Among these positive cases, 1 of 5 cases developed SSI in VCM group, while 3 of 26 in Control. Among the culture negative cases, 0 case in VCM and 6 cases in Control presented SSI. Finally, incidence of SSI was 0.3% (1/314 cases) in VCM group and 2.5% (9/354 cases) in control group. SSI was significantly less in VCM group than in Control group ( $p=0.01$ ). In VCM group, pathogenic bacterium was *Pseudomonas aeruginosa*. In Control, pathogenic bacteria were *MSSE* in 3 cases, *Serratia marcescens* in 1 case, MRSA in 1 case, and unknown in 4 cases.

### Discussion

In this study, VCM group presented statistically less incidence of positive bacterial culture of the drainage tubes, indicating that the amount of bacteria in the operative field was decreased by local application of VCM powder. However, incidence of positive culture of VCM resistant bacteria was not decreased by VCM powder. Therefore, prophylactic administering of antibiotics with broad spectrum cannot be excluded even if VCM powder is used. As well, incidence of SSI in VCM group was significantly lower compared to Control group. Importantly, pathogenic bacterium of SSI in VCM group was only VCM resistant bacterium supporting the efficacy of VCM powder. In conclusion, local application of VCM decreases the amount of bacteria in the operative field and leads to less incidence of SSI.

## REVISION SURGERY OF SYMPTOMATIC PSEUDARTHROSIS AFTER LUMBAR FUSION: A VIABLE TREATMENT OPTION?

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### Introduction

Pseudarthrosis is a rare complication after lumbar fusion that can be associated with pain and disability. Revision surgery for pseudarthrosis has unpredictable clinical and radiological outcome. The aim of the present study was to investigate patient-rated outcome, surgical strategy, and preoperative radiographic parameters in patients undergoing revision surgery for symptomatic pseudarthrosis after short lumbar fusion ( $\leq 3$  segments).

### Methods

This was a retrospective analysis of prospectively collected data from 95 patients in our local spine outcomes database (linked to the EUROSPINE Spine Tango Registry) who had undergone revision surgery for pseudarthrosis between 2005 and 2014. Patients were  $52 \pm 14$  years old at the time of the index surgery (50 male, 45 female). Inclusion criteria were prior lumbar fusion of one to three levels, symptomatic pseudarthrosis, and a minimum 6 months follow-up. Radiographic data were evaluated by two independent spine specialists. Surgical data were retrieved from the patient charts. The Core Outcome Measures Index (COMI) was used to assess patient-rated outcome at 3, 12, and 24 months postoperatively. The COMI includes the domains pain, back-specific function, symptom-specific well-being, general quality of life (QOL), work disability, and social disability. Differences between pre- and postoperative scores were analyzed using repeated measures analysis of variance.

### Results

The mean duration between initial and revision surgery was  $35.9 \pm 40.8$  months. 52/95 patients (55%) had originally been treated at our spine center, and 43/95 (45%) at other hospitals. In 91/95 (96%) patients posterior fusion was performed with pedicle or translaminar screws. In 63/95 (66%) patients, the initial interbody fusion was performed with a cage. Prior to revision, screw loosening or breakage was demonstrable in 51/93 (55%) available radiographs, and 47/64 (73%) CT images; cage loosening was detected in 21/63 (33%) and 17/45 (38%), respectively. Intraoperatively, the most commonly documented level of pseudarthrosis was L5/S1 (40/95; 42%), followed by L4/5 (29/95; 31%). Screw loosening or breakage could be confirmed in 72/91 (79%) patients, and cage loosening in 17/63 (27%). The TLIF technique was used as part of the revision strategy in 76/95 (80%) patients, and PLIF in 9/95 (9%). Screws were exchanged in 91/91 (100%) patients and cages in 24/63 (38%) of the patients. BMP was used in 20/95 (21%), and iliac bone graft in 57/95 (60%) of the patients. 18/95 (19%) patients underwent further revision at the same level since revision surgery.

The mean COMI score showed a small but statistically significant improvement ( $p < 0.05$ ) from  $8.6 \pm 1.3$  pre-revision to  $6.6 \pm 2.4$  at 3 months,  $6.5 \pm 2.8$  at 12 months and  $6.4 \pm 2.7$  at 24 months after revision. At 24 months, 35% had achieved a minimal clinically important change (MCIC) score in COMI of 2.2 points.

### Discussion

Revision surgery for symptomatic pseudarthrosis resulted in a small but statistically significant improvement in the multidimensional COMI score at 3, 12, and 24 months postoperatively, with approximately 35% patients achieving MCIC. Revision surgery may hence be a viable treatment option for some patients with suspected symptomatic pseudarthrosis. However, both patients and surgeons should be aware of the potentially marked, ongoing impairment at 2 years' follow-up.



## THE CHANGE OF PAIN CATASTROPHIZING IN PATIENTS WITH SPINE SURGERY

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**Introduction:** It is still unclear whether pain catastrophizing would be enduring stable construct or dynamic construct related to pain intensity. The purpose of this study was to clarify whether catastrophizing would be changeable in given a specific situational circumstance in the patient underwent spinal surgery for degenerative spinal disease, compared to preoperative state.

**Methods:** The present observational cohort had been set in the previous study, which consisted of 138 patients between the ages of 40 and 80 years who were scheduled to undergo surgery for LSS to investigate the influence pain catastrophizing on treatment outcomes after surgery for lumbar spinal stenosis. The pain catastrophizing scale (PCS) questionnaire was used for pain catastrophizing assessment before and 2 year after surgery. Oswestry disability index (ODI), Visual analog pain scale (VAS) for back and leg pain, and PCS was assessed 3, 6 months, 1 year, and 2 year after surgery. The correlations between variables was analyzed before surgery and 2 year after surgery, and the association between changes of symptom (VAS and ODI) and changes of PCS was also analyzed. To clarify the causal relationship, time-series and lagged analysis were also used.

**Results:** At 2 year after surgery, not only VAS for back and leg pain, ODI, but also PCS were significantly decreased. The correlation of PCS with VAS and ODI were significant both before surgery and 2 year after surgery. The correlation between change in pain intensity or disability and change in catastrophizing from baseline to 2 year after surgery was also significant. In the causal relationship between pain and catastrophizing, previous pain and disability were significant and robust predictor of future catastrophizing.

**Conclusion:** The present study clearly shows that pain catastrophizing can be changed in relation with the improvement of pain intensity after spine surgery. Therefore, catastrophizing is not enduring stable construct, but a dynamic construct.

## PLANNED TWO STAGE CORRECTIVE SPINAL SURGERY FOR ADULT SPINAL DEFORMITY DOES NOT INCREASE THE RISK OF COMPLICATION COMPARED TO ONE STAGE SURGERY

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### INTRODUCTION

We have performed two stage surgery for the adult spinal deformity patients who had severe deformity, poor general conditions and/or correction by combined with lateral lumbar interbody fusion (LLIF) and posterior fusion to reduce surgical invasiveness. However, staged surgery might be associated with totally longer operation time, infection, DVT and some additional complications. The purpose of this study was to compare the effect and safety of two stage surgery for adult spinal deformity patients.

### METHODS

We investigated 246 adult spinal deformity who underwent spinal corrective fusion over 5 vertebrae from 2010 to March 2016 at our hospital. Among them, 185 patients underwent 1 stage surgery (G1), whose surgical methods were: multiple posterior column osteotomies (91 cases), pedicle subtraction osteotomy (52 cases), and posterior vertebral column resection (42 cases). Sixty-one patients underwent two stage surgery, whose surgical methods were: anterior-posterior fusion (G2AP: 51 cases) and pedicle screw insertion in the first stage and posterior osteotomy and fusion in the second stage (G2P: 10 cases). Patients of G2AP underwent second surgery 1 or 2 weeks after the first surgery. Patients of G2P also had same interval between first and second surgery expect one case who underwent second surgery at 9 months after the first surgery because of very poor pulmonary function (25% vital capacity) and severe osteoporosis (young adult mean 43%). Total operation time, total blood loss, FDP, D-dimmer on the next day and 1 week after the surgery were investigated. Furthermore perioperative complications and the number of re-operation due to the complication within three months after the surgery were also analyzed. Statistical analysis for three groups was performed by ANOVA with post hoc test.

### RESULTS

Average operation time were G1:397minutes, G2AP:457 minutes and G2P:572 minutes. G2AP and G2P were significantly longer than G1 ( $P<0.01$ ). The amounts of blood loss were G1:1800 ml, G2AP:1083 ml and G2P:1624 ml. G2AP was significantly less than G1 and G2P ( $P<0.01$ ). There was no significant difference between G1 and G2P ( $P=0.69$ ). D-dimmer was not significantly difference among the three groups at the each time point ( $P>0.05$ ). Re-operations were performed in 17 (9%) in G1 and 2 (4%) in G2AP and 1(10%) in G2P. Surgical site infection occurred in 4 (2%) in G1, 2 (4%) in G2AP and 1 (10%) in G2P. Deep venous thrombosis occurred in 3 cases in G1 (2%). Complication rate was no difference among the three groups

### DISCUSSION

Previous reports suggested that planned two stage posterior spinal fusion for spinal deformity did not increase the general complication. However, few studies have reported the safety of two stage spinal fusion, including not only posterior but also anterior –posterior combined surgery. This study showed that although two stage surgery increased total operation time, the procedure did not increase total blood loss, incidence of DVT, and reoperation rate. Thus, the two stage procedure should be considered for severe spinal deformity and frail patients.

## A COMPARISON OF NON-SURGICAL TREATMENT METHODS FOR PATIENTS WITH LUMBAR SPINAL STENOSIS

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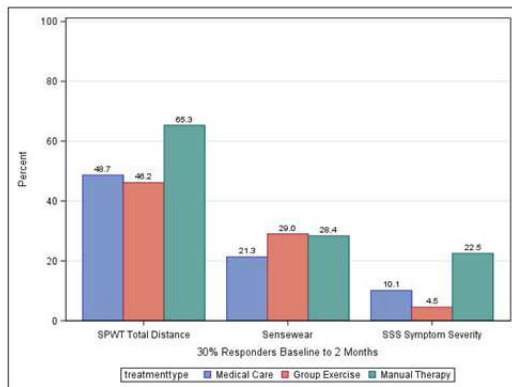
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**INTRODUCTION:** Lumbar spinal stenosis (LSS) is a highly prevalent condition in the senior citizen population. LSS is the most frequent indication for spinal surgery in patients over the age of 65 years. The fastest growth in lumbar surgery in the U.S. this past decade has occurred in older adults with LSS and the rate of complex fusion procedures has significantly increased. These surgical procedures are associated with significant health care costs, risks, complications, and re-hospitalization rates. Yet, evidence is lacking for the effectiveness of the various non-surgical treatment options offered to patients with LSS. This study was designed to help bridge this evidence gap. The objective of this study was to compare the clinical effectiveness of 3 common non-surgical approaches to the management of patients with lumbar spinal stenosis (LSS): 1) usual medical care (UMC); 2) non-specific group exercise classes (GE); or 3) combination of manual therapy and rehabilitative exercises specific to LSS (MTRE).

**METHODS:** Randomized controlled clinical trial of N=259 patients with LSS. Patients were randomized into 1 of the 3 groups described above, and treated for a total of 6 weeks. The primary outcome measures were symptom severity, measured by the Swiss Spinal Stenosis (SSS), and walking performance, measured by the 30-minute Self-Paced Walking Test (SPWT). The secondary outcome measure was daily physical activity measured by accelerometry (Sensewear). Outcome measures were taken at baseline, 2 months and 6 months. The primary end point was at 2 months. The primary analysis used linear mixed models to compare changes in each outcome measure between the groups. The secondary analysis was a comparison of the proportion of responders ( $\geq 30\%$  change) in each outcome measure by group using Chi Square test.

**RESULTS:** No serious adverse events were reported in any of the groups. There was a significantly greater reduction in mean SSS score in the MTRE group ( $-2.8 \pm 4.3$ ) at 2 months compared to UMC ( $-1.2 \pm 4.0$ ) or GE ( $-1.2 \pm 3.9$ ). The MTRE group had the most improvement in mean walking distance in meters at 2 months ( $267.8 \pm 507.8$ ) compared to UMC ( $130.5 \pm 478.7$ ) or GE ( $219.2 \pm 413.0$ ), but these differences were not statistically significant. There were no significant between-group differences in the mean amount of daily physical activity at 2 months. The responder analysis showed that the MTRE group had a significantly greater number of participants who improved above 30% in the SSS and SPWT (22.5%, 65.3%) at 2 months compared to UMC (10.1%, 48.7%) and GE (4.5%, 46.2%). There were no between-group differences in the proportion of responders based upon the measure of physical activity.



**DISCUSSION:** Patients with LSS can be safely and effectively treated with various non-surgical treatment approaches. Group exercise classes appear to be about as effective as medical care in reducing pain and improving walking performance. A combination of manual therapy and rehabilitative exercise leads to greater reduction in self-reported pain and improvement in walking performance.

Figure: SPWT=Self Paced Walking Test (meters); Sensewear=physical activity measured by accelerometry; SSS=Swiss Spinal Stenosis questionnaire (symptom severity).

## DETERIORATION IN QOL CAUSED BY LUMBAR SPINAL STENOSIS: A STUDY OF DISEASE SPECIFIC CHARACTERISTICS (LUMBAR SPINAL STENOSIS DIAGNOSIS SUPPORT TOOL: DISTO-PROJECT)

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### Introduction

Leg pain, numbness, and intermittent claudication caused by Lumbar Spinal Stenosis (LSS) induce a deterioration in Quality Of Life (QOL). However, it is still unclear how LSS effects the QOL deterioration, because aging itself can worsen comprehensive QOL. The purpose of this study was to elucidate the characteristics of deterioration of QOL caused by LSS through comparison of patients with and without LSS.

### Methods

This multicenter cross-sectional study was performed as the "Lumbar Spinal Stenosis Diagnosis Support Tool: DISTO-project" from December 2010 to December 2011 at 564 medical centers and clinics in Japan. Subjects comprised 8,338 patients aged 20 years and older who consulted outpatient clinics with low back pain as the chief complaint. Recently, we developed a simple clinical diagnostic support tool to identify patients with LSS (Konno et al. 2007). This tool consists of 12 simple items that can be clinically determined, and has a sensitivity of 92.8% and a specificity of 72.0%. This tool enables screening for LSS on a large scale. Patients who were diagnosed positive for LSS with this tool were included in the LSS group, while those who were diagnosed negative were included in the low back pain (LBP) group. The Japanese Orthopedic Association Back Pain Evaluation Questionnaire (JOABPEQ), which includes five domains: Pain related disorders, Lumbar dysfunction, Gait disturbances, Social life dysfunction, and Psychological disorders, was used to evaluate QOL due to low back pain. Scores in the five JOABPEQ domains were compared between the 2 groups stratified according to sex and age. Chi-square test and Fisher's exact test were used for statistical analysis.  $p < 0.05$  was considered significant.

### Results

The prevalence of LSS significantly increased with age in both males and females ( $p < 0.001$ ). In the LSS group, pain related disorder scores had a significantly low distribution in males aged 40-49 and those  $\geq 60$  years, and in females aged  $>30$  years. Lumbar dysfunction scores were significantly higher in males aged 50-59 with LSS. Gait disturbance scores were significantly low in all age groups for males and in  $\geq 30$ -year old females in the LSS group. Social life dysfunction scores were significantly low in the LSS group for males aged 20-29 and  $\geq 40$  and  $\geq 40$  for females. Psychological disorder scores were significantly low among all age groups, except males aged 30-39, and females aged 60-79.

### Discussion

We evaluated the deterioration in QOL with LBP using JOABPEQ in each QOL domain and successfully clarified the disease specific characteristics of deterioration in QOL in patients with LSS. The scores for Pain related disorders, Gait disturbances, Social life dysfunction, and Psychological disorders had a low distribution. This data can be used as baseline data for LSS patients stratified into sex and age groups. Thus, JOABPEQ is a useful tool to evaluate disease specific deterioration in QOL in patients with LSS.

## IS REDUCTION BETTER THAN ARTHRODESIS IN SITU IN SURGICAL MANAGEMENT OF LOW-GRADE SPONDYLOLISTHESIS? -A SYSTEM REVIEW AND META ANALYSIS

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**Introduction** Low-grade spondylolisthesis has always been considered a benign condition with a good outcome, and rarely requiring surgical intervention. However, in case of persistent symptomatology or those with neurological deficits, surgical treatment has proven to be superior over a conservative approach. Spinal arthrodesis is widely accepted for the treatment of mild spondylolisthesis; it is also generally considered safe, with good long-term results. However, reduction of the slipped vertebrae as a part of surgical approach is still debatable. There is a paucity of evidence based studies comparing treatment of low-grade spondylolisthesis with fusion in situ or reduction followed by fusion. This study was designed to compare the clinical and radiographic outcomes of arthrodesis in situ with arthrodesis after reduction in low-grade spondylolisthesis.

**Methods** We performed a comprehensive search of both observational and randomized clinical trials published up to April 2016 in PubMed, MEDLINE, Cochrane Library, and Embase databases. The outcomes included age, sex, operative time, blood loss, and at least 2 years clinical results of Oswestry disability index (ODI), visual analogue scale (VAS), lumbar lordosis, slippage, fusion rate, the rate of good and excellent and the complication rate. Two authors independently extracted the articles and the predefined data.

**Results** Seven eligible studies, involving four RCTs and three cohort studies were included in this systematic review and meta-analysis. Patients who underwent reduction did achieved better slippage correction comparing with arthrodesis in situ ( $P < 0.00001$ ). However, there was no significant difference in the case of operative time, blood loss, VAS ( $P = 0.36$ ), ODI ( $P = 0.50$ ), lumbar lordosis ( $P = 0.47$ ), the rate of good and excellent ( $P = 0.84$ ), fusion rate ( $p = 0.083$ ) and complication rate ( $p = 0.33$ ) between the arthrodesis in situ group and the reduction group.

**Conclusions** On the basis on this review, arthrodesis after reduction of low-grade spondylolisthesis potentially reduced vertebral slippage. Reduction was neither associated with a longer operative time nor more blood loss. There was no significant difference in the outcomes between reduction and arthrodesis in situ group. Both procedures could be expected to achieve good clinical result.

*Level of Evidence* Therapeutic Level IIa.

## WHEN AND HOW OFTEN SPONDYLOLISTHESIS OCCURS IN PATIENTS WITH OR WITHOUT SPONDYLOLYSIS.

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**Introduction:** Lumbar spondylolysis generally occurs in adolescent athletes. Acute symptoms of spondylolysis usually improve conservatively; however, spondylolysis patients have the potential to develop isthmic spondylolisthesis. In this study, the incidence of spondylolysis and spondylolisthesis was determined, and when and how often spondylolisthesis occurs in a general Japanese population with or without spondylolysis was established.

**Methods:** Patients undergoing computed tomography (CT) scans of abdominal or lumbar regions for reasons other than low back disorders were included (n=580). Patients visiting orthopaedic outpatient clinics whose ethnicity was not Japanese were excluded. Sagittal multiplanar reconstruction CT images were obtained and evaluated. First, the incidence of spondylolysis and vertebral slip (>3 mm) was examined. Second, the age-specific incidence of spondylolisthesis was examined in patients with or without spondylolysis.

**Results:** Of the 580 patients (mean age: 64.4 years-old; 336 men/244 women), 37 patients (6.4%; 26 men and 11 women) had spondylolysis. Five of 37 patients had spondylolysis on one side, and none of these five patients showed spondylolisthesis. Of the remaining 32 patients included in the spondylolysis group, 19 patients (59.4%) showed spondylolisthesis. Patients showing no spondylolysis were included in the non-spondylolysis group (n=543), which had a significantly lower incidence of spondylolisthesis (40 patients: 7.4%, p<0.05) than the spondylolysis group. In both groups, no patient younger than 50 years-old had spondylolisthesis. The age-specific incidence of spondylolisthesis is as follows (spondylolysis, non-spondylolysis groups): 50-59 years-old (1/5 patients, 1/65 patients); 60-69 (5/5, 7/117); 70-79 (4/5, 14/118), and ≥80 (9/10, 18/130). In the spondylolysis group, the majority of patients (90%) aged ≥60 years-old showed spondylolisthesis, whereas only 8.3% of patients <60 years-old showed spondylolisthesis (p<0.05). In the non-spondylolysis group, the incidence of spondylolisthesis in patients ≥80 years-old (13.8%) was significantly higher than patients aged 50-59 years-old, and showed a non-significant tendency towards higher incidence when compared with patients 60-69 years-old (p=0.067).

**Discussion:** The incidence of spondylolysis has been reported to be 3.5-54%, varying among ethnic groups. Our results revealed a similar incidence to previous studies performed on Japanese populations. Previous reports suggested that over half of spondylolysis patients develop spondylolisthesis. Our study, comparing the incidence of isthmic and degenerative spondylolisthesis in the same series convincingly revealed that spondylolisthesis occurs very frequently and may develop at a younger age when spondylolysis exists. Our results also suggest that spondylolisthesis is rarely present in patients younger than 50 years-old, and occurs between 50-60 years-old of age in spondylolysis patients and between 50-80 years-old in patients without spondylolysis. A limitation of our study is that we have no information about patients' symptoms; there may be a certain number of patients with isthmic spondylolisthesis who have no symptoms. In cases of isthmic spondylolisthesis requiring surgical treatment, spinal fusion is often indicated. However, none of patients with isthmic spondylolisthesis had received fusion surgery, suggesting that most of these patients didn't have a severe disability requiring surgical treatment. Our result that almost all bilateral spondylolysis patients developed spondylolisthesis is somewhat striking; however, care should be taken when interpreting our data to avoid excessive anxiety in patients.

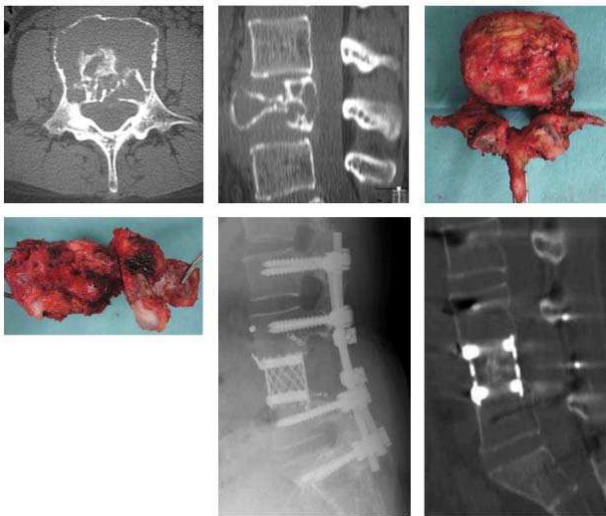
## TOTAL EN BLOC SPONDYLECTOMY FOR PRIMARY TUMORS OF THE LUMBAR SPINE

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**Introduction:** Total en bloc spondylectomy (TES) is an aggressive surgical technique that may be employed in the treatment of spinal neoplasms. TES in the lumbar spine is particularly challenging, owing to the unique anatomy of this region. In contrast to TES in the thoracic spine, lumbar tumors are typically removed in posterior/anterior combined procedures, and there is potential risk of lumbar plexus, major vessel, and/or bowel injury. For these reasons, the majority of descriptions of TES in the lumbar spine are case reports and small case series. The aim of this study was to report our experience with TES in the lumbar spine for patients with primary spinal tumors and the clinical outcomes.

**Methods:** We performed a retrospective review of 26 patients who underwent TES for a primary aggressive benign or primary malignant tumor of the lumbar spine between 1993 and 2015. We investigated perioperative complications, reoperation rates for instrumentation failure, local recurrence and overall survival.



**Results:** There were 12 men (46%) and 14 women (54%). The mean age at the time of surgery was 39.2 years (range; 6–66 years) and the mean follow-up period was 84 months. The 26 tumors included 12 giant cell tumors, 3 plasmacytomas, 3 hemangiomas, 2 chordomas, 2 chondrosarcomas, and one each of osteosarcoma, synovial sarcoma, osteoblastoma, and hemangiopericytoma. Seven patients underwent previous intralesional resection, 3 received previous chemotherapy, and 2 previously underwent radiation therapy. Twenty patients underwent a single vertebral resection, 2 patients underwent two, and four patients underwent three consecutive vertebral resection. Posterior approach alone was performed in 8 patients and combined posterior–anterior approach was performed in 18 patients. Eight patients underwent a two-staged operation and the others underwent single-staged operation; median total estimated blood loss was 1630 mL and median total operative time was 11 hours. Seventeen patients (65%) developed at least one perioperative complication. The most common complication was postoperative muscle weakness (9

patients: 35%), followed by wound infection (7 patients: 27%) and postoperative cerebrospinal fluid leakage (5 patients: 19%). Of the 9 patients of postoperative muscle weakness, all but one recovered within 6 months after the surgery, and all patients had preserved neurologic function at last follow-up. All 7 patients with wound infection required reoperation for debridement and one patient required exchange of spinal instrumentation. Revision surgery for instrumentation failure was required in 4 patients (15%) at the mean time of 41 months after the surgery. Local tumor recurrence and 5-year survival rate was 12% and 79%, respectively.

**Discussion:** In this study, TES in the lumbar spine resulted in relatively favorable oncological outcomes in terms of recurrence and overall survival. TES in the lumbar spine is a feasible procedure in carefully selected patients, but the risk for perioperative complication and late instrumentation failure should be acknowledged. Further investigation into ways to reduce perioperative complications and instrumentation failure is needed.

## PREOPERATIVE EMBOLIZATION IN PATIENTS WITH METASTATIC SPINAL CORD COMPRESSION: MANDATORY OR OPTIONAL?

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**Introduction:** Palliative decompression surgery for metastatic spinal cord compression (MSCC) is associated with problems such as potential massive bleeding and postoperative complications. Many authors have suggested that preoperative embolization could reduce intraoperative blood loss. However, the contribution of preoperative embolization in reducing intraoperative blood loss and its clinical importance are unclear. We aimed to compare the perioperative clinical outcomes based on whether preoperative embolization was performed and assess the role and safety of preoperative embolization in metastatic spinal cord compression (MSCC) patients.

**Methods:** We enrolled 52 patients (men, 37; women, 15) who underwent palliative decompression for MSCC. Demographic data, neurologic status, surgery-related data (operation time, estimated blood loss, and transfusion), complications, and survival time were recorded. Patients were categorized based on whether they received preoperative embolization: group E (embolization, n=18) and NE (non-embolization, n=34), and the clinical parameters were compared. Subgroup analysis was performed specifically for cases of hypervascular tumors (23/52, 44%).

**Results:** The mean patient age at the time of operation was 59.7±12.3 years. Among 18 patients who underwent preoperative embolization, complete or near-complete (>80%) embolization was possible in 13 cases (72.2%). Procedure-related complications were not found in all cases. The time period between embolization and the surgical procedure was 16.4±9.1 h. Preoperative neurologic status in the NE group was inferior to that in the E group (2.7 vs 3.6). The postoperative neurologic status was also different between the 2 groups (2.9 vs 3.8, P=0.042). However, the degree of neurologic improvement did not significantly differ (P=0.519). The transfusion degree was greater in the NE group (4.6 pints) than in the E group (2.5 pints, P=0.025); the other parameters did not differ between the groups.

However, massive bleeding (>2,000 mL) was more frequent in the NE group (10/34) than in the E group (0/18, P=0.010). Subgroup analysis indicated that intraoperative blood loss was greater in the NE group (1,988 mL) than in the E group (1,095 mL, P=0.042) in 23 hypervascular tumor patients. Although massive bleeding was more frequent among hypervascular tumor patients, 3 patients with non-hypervascularized tumors also exhibited massive bleeding (P=0.087).

**Discussion:** Intraoperative blood loss and perioperative transfusion can be reduced by preoperative embolization in MSCC patients. Neurologic recovery, operation time, and complications did not differ according to the application of embolization. In our present study, none of the patients showed procedure-related complications, including neurologic deficits. However, cord ischemia may be the most critical complication of the embolization. In fact, embolization was not performed in 2 patients because of the risk of cord infarction due to occlusion of the anterior spinal arteries in our series.

In summary, as preoperative embolization is relatively safe and effective for controlling intraoperative bleeding without any neurologic deterioration, it is highly recommended for hypervascular tumors. Moreover, it may also be effective for non-hypervascular tumors as massive bleeding may be noted in some cases.



## PATTERNS OF FAILURE OF FIXATION IN METASTATIC SPINAL DISEASE

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### Introduction:

Patients with spinal metastases have median survival of 10 months and effective palliation of symptoms is principle objective. Studies have focused on surgical decision making, management and complications of spine tumour surgeries(STS). Few focusing on the failure of fixation(FOF). This study presents the results of patterns of FOF in STS and factors leading to it.

### Material and Methods:

Retrospective analysis of 165 patients undergoing STS in a tertiary referral institution from 2005 to 2016 was carried out. Demographic data was collected from hospital electronic records and radiological investigations from Centricity Web(C Web). Medical history, radiological investigations (radiographs, CT, MRI) were assessed on presentation, inpatient, outpatient follow-up & at time of FOF. Radiological data included, type of lesion(lytic/mixed/sclerotic/none), level of fixation & derived SINS. Surgical data minimally invasive surgery (MIS)/open fixation, level and type of stabilisation & revision after FOF.

FOF was defined as increase in angular deformity; reduction in anterior column height; tilting or subsidence of cage; lysis around screw; back-out/ cut-out; breakage of the rod/screw. The endpoint of the evaluation was last follow-up/death. The upper and lower instrumented vertebra defined the construct-length (CL). CL were classified as short(1-7 levels), intermediate(7-12) or long(>12). Vertebra within the construct without anchor was considered as a level.

Exclusion criteria: Age <18yrs, infection of implant leading to failure, survival <30days.

### Result:

Lung(23.2%) was the most common followed by breast(16.7%) as primaries for STS. Most common symptoms on presentation was pain with weakness (76%), followed by weakness only.

The average follow-up was 330days(31-2758). Of 165 patients 15 died <30 days post-op, 12 lost to follow-up. 26.8%(37/138) had FOF. The most common failure was asymptomatic change in angular deformity 86.5%(32/37), back out 5%(2/37), cut out 5% ( 2/37), lysis 8%(3/37) , cage tilt 2.7%(1/37), Only 4 cases required revision of fixation due to progressive neurological deficit & pain.

There were no FOF in SIN score< 7. All FOF were in 7-14, of which 54% were SIN score >9.

### Discussion:

In STS non-fusion fixation is the norm; owing to poor survival, increase morbidity of auto-graft harvesting, poor host graft bed leading to poor fusion, associated adjuvant radiation & chemotherapy.

Renato et al have reported, FOF as 8.57% similar to the failure from other non-tumour pathologies. However in our study the FOF >3 times the non-tumour pathology, due to inclusion of asymptomatic failures.

Asymptomatic FOF are radiological failure exhibiting increase in angular deformity, reduction of anterior column height with/without cage displacement/sinkage. Increase angular deformity was increase in kyphosis but no altered coronal angulation.

The symptomatic presentation were screw back-out and cut-out in adjacent disc space presenting as pain and prominence of the screw head. One patient with anterior column reconstruction developed an increase in angular deformity due to placement of cage on diseased body.

We conclude that FOF though radiologically noticed as increasing angulation and reduction in anterior column height were asymptomatic not requiring revision. It may however be the early sign of complete FOF. FOF is found more than 3 times in STS than non-tumour surgery.

## LUMBAR INCIDENCE, TILT AND SLOPE - APPLICATIONS AND COMPARISON OF VALUES IN STANDING VERSUS SITTING

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### Introduction

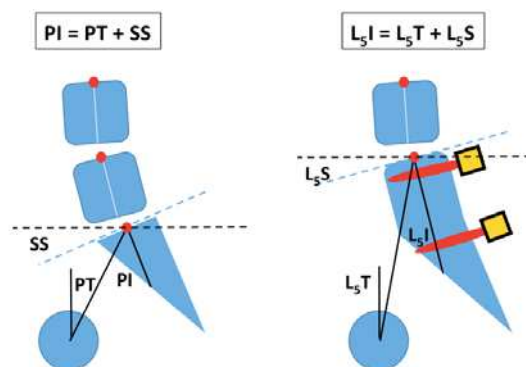
Sitting is a common posture we assume. However, spinopelvic correlation in the sitting profile remains unestablished.  $PI=PT+SS$  is a geometric formula, which can be applied to lumbar vertebrae in cases where the caudal spine is fused.

The purpose of this study is to investigate spinopelvic parameters in sitting and compare them with those of standing, and to apply the  $PI=PT+SS$  concept to the lumbar spine where  $LI=LT+LS$ .

### Methods

This is a prospective observational comparative study. Fifty-three young, healthy adults with first episode lower back pain without red flag symptoms or spinal deformity were recruited. Lateral standing and sitting. EOS® radiographs were obtained. Radiographic parameters measured included SVA, CL, TK, LL, PI, PT and SS. Extrapolating the concept of  $PI=PT+SS$ , variables for each lumbar vertebra in relation to the hip were also measured in both postures and termed lumbar incidence (LI), lumbar tilt (LT) and lumbar slope (LS). T-tests were performed to compare variables.

Pelvic Incidence (PI) → Lumbar Incidence (LI)  
Pelvic Tilt (PT) → Lumbar Tilt (LT)  
Sacral Slope (SS) → Lumbar Slope (LS)



### Results

The mean PI, PT and SS values were 47.28°, 12.73° and 34.45° for standing and 49.04°, 27.84° and 21.02° for sitting. While PI is a constant independent of posture, LI varies with posture, decreasing in value cranially. LI turns negative at L3 in standing, while remaining positive throughout the lumbar spine in sitting. LT is positive throughout the standing lumbar spine, with a nadir at L4. In sitting, LT progressively decreases cranially. LS turns negative at L3/4 in standing and at L1/2 in sitting. All spinopelvic parameters were significantly different between standing and sitting, with the exception of PI ( $p=0.376$ ) and  $L_1T$  ( $p=0.239$ ).

### Discussion

This study informs of the alignment of each lumbar vertebra relative to the hip during both standing and sitting, and provides further insight into selective lumbar fusion targets, spinopelvic compensation, and conditions involving vertebral translations. The trigonometric spinopelvic equation,  $PI = PT + SS$ , can be extrapolated to lumbar vertebrae such that  $LI = LT + LS$ . Quantifying LI may prove useful in determining lumbar lordosis correction targets for the remaining mobile segments

(if there is no intention to revise the already fused segments) in a caudally instrumented spine, or in patients with a sacralised L5 vertebra. Quantifying LT may facilitate estimation of the degree of compensation occurring at any lumbar vertebrae fused to the sacropelvis. Significant differences in LI, LT and LS values of each vertebra between sitting and standing further highlight spinopelvic alignment differences between both postures. This has not been previously shown.

## COMPARATIVE ANALYSIS OF OVER-CORRECTION, IDEAL-CORRECTION, AND UNDER-CORRECTION OF LUMBAR LORDOSIS FOR ADULT SPINAL DEFORMITY: ANALYSIS OF 458 CONSECUTIVE PATIENTS AT A TERTIARY SPINAL DEFORMITY CENTER

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**Introduction.** Sagittal malalignment in adult spinal deformity (ASD) is related to pain and disability. To restore global sagittal alignment, correction of lumbopelvic mismatch [pelvic incidence (PI) – lumbar lordosis (LL)] to  $<10^{\circ}$  is an important surgical goal. As outcomes in patients with over-correction of lumbar lordosis (i.e. PI-LL  $<-10^{\circ}$ ) are not well defined, we assess and compare radiographic data, complications, and health-related quality of life outcome (HRQoL) scores between ASD patients based on varying degrees of postoperative lumbopelvic mismatch.

**Methods.** Consecutive adults who underwent thoracolumbar fusions for ASD (2003-2013) at a single institution were reviewed. Inclusion criteria: instrumentation from pelvis to L1 or above, SVA  $<10$ cm, and minimum 2 years follow-up. Three groups were compared based on their post-operative PI-LL: “Over-Correction” (PI-LL  $<-10^{\circ}$ ), “Ideal-Correction” ( $-10^{\circ} \leq \text{PI-LL} \leq 10^{\circ}$ ), and “Under-Correction” (PI-LL  $>10^{\circ}$ ). Peri-operative spinal deformity parameters, proximal junctional angle (PJA: sagittal Cobb angle between UIV and UIV+2) complications (i.e. proximal junctional kyphosis), need for revision operation, and HRQoLs (SRS-22, SF-36, VAS back/leg pain) were assessed for each group and compared to each other using ANOVA tests and Kruskal-Wallis tests.

**Results.** Four hundred fifty-eight patients (“Over-Correction”: 65, “Ideal-Correction”: 227, “Under-Correction”: 166) met inclusion criteria. Pre-operative deformity characteristics averaged SVA  $> 8$ cm, PI-LL  $>20^{\circ}$ , PT  $>20^{\circ}$ , lumbar Cobb  $>30^{\circ}$ , and thoracic Cobb  $>30^{\circ}$ . The groups were similar with respect to demographics, PJA, pre-operative HRQoL scores, and surgical strategies, including upper instrumented vertebral level and average number of levels for interbody and posterior fusion. “Over-Correction” patients had significantly lower preoperative SVA, PI, PT, and PI-LL mismatch as well as significantly higher preoperative LL and TK than the other two groups.

At final follow-up (average 34.2months), “Over-Correction” patients had persistently lower post-operative SVA, PI-LL, and PT and higher LL and TK. While PJA was similar between groups at final follow-up, the percent change of PJA was significantly higher in “Over-Correction” (434%) than the other two groups (“Ideal-Correction”: 260%, “Under-Correction”: 298%) ( $p=0.035$ ). Average number of complications and PJK-related complications were similar between the groups. All HRQoL scores at final follow-up were similar among the three groups.

**Discussion.** In this heterogeneous cohort of adults with spinal deformity, over-correction of PI-LL ( $<-10^{\circ}$  post-op) occurred in patients with lower PIs and resulted in greater thoracic kyphosis and angulation at constructs’ proximal junction. Additionally, under-correction of PI-LL ( $>10^{\circ}$  post-op) was common in patients with higher PIs which translated to less than ideal correction of sagittal imbalance. This highlights the importance of tailoring surgical strategies to preoperative PI in order to achieve appropriate lumbopelvic and global sagittal alignment in patients with adult deformity.

## THE ADULT DEFORMITY SURGERY COMPLEXITY INDEX (ADSCI): A VALID TOOL TO QUANTIFY THE COMPLEXITY OF POSTERIOR ADULT SPINAL DEFORMITY SURGERY AND PREDICT POSTOPERATIVE COMPLICATIONS

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**Introduction:** In 2008, Mirza et al. designed and validated the first and only index capable of quantifying the complexity of spine surgery. However, this index is not fully applicable to Adult Spinal Deformity Surgery (ASDS), since it does not include the surgical techniques most commonly used and most strongly associated with perioperative complications in ASD patients. The objective of this study is to develop an "Adult Deformity Surgery Complexity Index" (ADSCI), to quantify objectively the complexity of the ASDS and thus be able to stratify the risk.

**Methods:** Patients included in this study were drawn from the multicenter ASD database of the European Spine Study Group (ESSG). Its development and validation was based on the construction and comparison of three different tools: ADSCI score constructed by three rounds of expert consensus (ADSCI-Delphi) and two multiple regression models (ADSCI-RM-Simple and ADSCI-RM-Mixed). Their predictive capability was compared by means of  $R^2$  values in the same subrogated of surgical complexity as in the Mirza index validation: intraoperative bleeding and duration of surgery. Sensitivity and specificity were evaluated using Receiver Operating Characteristics (ROC) curves and area under the curve (AUC) analysis. The external validity was also examined by evaluating its predictive capability in the data from a multicenter ASD database of comparable patients in the USA.

		General	ASA	Age	Center	AUCs	AUCs complications
ADSCI-Delphi	Blood-loss	$R^2$ : 0.27	ASA I $R^2$ : 0.26 ASA II $R^2$ : 0.24 ASA III $R^2$ : 0.34	<50 $R^2$ : 0.22 >50 $R^2$ : 0.27	$R^2$ : 0.10-0.60	AUC: 0.73	AUC: 0.66
	Surgical duration	$R^2$ : 0.23	ASA I $R^2$ : 0.16 ASA II $R^2$ : 0.24 ASA III $R^2$ : 0.44	<50 $R^2$ : 0.17 >50 $R^2$ : 0.32	$R^2$ : 0.24-0.79	AUC: 0.71	
ADSCI-RM-Simple	Blood-loss	$R^2$ : 0.35	ASA I $R^2$ : 0.37 ASA II $R^2$ : 0.36 ASA III $R^2$ : 0.57	<50 $R^2$ : 0.33 >50 $R^2$ : 0.40	$R^2$ : 0.24-0.81	AUC: 0.80	AUC: 0.72
	Surgical duration	$R^2$ : 0.31	ASA I $R^2$ : 0.32 ASA II $R^2$ : 0.35 ASA III $R^2$ : 0.45	<50 $R^2$ : 0.34 >50 $R^2$ : 0.38	$R^2$ : 0.37-0.85	AUC: 0.76	
ADSCI-RM-Mixed	Blood-loss	$R^2$ : 0.36	ASA I $R^2$ : 0.36 ASA II $R^2$ : 0.40 ASA III $R^2$ : 0.57	<50 $R^2$ : 0.31 >50 $R^2$ : 0.42	$R^2$ : 0.37-0.64	AUC: 0.80	AUC: 0.72
	Surgical duration	$R^2$ : 0.35	ASA I $R^2$ : 0.42 ASA II $R^2$ : 0.37 ASA III $R^2$ : 0.64	<50 $R^2$ : 0.42 >50 $R^2$ : 0.45	$R^2$ : 0.40-0.88	AUC: 0.80	
MIRZA	Blood-loss	$R^2$ : 0.15	ASA I $R^2$ : 0.14 ASA II $R^2$ : 0.19 ASA III $R^2$ : 0.20	<50 $R^2$ : 0.12 >50 $R^2$ : 0.22	$R^2$ : 0.0001-0.53	AUC: 0.64	AUC: 0.53
	Surgical duration	$R^2$ : 0.11	ASA I $R^2$ : 0.19 ASA II $R^2$ : 0.08 ASA III $R^2$ : 0.08	<50 $R^2$ : 0.22 >50 $R^2$ : 0.05	$R^2$ : 0.0036-0.71	AUC: 0.64	

**Results:** At the time of the study, the ESSG database included 1325 patients, 475 of whom had been treated surgically using a posterior approach only (52.2y SD20; 77.7% female; 85.4% ASA I/II). Average blood loss was 1422.8 ml (SD1093.0) and operating time 290.4 min (SD141.2). 86 patients developed at least one major complication during the first 90 postoperative days. 51 international experts participated in the Delphi-consensus process. The surgical variables selected by consensus and included in the equation were divided into actions and factors. Actions selected were: number of fused segments, decompressions, interbody fusions and cemented levels; number and type of posterior osteotomies and use of pelvic fixation. The factors included were: implant density, revision surgery and team experience. ADSCI-RM-Mixed (Regression model with Delphi formula interactions), provided the best estimates and predictive value. The explained variance varied depending on study centre and patient characteristics. The ADSCI-RM-Mixed, with greater AUCs, was also the

most sensitive and specific for both of the dependent variables studied and also with complications prediction (Figure). ADSCI-RM-Mixed obtained also the highest  $R^2$  values in the validation cohort in predicting blood loss ( $R^2=0.34$ ) and surgical time ( $R^2=0.26$ ) with similar effect sizes to those for the derivation cohort.

**Discussion:** Accurate prediction of perioperative risk is an important goal to enable informed consent for patients undergoing surgery. ADSCI is the first tool to be specifically developed for the preoperative assessment of the complexity of ASD surgery. This study confirm its validity, specificity and sensitivity and show that it has greater predictive capability than the more generic Mirza invasiveness index. ADSCI should be useful for quantitatively estimating the increased risk associated with more invasive surgery and adjusting for surgical case-mix when making safety comparisons in ASDS.

## GLOBAL ALIGNMENT AND PROPORTION (GAP) SCORE: DEVELOPMENT AND VALIDATION OF A NEW METHOD OF ANALYZING SPINOPELVIC ALIGNMENT TO PREDICT MECHANICAL COMPLICATIONS AFTER ADULT SPINAL DEFORMITY SURGERY

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### **Introduction:**

The restoration of normal sagittal alignment is a critical goal in adult spinal deformity surgery to achieve favorable outcomes and prevent mechanical complications. Schwab's sagittal modifiers have been accepted as targets for appropriate alignment but addressing these does not always prevent high mechanical complication/revision rates. This may be because the linear numerical parameters do not cover the whole pelvic incidence (PI) spectrum and, the distribution of lordosis, pelvic anteversion and negative malalignment are not considered as potential causes of failure. This study aimed to develop and validate a scoring system based on PI-based proportional parameters to better predict mechanical complications.

### **Methods:**

222 patients (168 women, 54 men) who had undergone posterior fusion  $\geq 4$  levels at least  $\geq 2$  years ago were included. Mean age was  $52.2 \pm 19.3$  (18-84) years, and mean follow-up was  $28.8 \pm 8.2$  (24-62) months. The global alignment and proportion (GAP) score was developed and validated in groups of patients randomly assigned to derivation (n=148, 66.6%) and validation (n=74, 33.3%) cohorts. GAP score parameters comprised Pelvic Version Index (Sacral Slope/Pelvic Incidence  $\times 100$ ), Ideal Lordosis Index (L1-S1 Lordosis/Ideal Lordosis  $\times 100$ ), Lordosis Distribution Index (L4-S1 lordosis/L1-S1 lordosis  $\times 100$ ), Relative Sagittal Alignment (Global Tilt-Ideal GT) and an age factor. Proximal and distal junctional kyphosis/failure, pseudarthrosis and implant-related complications were considered mechanical complications. The predictive accuracy of the GAP score was analyzed using receiver operating characteristics (ROC) analyses. Associations between GAP categories and mechanical complications and revisions were analyzed using Chi-squared tests.

### **Results:**

In the validation cohort, 30 patients (40.5%) experienced mechanical complications and 11 (14.8%) underwent mechanical revision. The area under ROC curve for the GAP score in predicting mechanical complications was 0.866 (SE:0.045,  $p < 0.001$ , 95%CI:0.777-0.955). Postoperatively GAP proportioned patients had a mechanical complication rate of 8.3%, while GAP moderately disproportioned and severely disproportioned patients had rates of 55.6% and 85%, respectively.

### **Discussion:**

The GAP Score is a new PI-based proportional scoring system for the sagittal plane that predicts mechanical complications in adult spinal deformity surgery. Setting surgical goals according to the GAP Score may decrease the incidence of mechanical complications.

## LUMBAR SPINE ALIGNMENT IN 6 COMMON POSTURES - A ROM ANALYSIS WITH IMPLICATIONS FOR DEFORMITY CORRECTION

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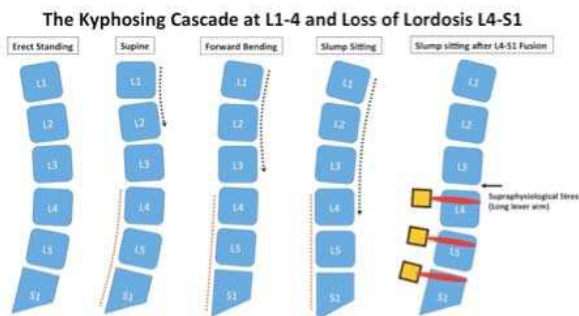
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### Introduction

The ideal position for fusion of the lumbar spine remains poorly understood. While surgical fusion is necessary to maintain deformity correction and symptom relief, the final position in which the vertebrae are immobilized should provide maximum residual function. This study aims to compare lumbar spine alignment in 6 common physiological postures, and estimate the loss in range of motion (ROM) relative to standing posture.

### Methods

This is a cross-sectional study with prospectively collected data. Seventy patients above the age of 45 years, with low back pain were recruited from a spine outpatient clinic over 1-year. All subjects had X-rays performed in 6 common human postures; namely slump sitting, forward bending, supine, half squatting, standing and backward bending postures. ROM quantified in terms of sagittal global and segmental Cobb angles was measured from L1 to S1. Loss in ROM relative to standing was calculated for each posture. ANOVA and unpaired t-tests were used to identify differences in alignment between postures. These postures were then ranked in order of global lordosis. The standing position was taken as reference to study important ROM changes occurring in the various non-standing postures.



### Results

Slump sitting gives the greatest lumbar flexion ( $p < 0.001$ ) followed by forward bending ( $p < 0.001$ ), and supine ( $p < 0.001$ ) postures. Significantly greater lumbar extension ( $p = 0.035$ ) occurs in backward bending as compared to standing. No significant differences were found between half-squatting and standing postures ( $p = 0.938$ ). Regardless of the posture, L4-L5 and L5-S1 levels remained in lordosis with L4-5 having a greater ROM compared to L5-S1. L1-2 turns kyphotic when a patient is lying supine, L2-3 during forward bending and L3-4 during slump sitting in the form of a "kyphosing cascade". Should the entire lumbar spine be fused in standing position from L1-S1, there would likely be a mean loss of  $47.6^\circ$  of lumbar flexion, and  $5.9^\circ$  of lumbar extension.

### Discussion

This study demonstrates the extent of flexibility required of the lumbar spine in assuming various postures. It also enables us to compare the differences in the degree of motion occurring in the lumbar spine, both across postures and across segments of the lumbar spine. If fusion based upon the lordotic profile of the standing lumbar spine occurs, significant loss in ROM, particularly flexion, is anticipated. This will lead to functional loss and possibly proximal junctional failure.

## TARGETED THERAPY OF 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 middle 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. 101 patients underwent PIPI (PIPI group) and 53 patients received nonoperative treatment (control group). The outcomes were evaluated using Visual analog scale (VAS) for LBP, and the Oswestry Disability Index (ODI). As the objective changes, we measured BME score. Mean follow-up period was 50.0±21.0 months.

**RESULTS:** In PIPI group, the mean VAS and ODI scores were 82.9±15.3 and 53.0±16.3 at the baseline. These scores were significantly improved at 1 month after PIPI (28.8±22.9, 31.2±18.1), and maintained for 2 years (30.0±25.4, 32.3±18.0). In control group, the mean VAS and ODI scores were 70.3±15.2, 49.7±16.1 at the baseline. These were not improved for 2 years (66.5±18.6, 47.0±15.1). 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:  $r=0.372$ ,  $P<0.001$ ). However, mean BME score was not changed in control group. In PIPI group, 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 (12 patients), and other level disorders (6 patients). In 53 patients with no recurrence of BME, the mean VAS and ODI scores were 29.6±18.3, 33.3±14.0 at the final follow-up (mean 45.6 months after PIPI).

**DISCUSSION:** LBP was improved immediately after PIPI compared with nonoperative treatments. PIPI could be a novel targeted therapy for LBP associated with *de novo* DLS in the elderly.

## COMPARISON OF THE CLINICAL OUTCOMES OF MINIMALLY INVASIVE DECOMPRESSION WITH THOSE OF MINIMALLY INVASIVE DECOMPRESSION AND FUSION IN PATIENTS WITH DEGENERATIVE SPONDYLOLISTHESIS WITH INSTABILITY -MEL VERSUS CBT-PLIF WITH A MINIMUM FOLLOW-UP OF 2 YEARS

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**Introduction:** The effectiveness of decompression alone for degenerative spondylolisthesis (DS) is controversial. However, previous reports only compared the clinical outcomes of conventional decompression alone with those of conventional decompression and fusion. Microendoscopic laminotomy (MEL) is representative of minimally invasive decompression surgery, and posterior lumbar interbody fusion with cortical bone trajectory (CBT-PLIF) is representative of minimally invasive decompression and fusion. Better clinical outcomes were reported following these two methods for the treatment of DS. However, no report has compared the clinical outcomes or invasiveness between them.

**Aim:** To compare the clinical outcomes of MEL and CBT-PLIF for degenerative spondylolisthesis with instability.

**Materials and Methods:** 40 patients with DS who met one of the following criteria were enrolled: (1) Meyerding grade 2; (2) segmental kyphosis of  $>5^\circ$  at flexion; or (3) anterior translation of  $>3$  mm at flexion. Generally, we would recommend decompression and fusion surgery for such patients. The patients were divided into two groups as follows: group C included 20 patients who underwent CBT-PLIF according to our recommendation, and group M included 19 patients who underwent MEL according to the patients' request. The same surgeon performed the operation in all the patients, who were followed-up for a minimum of 2 years. Patients who required hemodialysis, had Meyerding grade  $>3$  spondylolisthesis, or had symptoms owing to foraminal stenosis were excluded. We evaluated the clinical outcomes based on improvements in the Japanese Orthopaedic Association (JOA) score; visual analog scale scores (VAS) for back pain, leg pain, and leg numbness at 2 years; reoperation rate; and complications. In addition, operated and adjacent segment degeneration and diseases were also investigated.

**Results:** The mean operation times were similar between the groups. However, the amount of intraoperative blood loss and C-reactive protein level at 1 week after the operation were significantly higher in group C than in group M.

The improvement in the JOA score was 70.5% in group M and 72.6% in group C. No significant difference was found between the two groups. The improvements in the VAS scores for back pain, leg pain, and leg numbness also did not have significant differences (group M vs. group C: 23 vs. 27, 33 vs. 43, and 33 vs. 22, respectively).

In group M, disk height decreased by  $>1$  mm in 42% of the patients, and spondylolisthesis deteriorated by  $>1$  mm in 47%. Although no significant correlation was found between the clinical results and those radiographic changes, 2 patients (10%) needed reoperation for foraminal stenosis at the decompressed level after the primary operation.

In group C, nonunion and fused vertebral fractures were observed in 1 patient; however, none of the patients required reoperation. Other implant-related complications or adjacent segment degenerations and diseases were not observed.

**Conclusion:** The clinical outcomes of MEL for DS with instability were comparable with those of CBT-PLIF at the 2-year follow-up. MEL was less invasive than CBT-PLIF. However, foraminal stenosis at the decompressed level should be considered as a possible cause of reoperation after MEL.



## INTERSPINOUS DYNAMIC STABILIZATION ADJACENT TO FUSION VERSUS DOUBLE-SEGMENT FUSION FOR DEGENERATIVE LUMBAR DISEASES: MINIMUM THREE YEARS FOLLOW-UP

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**Introduction:** Rigid fixation and fusion surgery is viewed as the conventional treatment for lumbar degenerative disease. However, fusion surgery eliminates fixed segment motion, increases unfused adjacent segment motion, and then accelerates the degeneration of adjacent segments. The aim of this study was to assess the outcome of symptomatic lumbar degenerative disease treated with topping-off technique (Coflex combined with fusion) and compare two-segment fusion at mid-long term follow-up; and find out whether the topping-off technique can reduce the rate of adjacent segment degeneration (ASD) after fusion.

**Methods:** One hundred and fifty-four consecutive patients who received topping-off surgery (76 patients) and two-segment fusion surgery (88 patients) from March 2009 to March 2012 were studied. All patients included in the analysis had a minimum of three years of follow-up. Radiographic and clinical outcomes between the two groups were compared. A logistic regression analysis was used to analyze risk factors for developing radiographic ASD.

**Results:** Significant differences in clinical outcomes were observed between these two groups at three post-operative years (all,  $p < 0.05$ ). Compared with the fusion group, the topping-off group showed preserved mobility at the Coflex level ( $p=0.000$ ), which is associated with less blood loss ( $p = 0.000$ ), shorter duration of surgery ( $p = 0.000$ ) and lower incidence of ASD (Chi-square test, rate topping-off vs fusion = 13.2 vs 26.1 %,  $p = 0.039$ ). There were no differences in complications between the two groups.

**Discussion:** Mid-long term follow-up efficacy and safety between topping-off and fusion were similar, while topping-off reduced the rate of ASD. Under strict indications, topping-off surgery is an acceptable alternative to fusion surgery for the treatment of two-segment lumbar disease.

## A COMPARATIVE STUDY BETWEEN OPEN AND PERCUTANEOUS POSTERIOR FIXATION SURGERIES FOR EFFECTS OF THE PERFORMANCE STATUS, ACTIVITIES OF DAILY LIVING, AND QUALITY OF LIFE IN PATIENTS WITH SPINAL METASTASIS

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**Introduction:** Spinal metastasis can cause severe pain and/or neurological deficit, resulting in a drastic loss of the patients' performance status (PS), activities of daily living (ADL), and quality of life (QOL). We have performed open surgery (internal fixation and/or decompression) or only posterior fixation surgery using percutaneous pedicle screws (PPS) based on the severity of symptoms. However, surgical indication and clinical outcomes of PPS in spinal metastasis are still undetermined. Our objective was to clarify impacts of PPS surgery, compared to open surgery, on the PS, ADL, and QOL in patients with spinal metastasis.

**Methods:** Between 2013 and 2016, 60 patients who developed thoracic or lumbar spinal metastasis with pain and/or neurological complications were prospectively enrolled and underwent spinal surgery with optimal treatments including radiation, chemotherapy, cancer rehabilitation, and palliative care services. They consisted of 18 who took PPS surgery and 42 who received open surgery. Evaluation was performed at postoperative 0, 1, 3, and 6 months by the Frankel classification for the neurological status, Eastern Cooperative Oncology Group PS for the general well-being, Barthel index (BI) for the ADL, EQ-5D for the QOL. The  $\chi^2$  or Student t-test was used with significance of  $p < 0.05$ .

**Results:** No obvious differences in the patient age, sex, tumor origin, location and number of metastatic and operated vertebrae, and preoperative Tokuhashi and Katagiri classification scores were observed between patients with PPS and with open surgeries. 96.7%, 85.0%, 91.7%, and 91.7% of patients took radiation, chemotherapy, rehabilitation, and palliative cares, respectively, resulting in no significant differences between the groups. Significantly shorter operation time and smaller perioperative bleeding volume were observed in patients with PPS surgery ( $p=0.02$  and  $p<0.01$ , respectively), indicating less invasive surgery of PPS. Then, 94.4% of patients with PPS surgery but only 42.9% of those with open surgery showed preoperative Frankel grades DE, non-severe paralysis ( $p<0.01$ ); thus, PPS was applicable to patients with useful motor function. In addition, 83.3% of patients with PPS surgery and 81.6% of those with open surgery improved the Frankel grade  $\geq 1$  throughout postoperative 6 months. In the PS for the general well-being, no significant preoperative difference was observed. However, patients with PPS surgery showed the trend toward the improvement and maintenance of the PS throughout postoperative 6 months (94.4% vs. 73.8%,  $p=0.07$ ). Further, patients with PPS surgery demonstrated significantly higher scores of the preoperative BI for the ADL ( $p=0.049$ ) and a higher improvement rate of the BI throughout postoperative 6 months (100.0% vs. 66.7%,  $p<0.01$ ). Finally, although there was no significant preoperative difference in the EQ-5D for the QOL, a higher EQ-5D improvement rate postoperative throughout 6 months was found in patients with PPS (94.4% vs. 74.3%,  $p=0.08$ ).

**Discussion:** PPS surgery can improve and maintain ADL and potentially PS and QOL for minimum postoperative 6 months with a reduced invasion in spinal metastatic patients with preserved motor function, indicating PPS as an effective palliative therapy.

## IS DYNAMIC SURFACE ELECTROMYOGRAPHY TOPOGRAPHY AN INDICATION OF LOW BACK PAIN?

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**Introduction:** Dynamic surface electromyography (SEMG) topography was found to be altered during rehabilitation of low back pain (LBP), which tended to normal pattern with pain relief progress. SEMG topography was proposed as a quantitative and objective assessment of LBP rehabilitation. However, it is still a question whether SEMG topography is an indicator of pain or muscular strength improvement. Our hypothesis is that the change of SEMG topography is caused by pain relief instead of enhancement of muscle morphology. To verify this hypothesis, this study investigated the changes of SEMG topography immediately after local surface analgesic pain relief without changes of muscle morphology.

**Methods:** A total of 17 patients with non-specific LBP were recruited for this study. Each patient was asked to receive a topical anesthetic spray (Yunnan Baiyao spray, Yunnan Baiyao Ltd, Yunnan, China) on the lumbar area for reducing LBP. Visual analog scale (VAS) score was evaluated before and after surface anesthetic spray. Those patients reported VAS decreased more than 2 points (including 2 points) were classified as “responder” group, while those patients reported VAS decreased less than 2 points were classified as “non-responder” group. SEMG were recorded from an electrode-array on lumbar area of patient in two groups during flexion-extension movement before and after local analgesia. SEMG topography was calculated to obtain the root-mean-square difference (RMSD) values in comparison to healthy normal pattern established with an age and gender matched group of 35 healthy subjects from a previous database. The RMSD values included RMSD of relative area (RA), relative height (RH) and relative weight (RW). The values of RMSD were compared before and after local analgesia in these two groups by paired Student’s T-test. A linear correlation analysis was performed between changes of RMSD and VAS in LBP before and after local analgesia.

**Results:** Of 17 patients with LBP, 8 patients showed good response to local analgesia (“responder” group), while 9 patients did not show good response (“non-responder” group). The VAS score in “responder” group decreased from  $4.51 \pm 1.27$  to  $2.18 \pm 1.27$ , while VAS score in “non-responder” group changed from  $3.74 \pm 1.67$  to  $3.60 \pm 1.74$ . Visual inspection did not show difference in SEMG topography between “responder” and “non-responder” group. However, we could observe that the SEMG topography in “responder” group changed toward normal pattern after local analgesia. Significant higher reduction of RMSD could be seen in the “responder” group ( $p < 0.05$ ) in comparison to “non-responder” group. In all LBP patients, changes of RMSD RW during extension phase between local analgesia showed well correlation with reduction of VAS ( $r = 0.532$ ,  $p = 0.028$ ).

**Discussion:** Results of this study demonstrated that the SEMG topography changed in association with pain relief after local analgesia. Since the effect of local analgesia is a loss of nociception without changes of muscle morphology, this study well verified the hypothesis that changes of SEMG topography were pain-related rather than muscular function related. If further study can verify that SEMG topography do not change in association with changes of muscle morphology, we can prove dynamic SEMG topography as an indication of low back pain.

## USE OF THE LIMITING DILUTION METHOD FOR THE ISOLATION OF NUCLEUS PULPOSUS MESENCHYMAL STEM CELLS (NPMSCS) AND THE EFFECTS OF PLATING DENSITY ON BIOLOGICAL CHARACTERISTICS AND PLASTICITY (#102)

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**Introduction:** Recent studies have demonstrated that nucleus pulposus mesenchymal stem cells (NPMSCs) have great bioactivity and would be as the seed cells in tissue-engineering, which will take the important role in regeneration of nucleus pulposus (NP) regeneration. In our study we introduced a non-usual method, limiting dilution method, to isolate NPMSCs from NP, and we also evaluate its effect on biological characteristics and plating density in NPMSCs.

**Methods:** NP tissues were isolated from 12-week-old male Sprague–Dawley rats, and NPMSCs were isolated from the tissue with the limiting dilution method. The harvested cells were then classified into 3 groups according to the cell density of plating as follows: low density (LD) group, medium density (MD) group and high density (HD) group. NPMSC morphologies were observed and colony-forming units determined. The migration abilities, proliferative capacities, cell cycle percentages, multi-lineage differentiation capacities, stem cell biomarker expression levels and immunophenotyping were also examined each group.

**Results:** LD NPMSCs had higher morphological homogeneity, stronger colony-forming ability, highly cell proliferation capacity and could enhance the cell migration ability relative to the other two groups ( $p < 0.05$ ). Moreover, LD NPMSCs had much more cells entering S phase, with fewer cells arrested in G0/G1 phase ( $p < 0.05$ ). While all three density groups showed multi-lineage differentiation potential, the LD group showed a higher degree in cells observed and semi-quantified lineage specific staining ( $p < 0.05$ ). Furthermore, the LD NPMSCs displayed higher expression levels of stem cell biomarkers (Nanog, Oct4 and Sox2) and showed higher percentages of CD29+, CD44+ and CD90+ cells ( $p < 0.05$ ) following flow cytometry analysis.

**Discussion:** The limiting dilution method and a cell plating densities of 5 cells/cm<sup>2</sup> were suggested when isolating NPMSCs as a means of improving cell activity and plasticity. In our studies, we utilize a limiting dilution method when isolating NPMSCs under LD condition can yield a cell population with a higher proliferative capacity, activity and stemness. Therefore, this method can be chosen to isolate the NPMSCs and apply in tissue-engineering.

## REAL-TIME MONITORING OF GLUCOSE CONSUMPTION OF INTERVERTEBRAL DISC CELLS IN 3D CULTURE

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### Introduction

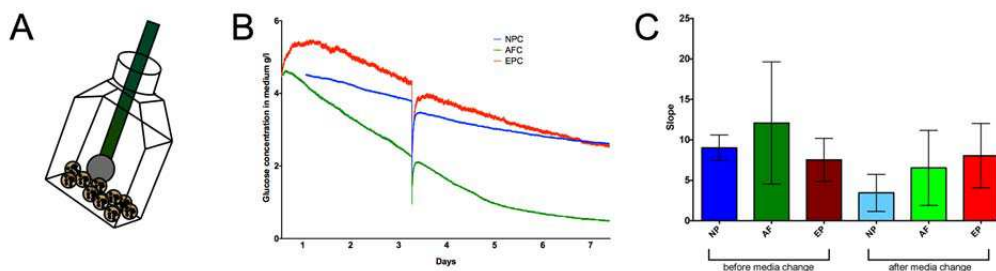
Glucose consumption is a key parameter for many cell types. However, this parameter seems to be crucial for cells dependent solely on passive diffusion such as intervertebral disc (IVD) cells [1, 2]. The limited nutrition hypothesis states that IVD cells die because of depletion of nutrients such as glucose by blockage of the main nutritional routes. Due to the location of the different cell types, i.e. the nucleus pulposus cells (NPC) in the center of the disc, the annulus fibrosus (AFC) and the cartilaginous endplate (CEP) cells, we hypothesized that the glucose consumption rate should be highest with cells being closer to blood vessel supply and the cells in the center (NPC) would require the lowest glucose consumption rate. Here, we test this hypothesis using freshly-isolated, clinical primary IVD cells isolated from trauma tissue in real-time.

### Methods

Human primary AFC, NPC and CEP were isolated from different lumbar levels using a mild two-step digestion protocol with pronase and collagenase 2. Cells were resuspended in passage 2 in 1.2% alginate at a density of 4Mio cells/ml and ~30ul beads were formed. 30 beads in 9ml DMEM supplemented with 4.5g/l glucose (hyperglycaemic condition) and 10% FCS were added to a T-25 culture flask that was equipped with a glucose sensor (C-CIT Sensors AG, Switzerland), Fig 1A. T-flasks were put on a shaker (10rpm) and glucose concentration was recorded over seven days. Media was replaced after 3-4 days. Cell activity (Alamar blue) was determined on day 1 and on day 7. Further, DNA (Hoechst assay) and glycosaminoglycan (GAG) (DMMB assay) content were determined.

### Results

Monitoring of real-time glucose was successful *in vitro*, Fig 1B. Glucose uptake was inferred from current (nA) and linear regression was performed. Slopes were used for comparison among cell types. Before media change EPC presented a higher glucose consumption than AFC and NPC, Fig 1C.



**Figure 1:** A Sketch of the glucose sensor in a T-flask. B Glucose consumption monitored in real-time over seven days for human AFC, NPC and EPC. C Slopes of current before and after media change of 5 experiments  $\pm$  SD.

### Discussion

There seems to be a difference in glucose consumption between the different cell types. Before media change cells consume glucose at a comparable rate. Nevertheless, after media exchange a trend towards higher glucose consumption by CEP compared to AFC and NPC could be observed. This could be explained by their location close to the nutrient transport route, i.e. the capillary system of the vertebrae. So they should be adapted to higher glucose levels than cells in the centre of the disc, which rely on pure diffusion. In the near future we plan to repeat this experiment and to vary glucose concentration to determine the ideal glucose range for cell culture and to investigate possible IVD treatment approaches.

### Acknowledgements

This project was supported by the Gebert R uf Foundation project # GRS-X028/13. We thank Stefan Spichiger and Ferdynand Cagayan from C-CIT Sensors AG. Further, we thank Eva Roth for assistance with IVD cell isolation.

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## HUMAN MESENCHYMAL STEM CELLS PRE-TREATED WITH IL-1 $\beta$ AND STIMULATED WITH BMP-3 GROWTH FACTOR ENHANCE CHONDROGENESIS *IN VITRO*

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**Background:** Low back pain is the most common pain condition in western countries afflicting more than 80% of the population and the main cause is believed to be degeneration of intervertebral discs (IVDs). Transplantation of human mesenchymal cells (hMSCs) to the discs has been suggested as a potential way to treat disc degeneration. To be able to optimize such treatment it is important to know the effect of different cytokines on hMSCs. IL-1 $\beta$  is a vital inflammatory cytokine found in abundance in degenerated discs environment where as BMP-3 is believed to promote chondrogenesis through the TGF- $\beta$  pathway.

**Aim:** The aim was to study the effects of BMP-3, IL-1 $\beta$  and combination (IL-1 $\beta$  pre-treatment) on hMSCs encapsulated in hydrogel (Phg) especially in the absence of TGF- $\beta$ , in order to investigate proliferation and differentiation ability of hMSCs over a 28 day period.

**Method:** 100 $\mu$ L of hMSCs cell suspension was encapsulated between two layers of 100  $\mu$ L Phg (sandwich-like structure). The encapsulated cells were supplied with media containing cytokine and growth factor according to Table 1. The samples were harvested at day 7, 14 and 28 and evaluated for cell viability, proteoglycan accumulation, differentiation, chondrogenesis and cellular proliferation pattern.

**Results:** Proliferation and differentiation of hMSCs into chondrocyte-like cells was observed in all samples. Proteoglycan accumulation was observed as early as in day 7 in pre-treatment samples in C media while in BMP-3 stimulated samples, it was observed in day 28. Instead of possessing negative signs of proliferation and differentiation in samples stimulated with IL-1 $\beta$  alone, the hMSCs were found unaffected, even in media deprived of TGF- $\beta$  (nC media). The protein and gene expression of the early and late indicator of chondrogenesis, SOX-9 and COL2A1 respectively, showed the occurrence of chondrogenesis in all samples.

**Conclusion:** Good cell viability, proliferation and differentiation is achieved in this *in vitro* model. Our finding confirms that BMP-3 alone in the absence of TGF- $\beta$  could drive hMSCs into chondrogenic lineage and in presence of TGF- $\beta$  seemed to further increase the extracellular matrix (ECM) production. Pre-treatment with IL-1 $\beta$  followed by BMP-3 stimulation resulted in high proteoglycans accumulation compared to stimulation with growth factors or cytokine alone, both in the presence (C media) and absence of TGF- $\beta$  (nC media).

**Table 1.**

Sets of Chondrogenic Media (C media)	Sets of non-chondrogenic media (nC media)
C media	-
10ng/ml BMP-3 in C media	10ng/ml BMP-3 in nC media
10ng/ml IL-1 $\beta$ in C media	10ng/ml IL-1 $\beta$ in nC media
Pre-treatment in IL-1 $\beta$ in C media for 24 hours + BMP-3 in C media	Pre-treatment in IL-1 $\beta$ in nC media for 24 hours + BMP-3 in nC media

**EFFECT OF GEOMETRY ON HUMAN LUMBAR INTERVERTEBRAL DISC SIX DEGREE OF FREEDOM MECHANICS**

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**Introduction:** Under daily activity the intervertebral disc is exposed to large multiaxial, or 6 degree-of-freedom (6DOF), loads. However, it remains unclear what relationships the disc’s geometry plays in its 6DOF mechanics. Therefore the objective of this study was to quantify the disc stiffness in 6DOF and relate them to disc height, aspect ratio, and area.

**Methods:** Lumbar human discs (n=10, Pfirrmann grade 2 and 3, age 35-59, Level L1-L5) were prepared by removing the posterior elements and measuring the height, anterior-posterior width, and lateral width with x-ray. Samples were thawed overnight in 50 N axial compression in 0.15M PBS with protease inhibitors. Discs were potted in PMMA, set up in a 6DOF hexapod robot [1], and preloaded to 0.2 MPa axial compression, which was held for 12 hrs at 37°C in 0.15M PBS with protease inhibitors. After preload, 6DOF dynamic mechanical testing was performed using sine waves under a 0.2 MPa axial compression load in the following order: lateral shear (±0.6 mm), anterior-posterior shear (±0.6 mm), axial rotation (±3°), lateral bending (±4°), flexion/extension (±3°) and axial compression (0.2 MPa to 1.1 MPa). Dynamic testing included 5 cycles at a fast (0.5 or 1 Hz), medium, and slow rate (0.005 or 0.01 Hz), where the higher rate was used in compression. There was an unloaded recovery for 30 min at 0.2 MPa after each loading direction. Stiffness was calculated between 80-100% of the maximum force of the final cycle. The relationship of stiffness to geometry (height, area, aspect ratio) was evaluated with a Pearson’s correlation.

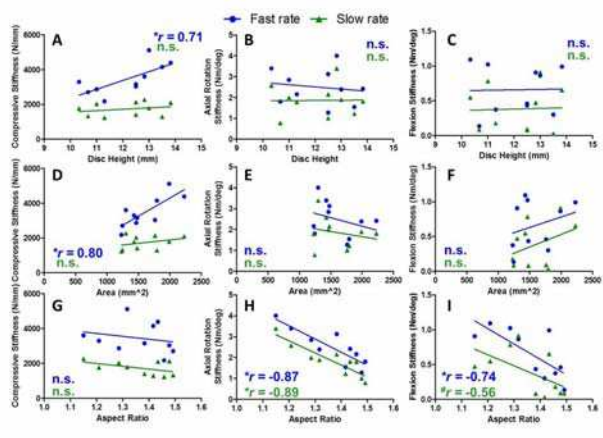


Figure 1: Comparison of 6DOF stiffness and disc height, disc aspect ratio, and disc area. \* Denotes significant correlation ( $p < 0.05$ ) while \* denotes trending correlation ( $p < 0.1$ ), and n.s. denotes not significant.

**Results:** Compressive stiffness correlated with height ( $r = 0.71$ ) and area ( $r = 0.80$ ) for fast rate loading. No measures were correlated with height for slow rate loading. The only other stiffness to correlate with area was anterior-posterior shear, which decreased for fast ( $r = -0.68$ ) and slow ( $r = -0.65$ ) rate loading. Stiffness in axial rotation ( $r = -0.87$ ), flexion ( $r = 0.74$ ), lateral shear ( $r = -0.76$ ), and anterior-posterior shear ( $r = -0.72$ ) were strongly correlated with the aspect ratio for fast rate loading. Stiffness in axial rotation ( $r = 0.89$ ), lateral shear ( $r = -0.92$ ), and anterior-posterior shear ( $r = -0.75$ ) were correlated with aspect ratio for slow rate loading. See Figure.

**Discussion:** This study correlated disc stiffnesses in 6DOF loading and with geometry. Surprisingly, only compression stiffness correlated with disc height and disc area. On the other hand, disc aspect ratio, a measure of the disc’s ellipsoid shape, was a significant predictor of the bending and torsional mechanics. This

suggests that the disc’s ellipsoid shape affects stress in the annulus fibrosus and may also affect mechanical signals cells experience in their local environment. These relationships between geometry and mechanics will be useful in validating finite element models of disc mechanics. Moreover, these relationships may be useful in diagnostic approaches for degeneration and low back pain.

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## EVEN MILD DEGENERATION OF THE LUMBAR SPINE IS ASSOCIATED WITH A LOSS OF THE HYDROSTATIC BEHAVIOR OF THE INTERVERTEBRAL DISC

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### Introduction

It is well known that advancing degeneration of the intervertebral disc reduces the water content of the nucleus pulposus (NP), evoking a solid-like instead of a fluid-like behavior of this structure (Inoue and Espinoza Orías, 2012). The changes of the NP can be indirectly quantified by the Intradiscal Pressure (IDP). Previous studies quantified the hydrostatic behavior by turning the sensor membrane inside the NP into vertical and horizontal positions (Nachemson et al., 1960; Sato et al., 1999). They concluded that degeneration either had no influence on the hydrostatic behavior or only at the severely degenerated stages of degeneration. However, in previous studies (Nachemson et al., 1979; Wilke et al., 2013), it was found that the response of the IDP to intervertebral motion is altered by degeneration. For this reason, the goal of this study was to investigate whether this parameter is superior in determining whether discs behave hydrostatic or not.

### Methods

The study was conducted using 10 human spine specimens (T12-S1) with a mean age of 53 years (34-64 years). The specimens were scanned with a 3T-MRI prior to preparation. Each disc was then graded according to the system by Pfirrmann and colleagues (2001). Prior to testing, flexible pressure sensors with a diameter of 1.5 mm were inserted centrally into the NP of each disc. Due to the anatomical symmetry of the spine in lateral bending and axial rotation, the specimens were loaded with pure moments of 7.5Nm in these motion direction to quantify the flexibility of the specimens. To determine whether the discs behave hydrostatically, the asymmetry of the pressures at maximal deflections (side-to-side comparison) was evaluated. Truly hydrostatic discs would only express minimal asymmetry of the maximal pressures (Fig. 1). The asymmetry was normalized to the individual IDP in neutral position to account for the differences between the specimens.

To determine whether the findings depend on the spinal level, Kruskal-Wallis tests were performed for each motion direction. Since no level-dependence was found, data were pooled and Mann-Whitney-U tests were performed to determine the influence of degeneration on the asymmetry of the maximal pressures. Significance level was set to  $\alpha=0.05$ .

### Results

We found a significant increase in asymmetry from degeneration grade II to grade III ( $p<0.001$ ), with no further significant changes with more severe degeneration. However, the variation within the degeneration groups generally increased with advancing degeneration (Fig. 2).

### Discussion

In this study, we found a significant increase in the side-to-side asymmetry of the IDP for segments of Pfirrmann grade III, which correspond to moderate degeneration. This contrasts with previous studies in which hydrostatic behavior was quantified by turning the sensor membrane within the NP. Since loss of hydrostatic behavior corresponds well with loss of water visible on MRI, we suggest that this method is more suitable to detect losses of hydrostatic behavior. Further, this study suggests that IDP curves from discs of grade III or worse are frequently paradoxical; thus no reliable information can be derived from such segments (Fig. 1).

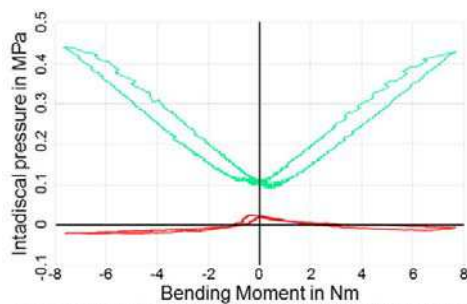


Fig 1. Representative IDP curves obtained in lateral bending. The Y-axis indicates the IDP, whereas the X-axis shows the bending moment. The light green curve is representative for non-degenerated discs, whereas the dark red curve was obtained from a degenerated intervertebral discs.

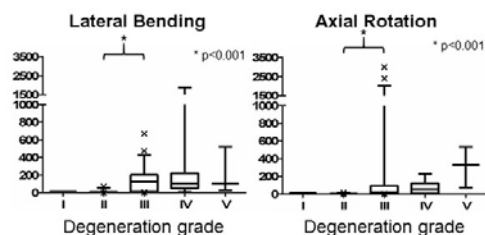


Fig 2. Relative asymmetry of IDP in lateral bending and axial rotation for each degeneration grade. Whether the higher value was measured in the positive or negative maximal deflection is not taken into account. Values are given in %. Box-whisker plots give the median value (horizontal line within the boxes), the upper and lower quartiles (box), and the upper and lower 95% percentiles (whiskers). Values outside this range are indicated by crosses. The Y-axis is split to account for the large range of results.

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## DOES AN ANNULAR PUNCTURE INFLUENCE THE HERNIATION PATHWAY? AN *IN VITRO* MECHANICAL AND STRUCTURAL INVESTIGATION

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**INTRODUCTION:** Discography involving an annular puncture is used to investigate the origin of disabling low back pain. However, 10 years post discography both degenerative changes and herniation have been shown to increase compared to untreated discs [1]. Also, future therapeutic interventions that include protein, gene, and cell-based therapies for the treatment of disc degeneration are likely to involve the use of an annular puncture. While the longer-term degenerative consequences of puncturing the disc have been widely investigated it remains unclear whether it places the disc under a greater risk of immediate or short-term herniation. New herniations in discs previously subjected to discography have been shown to occur most frequently at the site of puncture [1]. This raises the question whether localised damage created by an annular puncture can redirect the herniation pathway and thus increase the risk of it occurring at the puncture site independent of any longer term degenerative changes.

**OBJECTIVE:** To investigate whether an annular puncture increases the risk of immediate herniation at the site of needle damage.

**METHODS:** The posterolateral annulus of healthy ovine lumbar discs were punctured with either a 25-gauge (n=8) or 18-gauge (n=8) needle. Each motion segment was then compressed in a flexed posture of 10° to induce disc failure. The entire volume of the disc was assessed for annular damage and nuclear migration using a progressive transverse sectioning technique.

**RESULTS:** The mean failure loads for the 25- and 18-gauge puncture groups were 9.7 kN and 8.6 kN, respectively. This difference was not significant ( $p>0.05$ ). There was no association between the 25-gauge puncture site and disc disruption/herniation. In contrast, nuclear material was observed to migrate through the 18-gauge puncture. Further, a high prevalence of disruption at the lateral inner annulus was observed, even when the disc was punctured with the larger 18-gauge needle.

**DISCUSSION:** The immediate risk to herniation at the puncture site is dependent on the needle diameter used. The lack of influence of the 25-gauge needle on the herniation pathway suggests that the annulus is, to a degree, over-structured so as to provide a 'factor of safety' sufficient for it to cope with moderate overloading. Even with the posterolateral annular damage created by the 25- and 18-gauge needle punctures, the lateral inner annulus was the region most prone to disruption. This regional vulnerability is thought to arise from differential recruitment of the oblique-counter oblique fibre sets in the lateral annulus, generated by anterior shear induced in the flexed and compressed motion segment. In effect, at these lateral sites one fibre set is underloaded at the expense of the other being overloaded and therefore exposed to greater risk of disruption.

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**DIABETES' NEGATIVE IMPACT ON RADICULOPATHY INDUCED BY APPLICATION OF NUCLEUS PULPOSUS ONTO DRG IN SPONTANEOUS DIABETIC RATS****Takuya Kameda<sup>1</sup>, Miho Sekiguchi<sup>1</sup>, Yoichi Kaneuchi<sup>1</sup>, Shinichi Konno<sup>1</sup>***1. Fukushima Medical University, Fukushima, Japan*

**Introduction:** Previous clinical studies suggested negative effects of DM on radiculopathy due to LDH, and that inflammation and nerve regeneration could interact with DM and radiculopathy. The aim of this study is to evaluate the effect of diabetes mellitus (DM) on radiculopathy due to lumbar disc herniation (LDH) by investigating the pain-related behavior along with the expression of tumor necrosis factor-alpha (TNF- $\alpha$ ) and growth-associated protein 43 (GAP43) using nucleus pulposus (NP) applied to type 2 diabetic rats.

**Methods:** We applied autologous NP to the left L5 DRG of adult male Wistar rats (n = 129) and Goto-Kakizaki rats (n = 126). Behavioral testing measured the rats' mechanical withdrawal threshold. We evaluated the localization of ionized calcium-binding adapter molecule-1 (Iba-1), receptor of advanced glycation end products (RAGE), and TNF- $\alpha$  in DRGs by immunohistochemistry. TNF- $\alpha$  and GAP43 expressions in DRG were examined by quantitative real-time PCR and western blotting.

**Results:** The mechanical withdrawal threshold significantly declined in the non-DM NP group compared to the non-DM sham group for 28 days, whereas it declined in the DM NP group compared to the DM sham group for 35 days. RAGE and TNF- $\alpha$  expressions in DRGs were colocalized in Iba-1 positive cells. The non-DM NP rats had higher TNF- $\alpha$  protein expression levels versus the non-DM sham rats on day 7, and the DM NP group had higher levels versus the DM sham group for 14 days. The non-DM NP group had higher GAP43 mRNA expression levels versus that of the non-DM sham group for 28 days, while the DM NP group had higher level than that of the DM sham group for 35 days.

**Discussion:** DM prolongs the pain-related behavior caused by NP. The prolonged inflammation and nerve regeneration could elucidate the pathogenesis of continuous pain of radiculopathy initiated by LDH.

## REDUCED NEURAL MOVEMENT WITH THE STRAIGHT LEG RAISE TEST IN PATIENTS WITH LUMBAR INTERVERTEBRAL DISC HERNIATION.

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**INTRODUCTION:** Earlier studies have shown that during the Straight Leg Raise (SLR) test in asymptomatic volunteers tensile forces are consistently transmitted throughout the neural system and the spinal cord in the thoracolumbar region slides distally in response to the clinically applied test. We aim to explore whether impairment of neural excursion occurs in patients with sciatic symptoms due to lumbar intervertebral disc herniation (LIDH).

**METHODS:** In this controlled radiological study, fifteen voluntary patients with sciatic symptoms due to subacute LIDH were investigated with a 1.5T magnetic resonance (MR)scanner. First a spine specialist diagnosed the LIDH with conventional scanning sequences. Following this the subjects were scanned with the same 1.5T MR scanner using different scanning sequences for planning and for measurement purposes as part of the experimental protocol. Planning: T2 weighted turbo spin echo sequence (Sagittal slices were aligned with the spinal cord to allow better identification of the medullar cone). Measurement: T2 weighted spc 3D-sequence.

Coronal, axial and sagittal slices (slice thickness 1mm, approximately 70 slices per plane) were reconstructed from the native 3D sagittal scans using the MPR program available in Sectra PACS program.

The displacement of the medullar cone relative to the upper intervertebral surface of the adjacent vertebra was compared between maneuvers. Each movement was performed twice for evaluation of reproducibility. Measurements were performed by two different observers, allowing for evaluation of intra- and inter-observer reliability.

**RESULTS:** The number of subjects required to produce statistically significant results ( $p<.05$ ) was five for both symptomatic SLR, asymptomatic SLR and for bilateral SLR. The conus medullaris displaced caudally with the asymptomatic SLR by  $2.28 \pm 1$  mm (Mean $\pm$ SD) ( $p<.001$ ) 95% CI (-2.81, -1.75). However, the excursion produced by the symptomatic SLR was only  $0.76 \pm 0.34$  mm ( $p<.001$ ) 95% CI (-0.95, -0.58), a reduction of 66.6 %. Alternatively, the symptomatic produced only 33.3 % of cord excursion produced by the asymptomatic SLR. The bilateral SLR produced  $3.40 \pm 1.65$  mm of cord excursion ( $p<.001$ ) 95% CI (-3.63, -2.98).

Pearson correlations proved higher than 0.99 for inter-observer reliability as well as results reproducibility for each tested maneuver. Observed power was 1 for each tested maneuver.

**CONCLUSION:** The data collected suggests that in patients with LIDH, the neural displacement on the symptomatic side is significantly reduced by the compressing IVD herniation. With these results, the authors expect that the sliding of neural structures in the vertebral canal may represent a protective mechanism which preserves the spinal cord and neural roots from excessive strain. It seems plausible that physical therapies aiming at restoring normal amount of neural excursion might be employed. To our knowledge, these are the first data to objectively support the limitation of neural movements into the vertebral canal with LIDH in in-vivo and structurally intact human subjects. These findings clarify the mechanism of why the SLR test is considered a useful tool to assess neuromechanical impairment with sciatic patients.



**Figure 1.** MRI T2 sagittal and T2 axial slices showing L5-S1 single-level left posterolateral lumbar intervertebral disc herniation (LIDH).

**DEFECT SIZE AND LUMBAR REHERNIATION: IDENTIFYING THE HIGH-RISK PATIENT****Nikolaus Koegl<sup>1</sup>, Mark Arts<sup>2</sup>, Frederic Martens<sup>3</sup>, Javier Fandino<sup>4</sup>, P. Douglas Klassen<sup>5</sup>***1. Neurosurgery, Innsbruck Medical University, Innsbruck, Austria**2. Neurosurgery, Leiden University Medical Center, Leiden, The Netherlands**3. Neurosurgery, OLV Zeikenhuis, Aalst, Belgium**4. Neurosurgery, Kantonsspital Aarau, Aarau, Switzerland**5. Neurosurgery, St. Bonifatius Hospital GmbH, Lingen, Germany***Introduction**

Reported rates of lumbar reherniation after primary discectomy vary widely with ranges from 1%-27%. Carragee and Kim, et al found that in patients with wide anular defect, reherniation rates were as high as 27% compared to a 1% rate of reherniation in patients with slit or fissure type defects.

Aggressive discectomy in patients with large defects may reduce recurrence risk, however this technique can result in disc collapse, back pain, and accelerated disc degeneration. Limited discectomy in this patient population increases the risk of reherniation but may reduce the chance of developing subsequent degeneration and pain.

Measuring anular defect size during discectomy is straightforward, but is not typically performed and is rarely reported in the literature making confirmation of the relative risk level difficult. The current study seeks to confirm the higher risk of reherniation in patients with larger anular defects by comparing the results of the discectomy-only cohort from an ongoing, randomized, post-marketing study of an anular closure device.

**Methods**

Data from the control cohort of an ongoing randomized study was reviewed for symptomatic reherniations. Similar to the definition used by Carragee et al to define their 'massive defect' group, a key inclusion criterion for the study was an anular defect  $\geq 6$ mm wide (measured intra-operatively with graduated paddles). Limited discectomy technique was defined by Spengler. Symptomatic reherniations were reported by the site and through correlations of independent MRI imaging reads and patient symptoms. Kaplan-Meier survivorship was estimated based on time to symptomatic reherniation, and compared to the data presented by Carragee et al.

**Results**

278 patients were enrolled in the discectomy-only cohort. Interim analyses were performed in February of 2016. Mean time from surgery was 40 months, with a maximum of 62 months. Mean volume of nucleus removed was 1.3cc. Mean defect width was 8.0mm. Symptomatic reherniations were observed in 56 patients (20.1%). Kaplan-Meier estimates of survivorship were 84% at 18 months and 78% at three years, compared to 84% and 76% respectively in Carragee et al.

**Discussion**

Patients at high risk of reherniation can be identified early by measuring anular defect size intra-operatively after discectomy. These interim results from an ongoing study of discectomy patients confirm a high early recurrence risk in patients with large anular defects as predicted by Carragee and Kim.

## THE EFFECT OF REPEATED BENDING AND AXIAL ROTATION MOTIONS ON INTERNAL DISC STRAINS AND RISK OF HERNIATION IN DEGENERATED HUMAN CADAVER LUMBAR DISCS

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### INTRODUCTION

Gross disc injury can be caused by sudden overload or by damage accumulation via repetitive loading, which are a cause of acute low back pain and an accelerant of disc degeneration. The aim of this study was to determine for the *first time* the relationship between combined repetitive compression, flexion and axial rotation of degenerated lumbar spine segments, and measure the 3D intradiscal strains that may lead to disc herniation and macroscopic tissue damage.

### METHODS

Seven degenerated human lumbar segments underwent pre-test MRI, had a grid of tantalum wires inserted into the disc and were subjected to 20,000 cycles of repetitive loading in combined compression, flexion and right axial rotation in a six degree of freedom hexapod robot. Stereoradiographs were taken at regular cyclic intervals from which the maximum shear strains (MSS) were calculated and partitioned into nine disc regions. After testing the discs underwent post-test MRI and macroscopic assessment to identify tissue damage. A two-way repeated measures ANOVA was used to examine the effects of cycle number and disc region on MSS.

### RESULTS

No visible evidence of disc herniation occurred after 20,000 cycles, however circumferential annular tears and nucleus separation from the endplate were observed in all specimens in agreement with observed signal changes in post-test MRI images. There was a marginally significant effect of cycle number ( $p=0.08$ ) and non-adjusted pairwise comparisons indicated significantly higher MSS for the posterior and right posterior regions compared to the nucleus ( $p<0.05$ ).

### DISCUSSION

A significant increase in MSS was observed across the posterior regions compared to the nucleus after 20,000 repetitive loading cycles. No herniation was observed, although macroscopic and MRI evidence of circumferential annular tears and nuclear separation from the endplate occurred, suggesting internal disc tissue disorganisation that may indicate a progression towards herniation.

## Q-SPACE IMAGING IS A NOVEL TECHNIQUE TO EVALUATE INTERVERTEBRAL DISC DEGENERATION

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**INTRODUCTION** The grading of intervertebral disc (IVD) degeneration has historically been evaluated with the Pfirrmann classification on T2-weighted magnetic resonance imaging (MRI)<sup>1</sup>. However, it is still difficult to classify subtle changes of degeneration using this method, which is qualitative and based on morphological changes over the progression of degeneration. For this reason, a quantitative and more sensitive classification system has been sought. Q-space imaging (QSI) is a quantitative diffusion-weighted MRI procedure that makes it possible to detect delicate changes in the microstructure of environments in which free water movement is restricted<sup>2</sup>. We have previously verified the efficacy of antioxidant N-acetylcysteine (NAC) on rat IVD degeneration using a semi-quantitative molecular technique<sup>3</sup>. The purpose of this study was to explore the possibility of using QSI to detect delicate changes in rat IVD degeneration using this model.

**METHODS** A rat degenerative model was generated in which the IVD was punctured using a 23-gauge needle on the third through tenth coccygeal vertebral levels. NAC (1000mg/mL) was given orally to degenerative model rats 1 week before puncture. We designated rats without IVD puncture as the control group, punctured rats without oral administration of NAC as the puncture group, and rats punctured with NAC as the NAC group (n=5 in each group). All rats were transcardially perfused with 4% paraformaldehyde. MRI was performed using a 7-Tesla Biospec 70/16 MRI (Bruker BioSpin, Ettlingen, Germany). IVD areas were measured by in-house analyzing software (Fig. 1). IVD degeneration grading was evaluated by T2 mapping values [ms] and QSI parameters including probability at zero displacement (arbitrary unit [a.u.]), kurtosis (a.u.), and full width at half maximum (FWHM) [ $\mu$ m].

**RESULTS** There were significant differences in T2 mapping values and all QSI parameters between the control and puncture groups ( $p < 0.001$ ). However, T2 mapping values were not significantly different between the puncture and NAC groups. On the other hand, all QSI parameters in the NAC group were significantly decreased compared to the puncture group ( $p < 0.001$ ). Interestingly, probability at zero displacement measurements for the control and NAC groups showed little variance compared to the other parameters (Fig. 2).

**DISCUSSION** An established method for evaluation of the grading of IVD degeneration is necessary, along with the progression of both basic and clinical research for IVD degeneration. In this study using QSI, we succeeded in evaluating IVD degeneration grading, which was otherwise not distinguished by T2 values. Kurtosis and FWHM have been widely used independently as QSI parameters for the evaluation of demyelination<sup>4</sup> and historical characters of malignant tumors<sup>5</sup>. Meanwhile, probability at zero displacement has been used in combination with other parameters. However, in this study, probability at zero displacement was a useful parameter that worked well alone. Our findings lend strong support to the hypothesis that probability at zero displacement obtained from QSI is a novel method for evaluating IVD degeneration.

**CONCLUSION** Probability at zero displacement obtained from QSI is a novel biomarker of IVD degeneration.

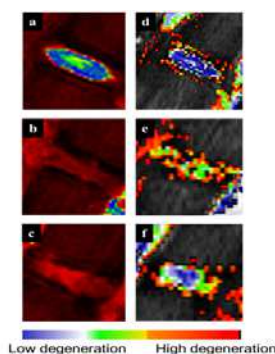


Figure 1 T2 mapping (a, b, and c) and probability at zero displacement maps (d, e, and f); control group (a and d); puncture group (b and e); N-acetylcysteine (NAC) group (c and f). The degeneration prevention effect of NAC is observed when comparing (e) to (f) but is not observed when comparing (b) to (c).

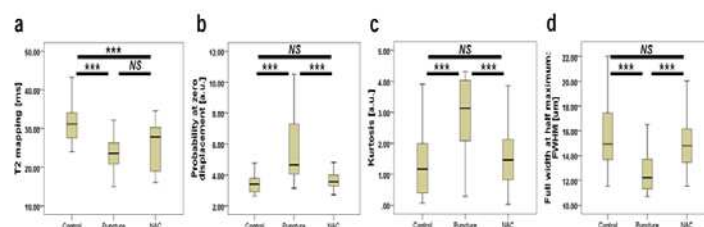


Figure 2 Box-and-whisker plot: the bottom and top of the box are the first and third quartiles; the band inside the box is the second quartile (the median). The ends of the whiskers represent the minimum and maximum of all of the data.

The Wilcoxon signed-rank test was used to evaluate the relationships among the control, puncture, and NAC groups for each imaging parameter: T2 mapping (a), probability at zero displacement (b), kurtosis (c), and full width at half maximum: FWHM (d), respectively. NS, not significant; \*\*\* $p < 0.001$ .

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## RISK FACTORS RELATED TO THE SEVERITY OF PAIN INTENSITY IN NON-SPECIFIC LOW-BACK PAIN PATIENTS OF SOUTHERN CHINA

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**Background:** Low back pain (LBP) is the leading cause of activity limitation and work absence throughout the world. Non-specific low back pain (NSLBP) accounts for over 85% of all LBP. However, the risk factors of NSLBP are still controversial. Full understanding the risk factors of NSLBP can help to provide early and prompt interventions during the acute phase to get better long-term results.

**Objectives:** This study determined to evaluate risk factors related to the severity of pain intensity in NSLBP patients of southern China.

**Study Design:** A cross-sectional study.

**Setting:** Self-assessment questionnaire survey was done from Jan 2014 to Jan 2016, which collected information about NSLBP, personal factors and physical factors. Participants were enrolled from health care centers around Guangzhou city.

**Methods:** Anonymous assessments included in a questionnaire to characterize the presence of NSLBP, weight, height, smoking habits, drinking habits, marital status, history of NSLBP in last year, the duration of last NSLBP, pain consultation at a hospital, NSLBP treatment in last year, occupation, history of heavy physical labor, long time driving or riding, history of exercise, sedentary lifestyle, long time standing. Standardized definition of non-specific LBP was used, MRI and medical history was taken to exclude patients with organic diseases (e.g. spinal tumor, fracture, inflammatory diseases, etc.). Associations between the severity of NSLBP and these potential risk factors were evaluated.

**Results:** Patients with only primary school education, higher BMI, long time driving, long time sitting, smoking habit, recurrent LBP have increased level of NSLBP VAS and ODI scores, with lower SF-36 scores ( $p < 0.01$ ). Workers and drivers compared with waiters group ( $p < 0.01$ ), and patients who lifted more than 10 Kg objects in 1/4 of their work time for more than 10 years have more NSLBP VAS and ODI scores, with lower SF-36 scores ( $p < 0.01$ ). In the multiple logistic regression model, Lower education, duration of current LBP for 1-7 days, long duration of LBP in last year, smoking (OR: 1.634, 95 % CI: 1.136, 2.350), long time driving (OR: 1.642, 95 % CI: 1.170, 2.304), higher BMI were associated with more severe NSLBP VAS score.

**Limitations:** The accuracy and completeness of the data within the database were dependent on the self-reported questionnaire, which may affect the internal validity of our study. One variable that may be related to LBP is socio-economic status.

**Conclusion:** The severity of NSLBP is associated with lower education, poor daily living, heavy physical labor, long time driving and sedentary lifestyle. Patients with recurrent NSLBP have more severe pain. So we should avoid obesity, heavy physical labor, long time driving or riding, sedentary lifestyle and smoking to prevent NSLBP.

**PRODUCTIVITY IMPAIRMENT AMONG WORKERS IN JAPAN WITH CHRONIC LOW BACK PAIN****Hiroki Sato<sup>1</sup>, Ko Matsudaira<sup>2</sup>, Toshinaga Tsuji<sup>1</sup>, Jeffrey Vietri<sup>3</sup>***1. Medical Affairs, Shionogi & Co., Ltd., Osaka, Japan**2. Medical Research and Management for Musculoskeletal Pain, 22nd Century Medical and Research Center, University of Tokyo, Tokyo, Japan**3. Kantar Health, Horsham, PENNSYLVANIA, United States*

**Introduction:** Chronic low back pain (CLBP) is associated with significant disability and impairments in health related quality of life (HRQoL), as well as reductions in overall functioning and productivity, including work productivity. Absenteeism (missing work due to illness) is low in Japan, but presenteeism (reductions in productivity while at work) may represent a more reliable source of information concerning the impact of CLBP on work impairment. The current study was conducted to measure the level of presenteeism among Japanese workers with CLBP and describe how presenteeism is related to other patient-reported health outcomes.

**Methods:** Data were obtained from the 2014 Japan National Health and Wellness Survey (NHWS), a large web-based survey of individuals age 18 and older which measures absenteeism and presenteeism using the Work Productivity and Activity Impairment (WPAI) questionnaire. Other outcomes included severity of pain measured through a numeric rating scale (NRS), HRQoL according to the Revised Short Form 36 (SF-36v2), and depression symptoms measured by the Patient Health Questionnaire-9 (PHQ-9) scale. Employed respondents with physician-diagnosed CLBP who reported any presenteeism were compared to those without any presenteeism using t-tests for continuous variables and chi-square tests for categorical variables. Correlations were calculated between presenteeism and other outcomes using Spearman's Rho was because of the non-normal distribution of presenteeism.

**Results:** Of the participants surveyed, 425 were identified as diagnosed with CLBP. Of these, 239 were employed respondents with CLBP with an average age of 51 years, 65% were male, experiencing back pain an average of 9 years. Presenteeism was reported by 77% of these respondents, who reported a mean of 41% loss of productivity due to health. Presenteeism was associated with more-severe pain in the prior week (4.5 vs. 3.6 on 0-10 NRS scale), greater depression according to the PHQ-9 score (6.1 vs 3.6), more numerous sites of pain (1.8 vs. 1.1), and lower health utility score (0.66 vs. 0.75, all  $p < 0.05$ ). Patients with presenteeism also had lower functional health status on seven of the eight SF-36v2 health profile scores using the Japanese norm-based scoring (all  $p < 0.001$ ). These relationships were also observed in correlation analyses between presenteeism and other outcomes; more-severe low back pain ( $r = 0.27$ ,  $p < 0.001$ ), more severe current pain on NRS ( $r = 0.25$ ,  $p < 0.001$ ), PHQ-9 ( $r = 0.34$ ,  $p < 0.001$ ), and all subscales of the SF-36v2 (all  $p < 0.01$ ).

**Discussion:** Most employed CLBP patients reported health-related work impairment, most notably in the form of presenteeism. The level of impairment by presenteeism was often high. The presenteeism of employed CLBP patients is likely due to high pain intensity, and the impairment extends beyond work-related factors to affect many domains of quality of life.



## INTERVERTEBRAL DISC HETEROGENEITY WITH MRI HISTOGRAMS - POTENTIAL MARKERS IN PATIENTS WITH LOW BACK PAIN?

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### Introduction

Intervertebral discs (IVD) exhibit strong intra- and inter-patient heterogeneity. The IVD heterogeneity can be displayed visually in T2-maps or T2-weighted (T2W) images as regional variation in the pixel grey scale. Histograms may have the feasibility to display regional variations in IVD heterogeneity, related to degeneration and thereby lumbar pain, that are not directly visible in the T2-maps or in T2W images. This work examines the feasibility of using histograms to decode IVD heterogeneity with the purpose to find new markers of pain in patients with low back pain (LBP).

### Methods

Ten LBP patients (6 males, 25-69y, 59 discs) were examined with T2-mapping, and with T1W and T2W MRI (sagittal, slice=3.5mm, pixel<1mm) on a 1.5T scanner. Each IVD was semi-automatically segmented on three mid-sagittal morphological T1W-images. The segmented "regions of interest" (ROIs) were transferred and rescaled to match the corresponding T2W-image and T2-map to produce grey scale distributions, *i.e.* histograms, of the pixel values within the ROIs. Heterogeneity features of the IVDs, such as the histogram shape and the separation between the high and low histogram peaks, were then extracted from the histograms. The histogram peak separation was correlated with Pfirrmann grade to find continuous markers of IVD degeneration. Mann-Whitney U-test was performed to examine whether the correlation was statistically significant ( $p < 0.05$  was considered significant).

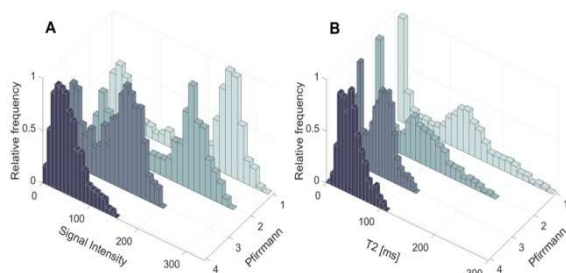
### Results

Both the T2-maps and T2W-images displayed similar histogram features (Figure 1). Histograms of well hydrated IVD's displayed two well separated peaks, one with low grey scale values from annulus fibrosis (AF) and one with high grey scale values from nucleus pulposus (NP). In histograms of degenerated IVD's, the distinction between AF and NP was reduced. This was displayed by increased number of pixels with intermediate grey scale values and decreased peak separation. The histogram peak separation was shown to correlate strongly with Pfirrmann grade 2 to 4 ( $p < 0.05$  for all groups). In addition, some degenerated IVD's within the same Pfirrmann grade displayed diametrically different histogram appearances (Figure 2).

### Discussion

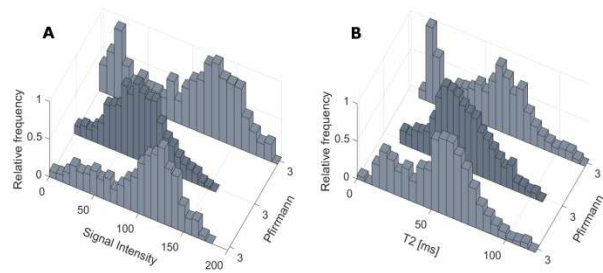
Decoding of the IVD heterogeneity with histogram analysis is feasible, not only with T2-mapping but also with conventional T2W-imaging. Since histogram features automatically display quantitative and continuous data that correlate well with IVD degeneration, it is a useful tool for detailed characterization of degenerative IVD changes. In contrast to Pfirrmann grading that includes IVD's with diametrically different heterogeneities in each grade, histogram analysis objectively can depict differences in IVD features, not only between different Pfirrmann grades but also within each grade. Thus, histogram analysis appears to be a sensitive tool for tissue characterization why it needs to be investigated in larger patient groups and correlated with pain patterns to reveal if it could be clinically useful.

Figure 1.



Typical IVD histograms for T2W-images (A) and T2-maps (B) for each Pfirrmann grade

Figure 2



T2W-images (A) and T2-maps (B) of IVD's with Pfirrmann grade 3 displaying that histogram analysis objectively can depict differences in IVD features, not only between different Pfirrmann grades but also within each grade.

## A PILOT STUDY COMPARING AN ONLINE BACK PAIN TRIAGE ALGORITHM WITH CLINICAL ASSESSMENT

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**Introduction:** Significant costs to national budgets are incurred by direct patient referral to hospital spinal clinics. Many patients could possibly be better served by triage to other health care professionals for rapid treatment to alleviate their symptoms. We aimed to determine whether an online assessment could substitute for clinical referral from primary care.

**Methods:** 75 patients (41 male ; 34 female ; mean age 53, range 16-96 yrs) referred to an orthopaedic spinal clinic were randomly allocated to complete an online assessment of their lower back symptoms before or after clinical consultation. The computer programme (Physiowizard®) assessed the patients' symptoms incorporating a 'red-flag' questionnaire - the STarT Back Screening Tool (SBST) and the Oswestry Disability Index (ODI). History and examination performed by the surgeon determined subsequent investigation, treatment, differential diagnosis and appropriateness of referral.

**Results:** The Physiowizard assessment took an average of 14 minutes to complete compared with a 30 minute surgical consultation. Red flags selected by patients on the computer correlated 100% (43/43) to suitable consultation with an orthopaedic surgeon. Following surgical assessment, 10 (23%) of these had symptoms requiring surgical treatment or steroid injection; 5 (12%) were referred for urgent MRI. 17 patients (39%) who selected a 'red flag' symptom on computer were deemed more appropriately treated by a physiotherapist than by the surgical team. The other 11 (26%) were considered appropriate for continued primary care consultation, pain management or no ongoing therapy.

Of those with no red-flag indicators on computer 21 patients (28%) were identified by both the surgical team and the Physiowizard as not requiring surgical referral and should have been seen by a Physiotherapist or Alternative Therapist.

11 (15%) were picked up as inappropriate referrals to an out-patient consultation as they were 'low risk' as measured by the SBST (ODI 22 +/- 14, mean +/- SD). The mean ODI for high risk patients was 54 +/- 16, and was 44 +/- 20 for those deemed appropriate for surgical consultation by the surgical team.

34 of the patients' primary source of pain was labelled radicular by the surgical team. Of these, Physiowizard correctly identified this element as a part of the differential diagnosis in 24 (71%) but only as the primary diagnosis in 17 (50%). The diagnosis of coccydynia was correctly matched in all 3 patients with this condition.

**Discussion:** The Physiowizard algorithm successfully triaged patients to appropriate care in most circumstances and was found to be 100% reliable at identifying red flag symptoms that all would agree are primary indicators for consultation with a surgeon. Refinement of the programme is required to build in a time line for referral. We believe that the system with modification will be appropriate for use as an on-line self-referral tool, or by central health care 'assessors' (such as the telephone NHS-24 in the UK) saving the patients and health services time and money.

## LUMBOSACRAL ORTHOSES FOR PREVENTING THE ONSET OF LOW BACK PAIN AMONG HEALTHY HOSPITAL NURSES: A RANDOMIZED CONTROLLED TRIAL

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**IMPORTANCE** The effectiveness of Lumbosacral Orthoses (LSO) for the prevention of low-back pain (LBP) is debatable due to the lack of quality randomized controlled trials (RCT).

**OBJECTIVE** To evaluate the effectiveness of prolonged LSO use for primary prevention of LBP among healthy hospital nurses.

**DESIGN, SETTING, AND PARTICIPANTS** Randomized clinical trial at Xiangya hospital in Hunan Province, PR China of 300 healthy nurses aged 20 to 25 years enrolled from November 2011 to June 2013 and randomly assigned to inelastic LSO (iLSO) (n=100), elastic LSO (eLSO) (n=100), or control groups (n=100).

**INTERVENTIONS** Participant in both iLSO and eLSO groups were recommended to wear LSO during working hours for 6-months. Control group involved no interventions during trial period. Subjects were evaluated at the end of the intervention with follow up at 6 and 12-months after intervention.

**MAIN OUTCOMES AND MEASURES** Primary outcome was the incidence of LBP and sick leave because of LBP. Secondary outcomes included changes in trunk (abdominal and back) muscle strength and spinal range-of-motion (ROM). Outcomes were assessed at 6-month and 12months after intervention.

**RESULTS** There were 300 randomized participants, 278 (92.7%) completed the 6-month intervention and 12-months follow-up assessment. From our analysis we found no statistically significant differences in LBP incidence among the three groups at 6-month (Overall p=0.74; relative risk [RR] for iLSO vs eLSO, 1.08 [95% CI, 0.66-1.78]; RR for iLSO vs Control, 1.03 [95% CI, 0.65-1.63]; RR for eLSO vs Control, 0.96 [95% CI, 0.61-1.50]) and 12-month follow up (Overall p=0.87; relative risk [RR] for iLSO vs eLSO, 1.08 [95% CI, 0.72-1.61]; RR for iLSO vs Control, 1.03 [95% CI, 0.66-1.61]; RR for eLSO vs Control, 1.11[95% CI, 0.74-1.66]). A significant increase in abdominal muscle strength was found in iLSO groups at 6-month (p=0.0098) and 12-month (p=0.0145) compared to baseline, whereas significant increase in abdominal muscle strength was only observed at the 12-month in eLSO group (p=0.0246). The observed improvement in back muscle strength persisted in the brace groups with no change at any point. In subgroups analysis of subjects for spinal ROM, flexion and extension motions had improved at 12-month in iLSO groups compared to baseline (flexion, p=0.007; extension, p=0.004), but not at 6-month, whereas only improvement in extension motion was observed at 12-month in eLSO group, (p=0.0014).

**CONCLUSIONS AND RELEVANCE** Among healthy hospital nurses, prolonged lumbar bracing with either iLSO or eLSO had no effect on the onset of LBP and also caused no trunk muscle atrophy. These findings suggest that LSO cannot be recommended in the primary prevention of LBP among healthy hospital nurses.

**TRIAL REGISTRATION** ClinicalTrials.gov identifier: NCT01483222.

## IDENTIFICATION OF A NMR BIOMARKER FOR *PROPIONIBACTERIUM ACNES* INFECTED INTERVERTEBRAL DISCS

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**Introduction.** Discogenic low back pain (LBP) often coincides with vertebral bone marrow lesions (Modic changes). Patients with Modic changes (MC) report a greater frequency and duration of LBP episodes, seek care more often, and have a higher risk for a poor outcome [1]. The reason for MC is unknown but bacterial infection of the intervertebral disc has been suggested as a potential reason in some MC phenotypes. In our previous experiments, we have shown that administration of *Propionibacterium acnes* (*P.acnes*) bacteria into intervertebral discs of rats cause pathological changes similar to those detected in patients with MC [2]. *P.acnes* produce propionic acid, which has a known NMR profile. The goal of this study was to test the feasibility of in vivo magnetic resonance spectroscopy (MRS) to detect *P.acnes* infected of intervertebral discs.

**Methods.** A colony of *P.acnes* was aseptically isolated from a human intervertebral disc with MC type 1. Two experiments were conducted: (i) *P.acnes* were anaerobically cultured and bacterial metabolites were extracted with 6% perchloric acid from dilution series of *P.acnes* [3]. High-resolution NMR at 14T were recorded. (ii) Intervertebral discs were isolated from fresh bovine tails and injected either with 50  $\mu$ l *P.acnes* ( $\sim 10^8$  bacteria) (n=3) or with 50  $\mu$ l of 650 mM propionic acid at pH7 (n=3). NMR spectra before and after injection were acquired with a 2 cm surface coil at 7T. Extracts from the discs tissues were prepared and analyzed by high-resolution NMR at 14T.

**Results.** (i) Extracts from *P.acnes* show NMR peaks at  $\sim 1.0$  and  $\sim 2.1$  ppm. Propionic acid also has peaks at  $\sim 1.0$  and  $\sim 2.1$  ppm. (Fig.A). The intensity of the peak at  $\sim 1.0$  ppm correlated linearly with the *P.acnes* concentration (Fig.B). (ii) After injection of *P.acnes* (Fig.C, red) and propionic acid (Fig.C, black) into bovine tail discs, MRS revealed an additional peak at  $\sim 1.0$  ppm.

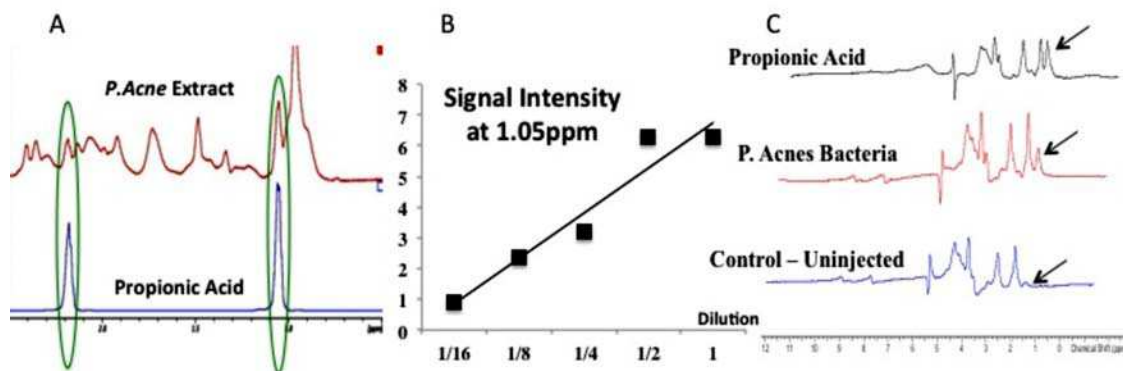


Fig. (A) NMR spectra of propionic acid and *P.acnes* extract. (B) Intensity of the signal at  $\sim 1.0$  ppm as a function of *P.acnes* concentration. (C) NMR spectra of uninjected bovine disk (blue), injected with *P.acnes* (red) and with propionic acid (black)

**Discussions.** In this study, we tested the feasibility of utilizing in vivo MRS to detect *P.acnes* infection of intervertebral discs. We found that extracts from *P.acnes* have NMR signals at  $\sim 1.0$  ppm and  $\sim 2.1$  ppm, which are characteristic for propionic acid. Since the  $\sim 1.0$  ppm peak correlated linearly with the *P.acnes* concentration, this peak is specific for *P.acnes* and could serve as potential biomarker. In-vivo MRS of *P.acnes* or propionic acid injected bovine tail revealed that the  $\sim 1.0$  ppm peak of propionic acid is detectable with in vivo MRS. The 2.1 ppm overlaps with proteoglycans and cannot be used as biomarker for *P.acnes* infection. In conclusion, this study suggests that *P.acnes* infection of intervertebral discs can be detected with in vivo MRS. NMR signal at 1.0 ppm can serve as biomarker for *P.acnes* infection.

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2. Dudli S, et al. J Orthop Res. 2016;34(8):1447-55
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**ANALYSIS OF FACTORS INFLUENCING LIGAMENTUM FLAVUM THICKNESS IN LUMBAR SPINE - A RADIOLOGICAL STUDY OF 1070 LEVELS IN 214 PATIENTS**

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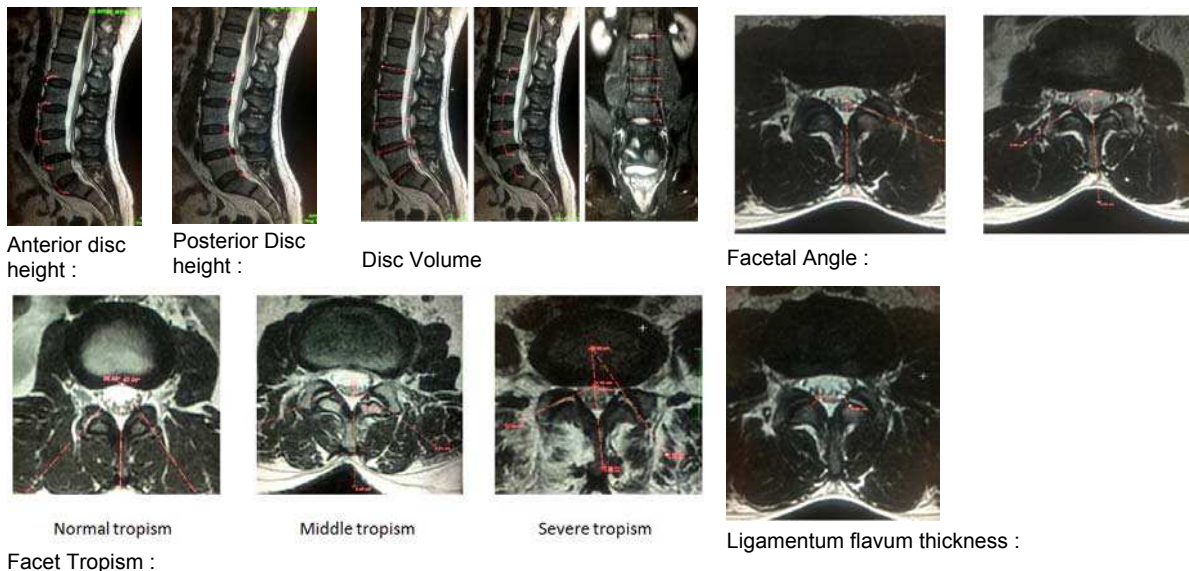
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**INTRODUCTION :** Ligamentum Flavum Hypertrophy (LFH) is known for its strong association with spinal canal stenosis by reducing the diameter of the spinal canal thereby compressing dural sac & nerve roots. Spinal canal stenosis due to LFH is common at the lumbar levels especially at L4-5. The pathomechanism & factors influencing hypertrophy of the Ligamentum flavum still requires a confident specificity. We aimed to analyse the association between various factors and Ligamentum Flavum Thickness (LFT) and also to investigate the major contributor for LFH at various levels in the lumbar spine.

**METHODS :** This is a retrospective study of the Magnetic Resonance Images of 1070 lumbar disc levels of 214 patients with chronic lower back ache. The following were evaluated at L1-L2,L2-L3,L3-L4,L4-L5 and L5-S1 levels: Pfirrmann's grade of the disc, anterior disc height and posterior disc height (measured by drawing longitudinal lines between the end plates of adjacent vertebrae in the anterior and posterior 1/3<sup>rd</sup> columns respectively in T2 midsagittal images), disc volume (disc was considered as a cuboid and the traditional formula was applied by measuring length, width and height in mid coronal and mid saggital planes), facet tropism (facetal angle was measured between two lines, one line drawn in the midsagittal axis and other drawn parallel to the facet joint and difference between both sides was calculated) and Ligamentum Flavum Thickness (thickest part of the ligamentum flavum was measured in mid axial T2 images). LFT more than 0.4cm was considered as hypertrophy. The data was subjected to statistical analysis with IBM-SPSS statistics software 23.0 version. Correlation between LFT and the rest of the parameters was done. Values with  $p < 0.05$  was considered statistically significant.

**RESULTS:** The mean age of the subjects is 52.57 years. There was an increase in the anterior disc height (0.98cm to 1.50cm), posterior disc height (0.84cm to 0.96cm), disc volume ( $7.17\text{cm}^3$  to  $14.6\text{cm}^3$ ), facetal angle ( $42.6^\circ$  to  $58.8^\circ$  on right side,  $41.7^\circ$  to  $56.4^\circ$  on left side) and LFT (0.32cm to 0.48cm on right side, 0.31cm to 0.44cm on right side) from L1-2 to L5-S1 levels. Highest frequency of LFT was seen at L4-5. Pfirrmann's grade of the disc & Anterior Disc Height had a statistically significant positive correlation with LFT at L1-L2,L2-L3,L3-L4,L4-L5 levels whereas facet tropism was strongly associated with LFT at L5-S1 level.

**CONCLUSION:** Higher Pfirrmann's grade and decreased anterior disc height can lead to ligamentum flavum hypertrophy at L1-L2, L2-L3,L3-L4,L4-L5 levels. Whereas at L5-S1 level, it is the presence of facet tropism which can cause LFH. Hence, patients with the presence of above mentioned factors at those respective levels have higher preponderance to develop Lumbar canal stenosis which can be identified at an early stage to prevent the progression of the same.



## HYPERLIPIDEMIA IS ASSOCIATED WITH IDIOPATHIC SPINAL EPIDURAL LIPOMATOSIS

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**Introduction :** Spinal epidural lipomatosis (SEL) is a relatively rare condition characterized by an abnormal accumulation of adipose tissue in the epidural space. Due to overt accumulation of epidural fat, SEL results in spinal cord or nerve root compression as observed in lumbar canal stenosis (LCS). Past studies have shown that SEL predominantly affects males, and obesity is potentially related to SEL. On the other hand, obesity is frequently accompanied by common lifestyle diseases, such as hypertension (HTN), diabetes mellitus (DM), hyperlipidemia (HL), and arteriosclerosis. Although any of these could possibly attribute to the development of SEL, it is not clear to what degree each of these factors is associated with SEL. The purpose of this study was to elucidate the factors potentially related to the development of SEL.

**Methods:** 122 male patients who underwent primary surgery for lumbar canal stenosis (LCS) between May 2013 and January 2015 were retrospectively reviewed. The epidural fat / spinal antero-posterior diameter (EF/SD) index was assessed based on the preoperative lumbar MRIs. Subjects were divided into three groups; No-lipomatosis, Medium, and Lipomatosis groups (henceforth referred to as N, M, and L groups, respectively) according to the EF/SD index. The numbers of subjects in each group were 13 (N), 85 (M), and 24 (L), respectively. We evaluated demographic data (age, BMI, and comorbidities of HTN, DM, and HL), preoperative blood examination (total-cholesterol (TC), high-density lipoprotein (HDL), triglycerides (TG), and HbA1c), arteriosclerotic indices including ankle-brachial index (ABI) and cardio ankle vascular index (CAVI) and the score of preoperative JOA back pain evaluation questionnaire (JOABPEQ) and Visual Analogue Scale. We examined the distribution of each factors related to SEL, by using Pearson's chi-square test or analysis of variance (ANOVA) after Bonferroni correction. To explore the independent association between metabolic factors and SEL, we included these factors simultaneously in the logistic regression model. HTN was defined as medical history of HTN. HL was defined as medical history of HL and/or TG  $\geq$  150 mg/dL and/or HDL  $<$  40 mg/dL. DM was defined as medical history of DM and/or HbA<sub>1c</sub>  $\geq$  6.5%.

**Results:** There was no significant difference in the demographic data except for BMI, where the mean BMI of L group was significantly higher. Laboratory examination showed that the serum TG was significantly elevated in L group. We also evaluated ABI and CAVI, however, neither showed any apparent trend. The preoperative questionnaires showed that the score for pain disorder in JOABPEQ was significantly lower in L group. As result the logistic regression analysis, we observed that HL only was significantly associated with SEL [OR: 3.63 (95%CI:1.30-10.12)].

**Discussion:** The current study demonstrated the clinical characteristics of SEL and HL could attribute to the development of SEL. The present study also showed that the male patients with SEL have more severe pain than non-SEL associated LCS patients in patient-based analysis. These observations support our hypotheses that the severe pain of SEL patients can be associated with the inflammatory cytokines which are overproduced in EF.

## 10 YEAR FOLLOW-UP OF LUMBAR SPINAL STENOSIS IN THE COMMUNITY. PART 1: TIME COURSE OF LUMBAR SPINAL STENOSIS SYMPTOM

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**Introduction:** Time course of lumbar spinal stenosis (LSS) symptom is still unclear. The purpose of this study was to assess the change of LSS symptom for 10 years using prospective cohort.

**Methods:** In 2004, 1599 people (male: 467, female: 1112, age ranging from 40 to 79y.o.) in the community were recruited and assessed LSS symptom by self-administrated and validated diagnostic support tool (LSS-DST) consisting of 10 yes/no questions. 1, 6 and 10 year follow-up were done by mail. People who received LSS surgery within this follow-up periods were judged as having LSS symptom.

### **Results:**

1) At one year follow-up, 101 of 224 with LSS symptom in the initial analysis (45.1%) still showed LSS symptom. Similarly, 89 at 6 year follow-up of 179 with LSS symptom in the initial analysis (49.7%) and 74 at 10 year follow-up of 192 with LSS symptom in the initial analysis (38.5%) showed LSS symptom.

2) At one year follow-up, 688 of 745 with no LSS symptom in the initial analysis (92.3%) still showed no LSS symptom. Similarly, 531 at 6 year follow-up of 631 with no LSS symptom in the initial analysis (84.2%) and 841 with no LSS symptom at 10 year follow-up of 962 in the initial analysis (87.4%) showed no LSS symptom.

3) Except for LSS surgery cases, 413 people had received all of 1, 4, and 10 year follow-up. Only 16 of 88 with LSS symptom in the initial analysis people (18.2%) showed LSS symptom in any follow-up period. Similarly, 286 of 325 with no LSS symptom in the initial analysis people (88%) showed no LSS symptom in any follow-up period.

4) 4 people within one year follow-up (0.4%), 31 people within 6 year follow-up (3.8%) and 46 people within 10 year follow-up (4.0%) received LSS surgery.

**Discussion:** Although many people in the community showed LSS symptom, LSS symptom was not always continuing. LSS symptom looks changeable. Only 4% received LSS surgery for 10 years. These results might strongly suggest that conservative treatment is the first choice for LSS symptom.

## 10 YEAR FOLLOW-UP OF LUMBAR SPINAL STENOSIS IN THE COMMUNITY. PART 2: RELATIONSHIP BETWEEN LUMBAR SPINAL STENOSIS SYMPTOM AND DURAL TUBE COMPRESSION ON MRI.

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**Introduction:** It is well known that anatomical dural tube compression does not always show lumbar spinal stenosis (LSS) symptom. However, there is still unclear how existence of anatomical dural tube compression cause LSS symptom. The purpose of this study was to clarify the relationship between LSS symptom, especially with/without surgery and dural tube compression on MRI using prospective cohort.

**Methods:** In 2004, 409 people ranging from 40 to 79y.o. in the community received conventional MRI of lumbar spine. 10 years later, 298 (male: 97, female: 201) were followed. Follow-up rate was 73%. 15 people received LSS surgery for 10 years. Dural sac cross-sectional area (DCSA)(mm<sup>2</sup>) of L1/2-L5/S1 disc level in T2-weighted image of 2004 was measured. The relationship between DCSA and with/without LSS surgery was assessed. For statistical analysis,  $\chi^2$  test and t-test were used. Less than 5% was judged as statistical significance.

**Results:** 1) 15 people received LSS surgery for 10 years (LSS surgery group).

2) The smallest DCSA of L1/2-L5/S1 was 75.5±32.1mm<sup>2</sup> in LSS surgery group and 72.3±41.6mm<sup>2</sup> in LSS non-surgery group. There was no statistical difference between two groups (p=0.5678).

3) The total DCSA of L1/2-L5/S1 was 626.4±179.3mm<sup>2</sup> in LSS surgery group and 614.2±223.8mm<sup>2</sup> in LSS non-surgery group. There was no statistical difference between two groups (p=0.8348).

4) 101 people showed the smallest DCSA less than 50 mm<sup>2</sup> which is judged as severe dural tube compression. Only 2 of those people received LSS surgery for 10 years.

**Discussion:** The clinical guidelines for degenerative lumbar spinal stenosis (LSS) by North American Spine Society (NASS) mention that LSS is a clinical syndrome which is associated with diminished space available for the neural and vascular elements in the lumbar spine. It is well known that dural tube compression is necessary for symptomatic LSS, however, dural tube compression does not always have symptoms. From this prospective cohort study, severe dural tube compression does not always induce LSS surgery for ten years. This fact suggests that other factors except for dural tube compression cause severe LSS symptom to receive operation.



## EFFECTIVENESS AND LIMITATIONS OF DECOMPRESSION WITHOUT FUSION FOR LUMBAR SPINAL STENOSIS WITH DEGENERATIVE SPONDYLOLISTHESIS: CAN A HIGHER SLIPPING RATE AFFECT SURGICAL OUTCOMES?

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**Introduction:** Decompression alone has been re-evaluated as an effective surgical option for lumbar spinal stenosis (LSS) with degenerative spondylolisthesis (DS). However, it is unknown whether decompression alone can provide a satisfactory surgical outcome, for any degree of slipping. The purpose of this study was to clarify whether decompression alone was effective, irrespective of the degree of slipping.

**Methods:** Patients that exhibited  $\geq 10\%$  slip in the neutral position on a standing radiograph were diagnosed with DS. We enrolled 56 patients with LSS that exhibited DS at L4/5 and had undergone microscopic decompression alone. We prospectively followed them up for three years. We performed a retrospective review, and excluded two patients that had required reoperation; the other 54 patients were evaluated in this study. The mean age was 68.2 years (range: 49-86); there were 18 men and 36 women. The mean % slip in the neutral position was 16.9% (range: 10-28). Patients were divided into two groups: group1: 39 patients that exhibited  $< 20\%$  slip, and group2: 15 patients that exhibited  $\geq 20\%$  slip. Surgical results were evaluated in each group and compared between the two groups annually. The clinical evaluations included the JOA score (15 points), a visual analogue scale (VAS) for low back pain (B-VAS: 0-10 points, where 10 indicated the most severe pain), and a VAS for leg symptoms (L-VAS: 0-20 points, where 20 indicated the most severe symptom). The radiographic evaluation, based on standing radiographs, included the % slip at each posture (flexion, neutral position, and extension), the %slip difference between flexion and extension ( $\Delta\%$ slip), and the range of motion (ROM) at L4/5.

**Results:** In each group, the JOA score increased significantly at 1 y post-surgery, but subsequently, it did not change. In group1, the B-VAS decreased significantly up to 2 y post-surgery, but did not change subsequently; however, the L-VAS decreased significantly each year. In group2, the B-VAS did not change in any year, but the L-VAS decreased significantly at 1 y and from 2-3 y post-surgery. In each group, the % slip at each posture increased significantly at 1 y post-surgery, but did not change subsequently; however, neither the  $\Delta\%$ slip nor the ROM changed in any year. The groups were not significantly different in the JOA score, B-VAS, or L-VAS, either preoperatively or during follow-up, except that the B-VAS was significantly lower in group1 than in group2 at 3 y post-surgery. The groups showed no difference in the  $\Delta\%$ slip or ROM for each year.

**Discussion:** Our results suggested that, although mobility at the level of DS level might not change, no further slip progression would be expected after about one year post-surgery. As a result, clinical symptoms can improve, even up to three years post-surgery. Back pain may not be relieved to the same extent as symptoms in the legs, particularly in patients with higher slipping rates. However, decompression alone is an effective surgical option for LSS with DS.

## RELATIONSHIPS BETWEEN PREOPERATIVE PSYCHOLOGICAL FACTORS AND PATIENT-REPORTED OUTCOMES IN PATIENTS WITH LUMBAR SPINAL STENOSIS

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**Introduction:** Preoperative depression in patients with lumbar spinal stenosis (LSS) is of concern because there are many reports that depression results in poor surgical outcomes. However, it is possible that not only depression, but also other patient psychological factors, such as pain catastrophizing, anxiety, fear and psychiatric disorders, could affect the preoperative symptoms and physical and lumbar spine function of patients with LSS. The objective of this prospective observational study was to investigate the relationships between these preoperative psychological factors and patient-reported outcomes for patients with LSS.

**Methods:** Patients with clinically and radiologically defined LSS were enrolled from September 2010 to March 2016. Patients with concomitant conditions that could compromise outcome assessment, such as trauma, osteoporosis, previous spine surgery, other spinal disorders, peripheral artery disorders, osteoarthritis of the knee and/or hip, cognitive impairment or a history of psychiatric illness, were excluded. In total, 346 patients (211 men, 135 women; mean age prior to surgery, 69 years) were recruited. All patients completed several questionnaires before surgery. For patient-reported outcomes (PROs), a self-administered visual analogue scale (VAS) was used to assess the intensity of low back pain, leg pain, and leg numbness; the Roland Morris Disability Questionnaire (RMDQ), five subdomains of the Japanese Orthopaedic Association Back Pain Questionnaire (JOABPEQ), and the Zurich Claudication Questionnaire (ZCQ) were also completed. Psychological factors were assessed using the Self-Rating Questionnaire for Depression (SRQ-D), the Hospital Anxiety and Depression Scale (HADS), the Pain Catastrophizing Scale, which includes rumination, magnification and helplessness, the Pain Anxiety Symptoms Scale-20, and the Brief Scale for Psychiatric Problems in Orthopaedic Patients (BS-POP). Spearman's rank correlation coefficient was used to evaluate correlations between PROs and psychological evaluation items. The Mann-Whitney *U* test was used to compare PROs in patients defined as psychologically abnormal based on the cut-off values for the psychological evaluation items with those in normal patients, while multiple regression analysis was used to evaluate relationships between PROs and preoperative psychological factors.

**Results:** No significant correlations were found between PROs and psychological evaluation items ( $|r| < 0.4$ ). However, in patients with abnormal scores in all psychological evaluation items, RMDQ scores, lumbar spine and social life dysfunction scores in the JOABPEQ subscales and the symptom severity scale of the ZCQ were significantly inferior to those in psychologically normal patients ( $P < 0.05$ ). Multiple regression analysis showed significant associations between RMDQ scores and pain-related disorders assessed by JOABPEQ subscales and patient scores for the SRQ-D and BS-POP, respectively, between lumbar spine function, gait and social life assessed by JOABPEQ subscales and HADS depression score, and between the physical function scale of the ZCQ and HADS anxiety score ( $P < 0.05$ ).

**Discussion:** This study demonstrated that not only physical function, but also lumbar spine function, was affected by preoperative depression, anxiety and psychiatric problems in patients with LSS. Preoperative evaluation of depression, anxiety and psychiatric disorders should be performed prior to surgery, and preoperative therapeutic intervention for psychological distress may result in improvement of physical and lumbar spine function in patients with LSS.

## HISTOLOGICAL ANALYSIS OF BONE REGENERATION WITH DIFFERENT DOSES OF rhBMP-2 IN AN OVINE LUMBAR INTERBODY FUSION MODEL

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The objective of this study was to investigate the effects of different doses rhBMP-2 on bone healing in an ovine lumbar interbody fusion model.

**Methods:** In this study 22 sheep underwent two level lumbar interbody fusion using a ventrolateral approach with secondary dorsal fixation at L1/2 and L3/4. After randomization in one level a PEEK-cage was implanted filled with one of three doses rhBMP-2 (0,5mg; 1mg; 2mg) delivered on an ACS. The other level received an empty PEEK-cage or ACS filled cage. Animals were sacrificed after 3 and 6 months and decalcified histology was performed. This included histomorphological analysis as well as histomorphometry of the tissues within the cage.

**Results:** At 3 months after surgery the groups treated with rhBMP-2 showed higher amounts of bone tissue within the cage. At 6 months the amounts of bone tissue increased in all groups, but were still lower in the groups without growth factor. At 3 months there was only one active osteolysis in the cage/ACS. 7 of 8 segments of the rhBMP-2 groups had a compromised bone structure around the implant. These areas were filled with fibrous tissue and fibrocartilage. This finding was not detected in the groups without rhBMP-2 at 3 months. At 6 months most of the segments with an empty cage or cage/ACS showed a chronic inflammation. Predominant cells were macrophages and giant cells. The groups treated with rhBMP-2 showed only a few mild chronic inflammatory reactions.

**Discussion:** The well-known dose dependent effect of rhBMP-2 on bone healing could also be recognized in our study. Attention has to be paid for the proinflammatory properties of the growth factor. Consistent with other studies we found 2 strong inflammatory reactions, each one in the lowest and highest dose group. Also the potential for causing transient bone resorptions, according to the results of others, was demonstrated. At 3 months 7 of 8 segments treated with rhBMP-2 showed compromised peri-implant bone. Osteoblasts, but not osteoclasts, were seen in the periphery of these areas. It can be concluded that there were bone resorptions which already merged into an increased osteoblastic activity. Usually resorptions occur between 2 and 12 weeks and are followed by a period of increased osteoblastic activity. This finding wasn't recognized at 6 months anymore.

Striking is that at 6 months most of the segments without rhBMP-2 showed a compromised bone structure around the implant with a mild to mainly moderate chronic inflammatory reaction. This cannot be attributed to the growth factor. Also the ACS is degraded at 6 months and is unlikely a possible explanation. Therefore, the cage as a reason must be considered and it has to be questioned whether PEEK is the optimal material for interbody cages.

## EARLY REDUCTION OF LIGAMENTUM FLAVUM AFTER POSTERIOR FUSION WITHOUT NEURAL DECOMPRESSION FOR UNSTABLE DEGENERATIVE LUMBAR SPONDYLOLISTHESIS

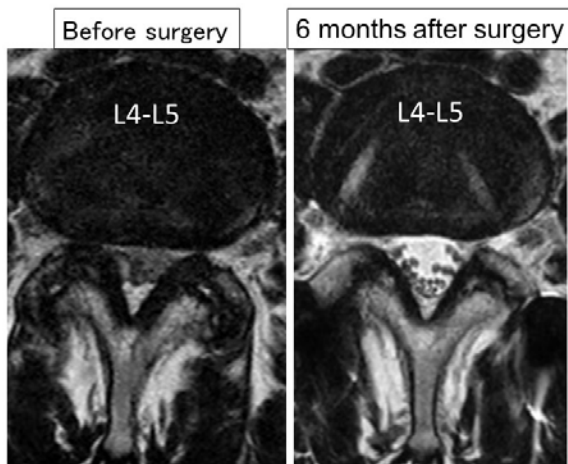
Hiromi Ataka<sup>1</sup>, Tomoihiro Miyashita<sup>2</sup>, Kei Kato<sup>2</sup>, Hiromitsu Takaoka<sup>1</sup>, Takaaki Tanno<sup>1</sup>

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**Introduction:** On the basis of clinical studies of instrumented facet fusion (i-FF)—that is, *in situ* posterior fusion in the alignment achieved by posture reduction—for degenerative lumbar spondylolisthesis (DLS), we devised a new, minimally invasive i-FF without neural decompression for radicular symptoms caused by unstable DLS. The fusion procedure without direct posterior decompression, lateral lumbar interbody fusion (LLIF), is widely performed, and its effect of indirect neural decompression by interbody distraction has been reported. However, little is known about the morphological changes of ligamentum flavum (LF) after fusion without decompression. The purpose of this study was to evaluate radiologically the changes of the LF after i-FF without decompression for unstable DLS.

**Methods:** Twenty consecutive patients with unstable DLS underwent i-FF via a bilateral intramultifidus muscular approach without posterior laminectomy. Cross-sectional area of the LF (LFA), thickness of the LF at lateral recesses (LFT), and cross-sectional area of the thecal sac (TSA) were measured on MR images preoperatively and at 3–6 months postoperatively. Disc height (DH) and disc angle (DA) were measured on plane lateral radiographs. The early clinical outcomes at 3–6 months after surgery were assessed using a visual analogue scale (VAS) for leg pain and the Japanese Orthopaedic Association Back Pain Evaluation Questionnaire (JOABPEQ).



**Results:** In all patients, radicular symptoms resolved immediately after surgery. JOABPEQ category scores demonstrated therapeutic effectiveness in 100% of the patients for walking ability, in 82% for low back pain, and in 82% for social life function. VAS scores were reduced to 15% of their preoperative values. No patient required a second procedure for additional posterior decompression. DH and DA did not show significant change postoperatively. At 3–6 months after surgery, significant decreases in the LFA (53% on the right side, 52% on the left), and LFT (57% on the right side, 65% on the left) were observed. TSA was markedly increased by 78%.

**Discussion:** Early reduction of the LFA and LFT, and a significant increase in TSA were observed 3–6 months after i-FF without neural decompression, despite a lack of change in DH and DA. This mechanism for enlargement of the spinal canal is quite different from the effect of indirect decompression through LLIF. Stabilization of the unstable segment may have reduced the mechanical stress on the nerve roots and surrounding tissues in the spinal canal, which

may have resulted in the reduction of LF and the canal enlargement, leading to good clinical outcomes. Thus, *in situ* posterior fusion without decompression may be sufficient and appropriate for managing unstable DLS, questioning the need for both direct and indirect decompression.

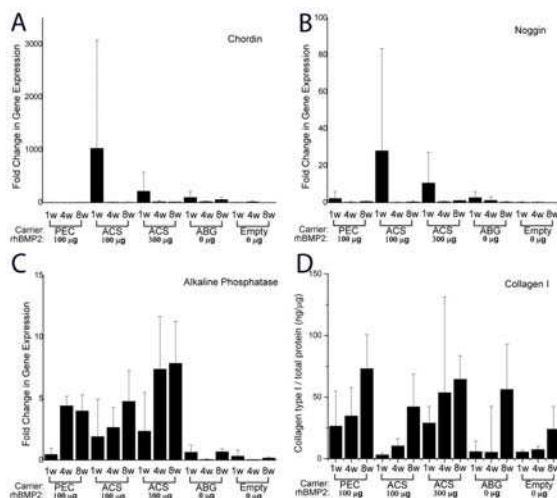
## BMP-2 CARRIER AND INTERBODY SPINAL FUSION OUTCOME: RABBIT SPINAL FUSION CHAMBER STUDY ON BMP ANTAGONIST

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**Introduction:** Recombinant human bone morphogenetic protein (rhBMP-2) has been widely used in clinical practice to enhance spinal fusion surgery. Supraphysiological doses of rhBMP-2 are required to achieve the consistent fusion rate which in turn has led to side effects such as heterotrophic bone formation and seroma formation. To address these problems, various carriers have been developed to optimize rhBMP-2 delivery. From our previous study, PEC can control the release of rhBMP-2 by optimizing the pharmacokinetics of the carrier, thereby lowering the dose of rhBMP-2 required to achieve fusion, and mitigating side effects. However, the molecular events underlying the two releasing systems, pertaining to the different healing outcomes remain unknown. In this study, a rabbit interbody spinal fusion chamber was designed to provide a sealed and stable environment in the repair tissues, to compare the expression level of osteogenic markers and molecular antagonists of BMP signaling, between controlled release carrier PEC and burst release carrier ACS.

**Methods:** Seventy-six rabbits were allocated to following groups: Group 1, PEC + 100µg rhBMP-2 (n=16); Group2, ACS + 100µg rhBMP-2 (n=16); Group 3 ACS + 300µg rhBMP-2 (n=12) Group 4 autologous bone graft (n=16) and Group 5 empty chamber (n=16). A retroperitoneal approach was used to expose the L5/6 intervertebral disc and the intervertebral disc defect was created using a trephine saw. Poly-ether-ketone-ketone spinal fusion chambers with the relevant carriers were implanted into the disc defect and secured with screws and sutures. The rabbits were sacrificed at the 1, 4 and 8 weeks. Fusion was assessed by manual palpation and µCT scan. Tissues within the chamber channel were harvested for the evaluation of the target genes and proteins. BMP antagonists and osteogenic markers were analyzed by real-time PCR and ELISA.



**Results:** Manual palpation showed that all the samples in Groups 1 and 3 and 50% of the samples from Group 2 achieved interbody spinal fusion while the rest of groups were not fused. Quantitative µCT parameters and resin histology confirmed the manual palpation results. PCR Array profiling indicated that at the 1-week time point, the BMP antagonist (Chordin and Noggin) was highly upregulated in Groups 2 and 3, and was down-regulated at Weeks 4 and 8. The osteogenic marker alkaline phosphatase was in the order of Group 3 > Group 1 > Group 2 > Group 4. Expression of the late osteogenic marker, COL1, correlated well with ALP expression pattern.

**Discussion and Conclusion:** Using the rabbit interbody spinal fusion chamber, analysis of the expression of osteogenic markers and BMP-2 antagonists showed that high BMP-2 antagonist expression was coupled with low expression of osteogenic markers in the burst release delivery of BMP2 which resulted in non-fusion. Conversely, the low antagonist expression coupled with strong expression of osteogenic markers in controlled release of

BMP-2 achieved fusion. These results are consistent with the high antagonist expressions in fracture non-union<sup>[1]</sup>. We speculate that the manner of BMP2 release at the interbody spinal defect site could re-balance the *in-situ* osteogenic and anti-osteogenic activities and affect the fusion outcomes.

1. Marc Fajardo et al. Levels of expression for BMP-7 and several BMP antagonists may play an integral role in a fracture nonunion. Clin Orthop Relat Res, 2009, 467, 3071-375.

## BALANCING BONE RESORPTION AND OVERZEALOUS BONE GROWTH IN LUMBAR INTERBODY FUSION WITH rhBMP-2 IN THE SHEEP MODEL- A QUESTION OF DOSE AND/OR CONCENTRATION?

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**Question:** Is there a dose- and/or concentration-dependent effect of rhBMP-2 on bone resorption and overzealous bone growth in anterior lumbar interbody fusion (ALIF)?

**Methods:** Thirty-six Merino sheep underwent right-anterior lumbar interbody fusion at L1-L2 and L3-L4 with the addition of a polyetheretherketone (PEEK) cage either filled with one of four different concentrations/doses of rhBMP-2 (interventional groups: 4.0 mg/ml, total dose of 4.0 mg; 2.0 mg/ml, total dose of 2.0 mg; 1.0 mg/ml, total dose of 1.0 mg; 0.5 mg/ml, total dose of 0.5 mg) or in the control group filled with an absorbable collagen sponge (ACS) or left empty. A pedicle-screw system was implanted in all surgical levels. Thin-cut CT image were taken directly postoperatively, after 3 months, 6 months and 12 months to assess bone resorption, cage subsidence and migration (indirect marker of bone resorption), and overzealous bone growth.

**Results:** In comparison with the control group, rhBMP-2 groups showed a higher fusion rate at 3 (72% vs. 13%), 6 (90% vs. 30%) and 12 (95% vs. 70%) months CT scans. Overzealous bone growth was detected at the right ventral circumference of the vertebral body as sign of the direct operative access. No ectope ossification was detected in all groups. The incidence of bone resorption as well as cage migration and cage subsidence as indirect marker of bone resorption were higher in the BMP-2 groups.

However, no clear dose-concentration-dependency of these adverse effects could be established. The side effects were less in the BMP-2 group treated with 0.5mg rhBMP-2.

**Conclusion** In this animal model the application of rhBMP-2 in different concentrations/doses showed much better fusion rates compared with the control group. These results could be shown in the 0.5mg BMP-2 group with clear reduction of adverse effects. Higher doses of BMP-2 doesn't cause a benefit in fusion rate but an increase in side effects like cage migration and subsidence as maker of higher bone resorption. No inflammation reaction or systemic side effects were detected in the BMP-2 group.

**CREATING LORDOSIS IN TRANSFORAMINAL AND POSTERIOR LUMBAR INTERBODY FUSION (TLIF/PLIF) – THE IMPACT OF SURGICAL TECHNIQUE – A CONTROLLED CADAVERIC STUDY**

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**Introduction:** Transforaminal and Posterior Lumbar Interbody Fusion (TLIF/PLIF) are widely used for lumbar spinal fusion, anterior column support and potentially lordosis control. Recreating lordosis is increasingly recognized as a critical factor in these procedures. The advantage of TLIF vs PLIF and the effect of various surgical stages between a unilateral and bilateral procedure are unknown. This study performed a controlled stepwise surgical simulation of cadaveric TLIF/PLIF to assess the impact of progressive surgical intervention.

**Method:** Eight cadaveric motion segments (four at L3/4 and four at L5/S1) underwent stepwise-simulated surgery. The steps progressed from a unilateral TLIF (18° lordosis, 27mm length) at three stages of resection (unilateral facetectomy, bilateral facetectomy, then a wide posterior decompression/posterior column osteotomy) to a bilateral PLIF (22mm length) with 18° then 24° lordotic cages. Dorsal compression across pedicle screws (bicortical and cement reinforced to resist loosening on multiple retesting) and rods provided stability before segmental lordosis was captured with lateral radiography. Repeated-measures ANOVA was used to compare across specimens and procedures.

**Results:** Pre-operative lordosis (pooled) was 8.6±6.1° (mean±SD), and maximum post-surgical lordosis was 20.4±6.3° with the 24° cage. No statistical increase in lordosis was achieved with unilateral TLIF and minimal bone resection (10.1±6.3°, 18% increase, p=0.9). Stepwise increase in lordosis occurred with progressive bone resection from unilateral TLIF with bilateral facetectomy (50%) and posterior wide decompression/posterior column osteotomy (12%) to bilateral PLIF (18%) with the 18° cage (15.2±8.2°, 17.0±4.7°, to 20.1±6.3°, respectively). The techniques with wide posterior decompression had significantly greater lordosis than the pre-operative and unilateral TLIF conditions (p<0.01).

**Discussion:** This cadaveric study demonstrated that operation type (TLIF v PLIF), posterior bone resection, and implant selection influence lordosis control in the lumbar spine. PLIF created more lordosis than TLIF, although TLIF lordosis can be increased with progressive bone resection of contralateral facet and midline structures. This cadaveric study strongly suggested, that along with lordotic cages, operation type and extent of bone resection contribute to lordosis control in interbody fusion using TLIF/PLIF techniques.

**Figure:**

Lordosis before and after respective surgical procedures:

Intact = Preop

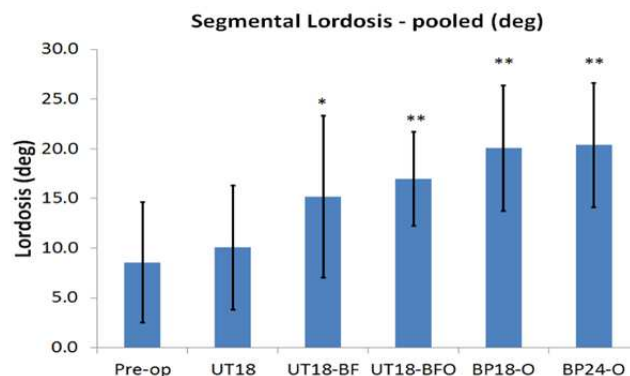
UT18 = Unilateral TLIF with 18deg x 27mm cage

UT18BF = TLIF with Bilateral Facetectomy with 18deg x 27mm cage

UT18BFO = TLIF with Bilateral Facetectomy and Posterior Column Osteotomy with 18deg x 27mm cage

BP18 = Bilateral PLIF with 18deg x 22mm cage

BP24 = Bilateral PLIF with 24deg x 22mm cage



## FACTORS AFFECTING THE BONY UNION OF THE DEFECTS IN THE PARS INTERARTICULARIS OF L5 UNILATERAL SPONDYLOLYSIS

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**Introduction:** Spondylolysis is a fatigue fracture of the pars interarticularis which occurs most commonly at L5. The purpose of this study was to investigate the factors affecting the bony union of the defects in the pars interarticularis of L5 unilateral spondylolysis.

**Methods:** Forty junior athletes with unilateral L5 spondylolysis based on CT and MRI were reviewed. They consisted of 32 men with a mean age of 14.8 years (12 to 18) and 8 women with a mean age of 13.0 years (10 to 16). The junior athletes with previous spine surgery and/or multilevel spondylolysis were ineligible. Using multislice CT, we measured the sagittal orientation of L4/5 and L5/S1 facet joint angles from the axial sections. All junior athletes were asked to discontinue their sporting activities and to wear a corset. We assessed that union of the defect had occurred or not by CT. All junior athletes were classified into two groups: the union group and the nonunion group. The gender differences, the L5 skeletal age, the side of the defect, the stage of the pars defect, and the number of junior athletes who underwent the hip joint stretch and exercise during the bracing were statistically compared between the union and nonunion groups by  $\chi^2$  test. The age, the interval between the onset and the bracing, the duration of the bracing, L4/5 and L5/S1 facet joint angles, and the differences between the left and right angles of L4/5 and L5/S1 facet joints were statistically compared between the union and nonunion groups by Mann-Whitney U test. A P value < 0.05 was considered statistically significant. The odds ratios for significant variables and the 95% confidence intervals were calculated by multivariate logistic regression analysis.

Fig. Summary of the results

		Union (n = 29)	Nonunion (n = 11)	P value
Gender	Male : Female	22 : 7	10 : 1	0.288
Age (years) <sup>*</sup>		14.4 ± 1.9	14.5 ± 2.7	0.722
L5 skeletal age	Cartilaginous : Aooohyseal : Eotohyseal	1 : 18 : 10	1 : 7 : 3	0.727
Side of defect	Right : Left	9 : 20	5 : 6	0.393
Stage of the pars defect				
	Very early : Late early : Progressive	5 : 19 : 5	0 : 7 : 4	0.202
Interval between the onset and the bracing (days) <sup>*</sup>		56.9 ± 37.5	74.5 ± 60.8	0.539
Duration of the bracing (days) <sup>*</sup>		101.3 ± 42.9	127.4 ± 78.1	0.606
Number of junior athletes who underwent the hip joint stretch and exercise during the bracing (cases)		13	5	0.972
Facet joint angles <sup>*</sup>				
	L4/5 spondylolysis side	48.1 ± 7.6 <sup>†</sup>	52.0 ± 10.1 <sup>†</sup>	0.051
	normal side	48.9 ± 8.0 <sup>†</sup>	51.6 ± 10.0 <sup>†</sup>	0.477
	L5/S1 spondylolysis side	51.3 ± 8.7 <sup>†</sup>	54.8 ± 13.9 <sup>†</sup>	0.952
	normal side	50.5 ± 8.0 <sup>†</sup>	53.2 ± 10.8 <sup>†</sup>	0.617
The differences between the left and right angles of the facet joints <sup>*</sup>				
	L4/S <sup>†</sup>	4.1 ± 3.2 <sup>*</sup>	7.4 ± 5.0 <sup>*</sup>	0.049
	L5/S1	6.2 ± 4.5 <sup>†</sup>	6.5 ± 5.9 <sup>†</sup>	0.844

<sup>\*</sup>Values are expressed as mean ± sd.

<sup>†</sup>Statistically different between the two groups.

**Results:** The differences between the left and right L4/5 facet joint angles were significantly larger in the nonunion group than in the union group (P=0.049). However, there were no statistical differences between the union and nonunion groups concerning the other data (Fig.). Multivariate logistic regression analysis showed that the differences between the left and right angles of L4/5 facet joint was the important factor affecting the bony union of the defects (odds ratio=1.26, P=0.025).

**Discussion:** From the results of this study, the differences between the left and right L4/5 facet joint angles were significantly larger in the nonunion group than in the union group. Therefore, asymmetry in L4/5 facet joint orientation was significantly greater in the nonunion group than in the union group. We reported that a more asymmetry in L4/5 facet joint orientation was likely to increase the point

loading through the L5 pars interarticularis in extension and rotation ('16, ISSLS). We think that a more asymmetry in L4/5 facet joint orientation is likely to increase the point loading through the L5 pars interarticularis. Therefore, if a subject has asymmetrically orientated L4/5 facet joint, this may be the risk of the bony nonunion of the defects in the pars interarticularis of L5 unilateral spondylolysis.



**MANUALLY DEFINING REGIONS OF INTEREST WHEN QUANTIFYING PARAVERTEBRAL MUSCLES FATTY INFILTRATION FROM AXIAL MAGNETIC RESONANCE IMAGING: A PROPOSED METHOD FOR THE LUMBAR SPINE WITH ANATOMICAL CROSS-REFERENCE**

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**Introduction:** There is increasing interest in paravertebral muscle composition as a potential prognostic and diagnostic element in lumbar spine health. As a consequence, it has become popular to use magnetic resonance imaging (MRI) to examine muscle volume and fatty infiltration in lumbar paravertebral muscles to assess both age-related change and their clinical relevance in low back pain. A variety of imaging methods exist for measuring key variables (including fat and muscle) and for defining regions of interest, making pooled comparisons between studies difficult and rendering post-production analysis of MRIs confusing. We propose a method for standardizing the quantification of lumbar spine muscle quality from axial MRIs.

**Methods:** We explain our method by providing an examination of regional lumbar morphology, followed by a detailed description of the proposed technique. Identification of paravertebral muscles and vertebral anatomy includes axial E12 sheet-plastinates from cadaveric material (Figure 1), combined with a series of axial MRIs that encompass sequencing commonly used for investigations of muscle quality (fat-water DIXON, T1-, and T2-weighted) to illustrate regional morphology; these images are shown for L1 (Figure 2) and L4 (Figure 3) to highlight differences according to level. The method for defining regions of interest (ROI) for spinotransverse muscles and the erector spinae is described in relation to existing literature.

**Results:** Our method for defining ROIs for lumbar paravertebral muscles on axial MRIs is outlined with reference to high quality cadaver-based and MRI imaging. Features of potential contention and/or with unclear representation in the literature are highlighted, such as whether and how to include the lumbar intertransversarii given the typical lack of distinction between these and the most commonly examined paravertebral muscles.

**Discussion:** This proposed method contributes to standardising the global effort towards defining ROIs using axial MRI data for lumbar paravertebral muscle quality and particularly fatty infiltration.



**Figure 1.**

Axial E12 plastinated sections (A, C) and schematic illustrations (B, D) at approximately L1 (A, B) and L4 (C, D) highlighting anatomical structures at these vertebral levels. B, D: Dotted lines and shading, Green - psoas major muscle; Blue - quadratus lumborum muscle; Purple - erector spinae muscles; Red - spinotransverse muscles. B: round white dotted regions (bilateral) denote 12th rib. D: square dotted box surrounds enlarged inset; round dotted circle indicates morphological feature of interest (ILB fatty 'tent'). Legend: A - aorta; ES - erector spinae muscles; ESA - erector spinae aponeurosis; ILB - iliocostalis - longissimus boundary and indentation; ISL - interspinous ligament; IT - intertransversarii muscle; IVC - inferior vena cava; K - kidney; L - liver; P - psoas major muscle; QL - quadratus lumborum muscle; SAF - superior articular facet; SP - spinous process; SPC - spinal canal; SPT - spinotransverse muscle group; ZJ - zygapophysial joint.

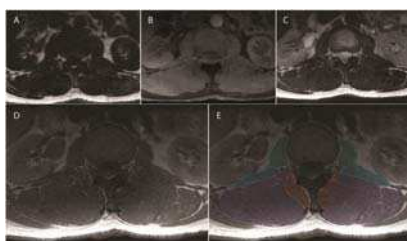


Figure 2. Axial MRIs at the L1/2 disc level of a 47 year old male depicting fat- (A) and water-separated (B) chemical shift, and T2- (C) and T1-weighted (D and E, same) images.

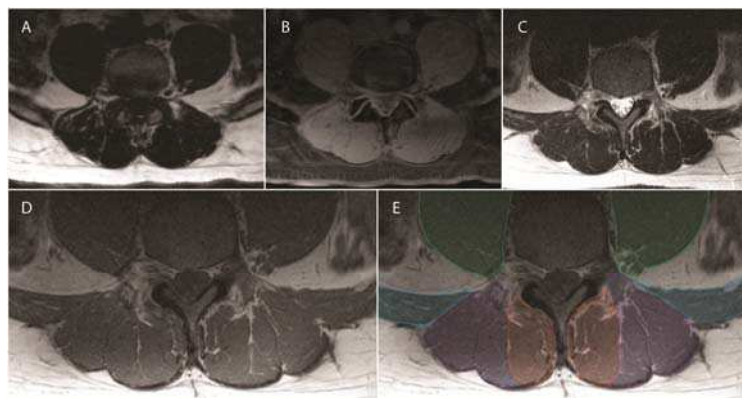


Figure 3. Axial MRIs at the L4/5 disc level

## LUMBAR PARAVERTEBRAL MUSCLE FATTY INFILTRATION: RELATIONSHIP OF DISTRIBUTION PATTERNS TO DEMOGRAPHICS, DISABILITY AND PAIN

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**Introduction:** Paravertebral muscle fatty infiltration (FI) has been associated with low back pain (LBP) and degenerative features of the vertebra and disc, yet relationships are confounded by age and spinal curvature. While FI is an established marker of muscle tissue decline, its etiology is ill-understood and mechanistic models are not confirmed. Identifying where fat has a propensity to accumulate and characteristics that influence its geography may better inform the role of, and interventions for, paravertebral muscles in optimising spinal health. We aimed to quantify lumbar paravertebral muscle FI in a representative cohort to identify whether demographics, disability and temporal LBP contribute to its spatial distribution.

**Methods:** Cross-sectional, cohort study quantifying erector spinae (multifidus, longissimus, and iliocostalis together) FI from axial T1-weighted MRIs of L1-S1 in 107 adult Asians. Most subjects reported LBP (yes/no) in their lifetime, with diminished proportions reporting pain in the preceding year, month, week, and day. Single-slices at the vertebral inferior end-plate per lumbar level were quantified for medial-to-lateral quartiled FI. Dependencies based on lumbar level, quartile, sex, age, BMI, disability (Oswestry Disability Index (ODI)  $\geq$  20%), LBP (lifetime, year, month, week, day) and pain location (none, LBP, sciatica, or LBP&sciatica) were examined using sex-specific generalized estimating equations (GEE) adjusting for clustering.

**Results:** The sample comprised 54 women (f: 53.7 $\pm$ 7yrs) and 53 men (m: 51.3 $\pm$ 8yrs). Average FI was higher in women (f: 31.5 $\pm$ 5.9%; m: 26.3 $\pm$ 5.4%;  $p < 0.001$ ), on the right (by f/m: 0.92/0.47, CI: 0.61-1.24/0.19-0.76%;  $p < 0.01$ ), increased per level caudally ( $p < 0.01$ ), and per quartile laterally, more-so in men ( $p < 0.01$ ) (Figure 1). FI linearly increased with age for both sexes (f: 1.5%/10yrs, CI: 0.3-2.6%,  $p = 0.013$ ; m: 1.3%/10yrs, CI: 0.34-2.24%,  $p < 0.01$ ) and was notably higher at L4&5 than L1,2&3 for cases aged 40-65yrs (Figure 2). BMI was unrelated to FI in women and showed an inverse relationship in men (-0.63%/BMI<sub>unit</sub>, CI: -0.92- -0.33,  $p < 0.001$ ) (Figure 3). Back disability (total ODI & ODI $\geq$ 20%) was unrelated to FI for both sexes but trended for men (f:  $p = 0.69$ ; m:  $p = 0.06$ ). Women with LBP<sub>week</sub> had 1.72% (CI: -3.37 - -0.06%,  $p < 0.05$ ) less average FI than those without pain at that time-point. Men showed insignificant association between FI and pain, but those with LBP had less FI than those reporting no locatable pain (-3.86%, CI: -5.68 - -0.04,  $p < 0.001$ ).

**Discussion:** Our large-scale study assessing lumbar paravertebral muscle FI shows predominant FI in the low lumbar spine, notably for those aged 40-65, which appears less dependent on quartile than lumbar level. Higher FI in women and differences of average FI between sexes for BMI, disabling ODI, and LBP suggest sex-differential fat accumulation patterns. Our findings appear inconsistent with pain models explaining lumbar paravertebral muscle FI and perhaps better reflect a normative sex-dependent feature of the degenerative cascade. However, the limited relationship between paravertebral muscle FI and pain shown here may relate to the complexity of measuring LBP rather than lack of association. Further examination of the quality of paravertebral muscles appears warranted in better understanding its capacity for modification in improving outcomes for spinal health.

Figure 1.

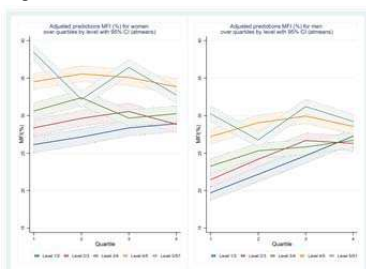


Figure 2.

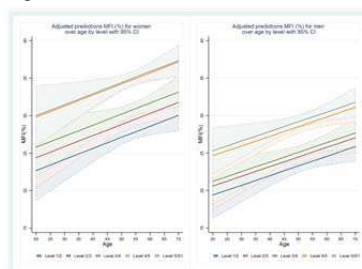
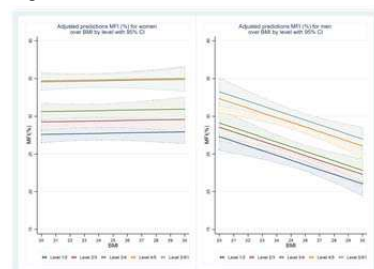


Figure 3.



## DO SITTING POSTURES REALLY AFFECT SPINAL BIOMECHANICS OF ASYMPTOMATIC INDIVIDUALS?

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### Introduction

Low back pain (LBP) is the most prevailing cause of work-related disability among office workers aged under 45 years. While previous observational research has suggested that prolonged slouched sitting may increase the risk of LBP development, the mechanisms underlying such observation remain speculative. Although it is generally thought that an awkward sitting posture may elicit abnormal spinal biomechanical responses, there is a paucity of research that has evaluated the impacts of various sitting postures on lumbar biomechanics. As such, the current study aimed to compare the effects of different sitting postures on trunk proprioception, lumbar range of motion, and trunk muscle activity.

### Method

Sixteen male and 14 female asymptomatic individuals were randomised into one of the three typical sitting postures (i.e. slouched, upright, and sitting with a backrest) with 10 participants per group. Participants remained in the assigned sitting posture for 20 minutes. Pre- and post-sitting spinal assessments were conducted to quantify post-sitting changes in spinal biomechanics. The spinal assessments included: (1) an established proprioception test on a force plate, and (2) evaluations of active lumbar full flexion range of motion in standing using motion sensors attached to T10 and S2 spinous processes. Additionally, muscle activity of bilateral obliquus externus, obliquus internus/transversus abdominis, and erector spinae at the L3 level during sitting were assessed by surface electromyography.

The proprioception test entailed six conditions requiring the participant to stand with eye opened/closed on the force plate or on a foam, with and without vibration to bilateral L5 lumbar multifidi/triceps surae. A larger displacement of center of pressure (CoP) during standing with multifidi vibration than that with triceps surae vibration indicated that the participant relied more on proprioceptive input of multifidi for postural control. Within-subject and between-group differences in various spinal biomechanical parameters were evaluated by separate two-way repeated measures ANOVAs.

### Results

Slouched sitting caused significant decreases in bilateral obliquus internus/transversus abdominis activity as compared to other postures ( $p < 0.05$ ). No such changes were noted in the other sitting postures. There were no significant temporal changes in the reliance of multifidus muscle proprioceptive signals for postural control nor changes in lumbar flexion range of motion following sitting in any of the three postures. No participant complained of post-sitting LBP.

### Discussion

Decreased bilateral obliquus internus/transversus abdominis activity in slouched sitting concurred with prior findings, indicating that reduced deep trunk muscle activation during slouched sitting may transfer the upper body loading to passive lumbar tissues and increases the risk of LBP. Interestingly, although slouched sitting has long been suggested to cause creep in viscoelastic lumbar tissues that may engender increased lumbar flexibility and altered trunk position sense, our findings did not support this premise. While a brief period of awkward sitting has no significant effects on lumbar biomechanics or symptoms, future research should determine whether prolonged sitting in awkward postures can jeopardise lumbar biomechanics and cause LBP.

## AXIAL LOADING DURING MRI INDUCES SIGNIFICANT EFFECTS ON VERTEBRAL ENDPLATE T2-VALUES - A FEASIBILITY STUDY ON PATIENTS WITH LOW BACK PAIN

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### Introduction:

The condition of the endplate (EP) is the most important factor influencing nutritional supply to the avascular intervertebral disc (IVD). Since dynamic load facilitates transport of nutrients over the EP it was hypothesized that axial loading during MRI (aIMRI) can induce such dynamic behavior. It is desired to have a non-invasive method to assess functional behavior of the EP in order to understand its relation to IVD degeneration. The aim of this study was to investigate if aIMRI instantaneously affect the EP's quantitatively but also to gain reference values regarding quantitative T2-values of human EP's.

### Methods:

T2 mapping of 55 EP's in 5 low back pain patients (L1-S1, 30 vertebrae) was performed during conventional unloaded MRI and subsequent aIMRI. Each vertebral EP was manually segmented at multiple consecutive midsagittal views, generating volumetric regions of interest (ROI), covering the entire EP except the outermost lateral parts. EP abnormalities, defined as signal changes or Schmorl's nodules, were registered. Also Modic changes (MC) adjacent to EP's were registered. EP mean T2-values were compared between unloaded MRI and aIMRI and the relationship with MC and EP abnormalities investigated. Of the 24 IVD's (1 sacralized) adjacent to the EP's 8 were degenerated (Pfirrmann grade $\geq$ 3).

### Results:

aIMRI induced significantly higher ( $p=0.01$ ) mean T2-values of the 55 EP's (43ms, SD 17) compared with unloaded MRI (36ms, SD 12). Significantly higher mean T2-values were also seen in inferior EP's compared with superior EP's, both with unloaded MRI (42ms vs. 31ms,  $p<0.01$ ) and with aIMRI (48ms vs 38ms;  $p<0.05$ ). MC (type 1) were found adjacent to 7 EP's. 11 EP abnormalities were registered, of which 10 were adjacent to MC's and 9 adjacent to degenerated IVD's. Comparing EP's with abnormalities with EP's without a significant difference between unloaded MRI and aIMRI was seen in normal EP's ( $p<0.05$ ) but not in EP's with abnormalities ( $p=0.4$ ). In EP's on vertebrae without MC ( $n=48$ ) a significant aIMRI-induced change was registered ( $p<0.02$ ) but no significant aIMRI-induced change in EP's adjacent to MC's was found ( $p=0.7$ ).

### Discussion:

This study shows, for the first time, that aIMRI induce significant changes in EP's and that the known biomechanical difference between superior and inferior EP's can be displayed with T2 mapping. The higher aIMRI T2-values in the EP's potentially represents an instantaneous change in EP diffusion. The lack of aIMRI-induced changes in EP's with abnormalities or adjacent to MC and degenerated IVD's, might represent restricted nutritional diffusion. To evaluate potential clinical application of the method, larger studies comparing aIMRI-induced patterns in EP's with various morphological features, in patients with low back pain and controls, are needed.

## ASCORBIC ACID ATTENUATES MULTIFIDUS MUSCLES INJURY AND ATROPHY AFTER POSTERIOR LUMBAR SPINE SURGERY BY SUPPRESSING INFLAMMATION AND OXIDATIVE STRESS IN A RAT MODEL

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### Introduction

Previous studies have showed oxidative stress and inflammation are the two main molecular mechanisms in multifidus muscle injury and atrophy after posterior lumbar surgery. Ascorbic acid (AA) is a physiological antioxidant and anti-inflammatory agent commonly used in clinic and many studies. The AA may have a potential protective effect in multifidus muscle injury and atrophy after posterior lumbar surgery.

### Methods

Fifty Sprague–Dawley rats were divided into two groups: control group and AA group. The lumbodorsal fascia were opened at the midline from the spinous processes from L2 to L6, and the bilateral multifidus muscles were splitting up from the osseous structures, and then the bilateral multifidus muscles were retracted using one eye speculum continuously for 2 hours. In the AA group, AA was administered via oral gavage at a dose of 2 g/kg daily in the first week. Then we stop the AA treatment and observed the rats until euthanized. In the control group, only drinking water was administered. On day 1, 3, 7, 14 and 28, rats were euthanized (5 rats at every time point in each group). Multifidus muscles were excised from the osseous structures of L3 to L5. In each group, the oxidative stress was evaluated by measuring MDA and T-SOD in the first week. The edema, inflammation, autophagy, fibrosis and fat degeneration of multifidus muscle were evaluated by Q-PCR of relative molecular markers, histology or immunohistochemical.

### Results

In the first week, T-SOD activity was significantly lower in the control group than that in the AA group on day 1, 3 and 7 postoperatively ( $P < 0.05$ ). On the contrary, MDA was significantly higher in the AA group ( $P < 0.05$ ). The molecular and biochemical markers of inflammation (IL-6 and TNF- $\alpha$ ) in multifidus muscles also show significant lower levels when treated with AA on day 1, 3 and 7 postoperatively ( $P < 0.05$ ). The edema, inflammation and necrosis score on histology were significantly lower in the AA group than those in the control group on day 1, 3 and 7 postoperatively ( $P < 0.01$ ). During the period of observation, the molecular and biochemical markers of fibrosis (fibronectin and  $\alpha$ -SMA) and fat degeneration (CD36 and perilipin-1) showed markedly differences between the two groups on the 14<sup>th</sup> and 28<sup>th</sup> day postoperatively. The fibrosis and fat degeneration scores were significantly lower in the AA group than those in the control group on day 14 and 28 postoperatively ( $P < 0.01$ ).

### Discussion

In this study, we explored the potential effect of AA in the postoperative multifidus muscles, the results suggest that AA attenuated the oxidative stress and inflammation response in the postoperative multifidus muscles, and remarkable differences were observed from the histological assessment and related genes expression. Our results provided important insight into the anti-inflammatory and anti-oxidative effects of AA in the postoperative multifidus muscles.

## CORRELATION OF PREOPERATIVE LUMBAR PARASPINAL EXTENSOR MUSCLE CONDITIONS WITH SEVERITY OF DEGENERATIVE FLAT BACK AND ITS IMPROVEMENT AFTER CORRECTIVE FUSION SURGERY

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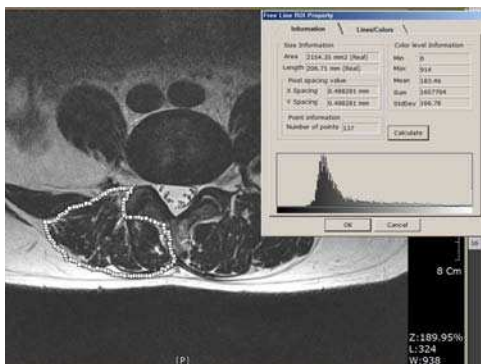
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**Introduction :** Degenerative flat back(DFB) is characterized by sagittal imbalance resulting from loss of lumbar lordosis. Extensive degeneration and weakness of lumbar paraspinal extensor muscle(PSE) are thought to be main cause of DFB. This study is to evaluate correlation between preoperative PSE conditions(atrophy and fat infiltration) on magnetic resonance image(MRI) and angular severity of DFB and to evaluate correlation between preoperative PSE conditions and degree of improvement of DFB obtained by corrective surgery in terms of static and dynamic parameters.

**Methods :** Forty-five patients with DFB who took MRI preoperatively and conducted simple radiography and three dimensional gait analysis before and 6 month after corrective surgery were included. To determine the severity of PSE atrophy, the ratio between cross sectional area of PSE and disc was calculated from L1-2 to L4-5 on MRI. To assess the degree of fat infiltration, mean value of the signal intensity was also measured within paraspinal extensor muscle, using histogram of MRI.(Fig.1) Static parameters of spinopelvic segment were measured by simple radiography. ; spinal parameters such as (A) thoracic kyphosis (TK), (B) thoracolumbar junction(TLJ), and (C) lumbar lordosis(LL), (Fig.2) and pelvic parameters including (A) pelvic tilt (PT), (B) pelvic incidence (PI), and (C) sacral slope(SS).(Fig.3) Dynamic parameters of spinopelvic and lower limb joints were obtained by three dimensional gait analysis.

**Results :** In static parameters, thoracic angle were correlated with atrophy and fat infiltration of upper PSE. Thoracic angle was less improved after surgery, as atrophy of upper PSE was more severe. In dynamic parameters, thoracic angle showed correlation with upper PSE conditions, whereas lumbar angle had correlation with middle to lower PSE conditions. While thoracic kyphosis was less improved after surgery, as atrophy of upper PSE was more severe, lumbar lordosis was less improved, as atrophy and fat infiltration of PSE from L1-2 to L4-5 were more severe. In lower limb dynamic parameters, increased posterior pelvic tilt, hip and knee flexion or ankle dorsiflexion angle was sometimes correlated with PSE conditions. After surgery, hip flexion angle was less improved as PSE atrophy was more severe.

**Discussion :** The severity of atrophy or fat infiltration of PSE show correlation with degree of angular deformity in patients with DFB and with less improvement after corrective surgery. Dynamic parameters showed more prominent correlation with PSE conditions than static parameters and also showed segmental specificity between PSE and angular deformity.



## MINIMALLY INVASIVE DECOMPRESSION SURGERY FOR LUMBAR SPINAL STENOSIS WITH DEGENERATIVE SCOLIOSIS: PREDICTIVE FACTORS OF RADIOGRAPHIC AND CLINICAL OUTCOMES

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**Background:** There is ongoing controversy regarding the most appropriate surgical treatment for lumbar spinal stenosis (LSS) with concurrent degenerative lumbar scoliosis (DLS): decompression alone, decompression with limited spinal fusion, or long spinal fusion for deformity correction. The coexistence of degenerative stenosis and deformity is a common scenario; Nonetheless, selecting the appropriate surgical intervention requires thorough understanding of the patients clinical symptomatology as well as radiographic parameters. Minimally invasive (MIS) decompression surgery was performed for LSS patients with DLS. The aims of this study were (1) to investigate the clinical outcomes of MIS decompression surgery in LSS patients with DLS, and (2) to identify the predictive factors for both radiographic and clinical outcomes after MIS surgery.

**Methods:** 438 consecutive patients were enrolled in this study if they had an evidence of LSS. All enrolled patients underwent the endoscope-assisted decompression surgery for LSS. Inclusion criteria was evidence of LSS and DLS with coronal curvature measuring greater than 10°. The Japanese Orthopaedic Association (JOA) score, JOA recovery rate, low back pain (LBP), and radiographic features were evaluated preoperatively and at over 2 years postoperatively. Spinopelvic parameters, including lumbar lordosis (LL), sacral slope (SS), pelvic tilt (PT), and pelvic incidence (PI) were measured on lateral standing radiographs of the entire spine.

**Results:** Of the 438 patients, 122 were included in final analysis, with a mean follow-up of 2.4 years. The JOA recovery rate was 47.6%. LBP was significantly improved at final follow-up. Cobb angle was maintained for 2 years postoperatively ( $p=0.159$ ). Clinical outcomes in foraminal stenosis patients were significantly related to sex, preoperative high Cobb angle and progression of scoliosis ( $p=0.008$ ). In the severe scoliosis patients, the JOA recovery was 44%, and was significantly depended on progression of scoliosis (Cobb angle: preoperation 29.6°, 2-years follow-up 36.9°) and mismatch between the pelvic incidence (PI) and the lumbar lordosis (LL) (preoperative PI-LL 35.5±21.2°) ( $p=0.028$ ).

**Conclusions:** This study investigated clinical outcomes of MIS decompression surgery in LSS patients with DLS. The predictive risk factors of clinical outcomes were severe scoliosis, progressive scoliosis and large mismatch of PI-LL.



## THE IMPACT OF HYPERTENSION ON THE OCCURRENCE OF POSTOPERATIVE SPINAL EPIDURAL HEMATOMA FOLLOWING AFTER SINGLE LEVEL MICROSCOPIC POSTERIOR LUMBAR DECOMPRESSION SURGERY

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**Purpose** Postoperative spinal epidural hematoma (PSEH) is one of the most hazardous complications after spine surgeries. Although numerous risk factors have been investigated, it is still controversial due to the inconsistent opinions of previous researchers. A recent study have reported that a  $\geq 50$  mmHg increase in systolic blood pressure after extubation was a significant risk factor for symptomatic PSEH; however, the impact of preoperative hypertension was still controversial. In this paper, the impact of hypertension for PSEH occurrence was investigated.

**Methods.** Among a total of 2,468 patients underwent single level microscopic posterior decompression surgery for lumbar spinal stenosis in a single institute, 15 (0.6%) received evacuation surgery for PSEH. Those 15 patients were investigated statistically compared with a randomly selected control group (n=46) using Mann-Whitney U test and Multiple logistic regression analysis. The rate of the patients who had hypertension treatment, high blood pressure value ( $>140 / 90$ mmHg) at pre-operation, before extubation, after extubation and after surgery.

**Results.** Their symptoms occurred on an average of 1.6 days (range 0-3) and evacuation surgery was performed on an average of 5.3 days (range 0-12) after primary surgery. All patients complained of severe pain. Motor deterioration occurred in five cases (33.3%). Bladder dysfunction only occurred in 1 patient (6.7%). After evacuation surgery, pain reduced to the acceptable level soon, and motor and bladder disturbance recovered within 3 months in all cases. There were no significant difference in age, gender, BMI, pre-operative anti-coagulant usage, intraoperative blood loss, and operation time between PSEH and control groups. Also, there was no statistical difference in the rate of patients who receive pre-operative hypertension treatment and blood pressure before extubation, but there were significant differences in the rate of patients who showed high blood pressure at admission (66.7% in the PSEH group vs 6.5% in the control group) and  $>50$ mmHg increase of blood pressure after extubation (53.3% vs 17.4%). Postoperatively, there is statistical difference in the amount of post-operative drainage. Multiple logistic regression analysis showed that blood pressure at admission and poor postoperative drainage were the essential risk factors.

**Discussion.** Our results demonstrated that the pre-operative high blood pressure value, poor postoperative drainage and increase of blood pressure after extubation are the essential risk factors for PSEH, although there was no difference in the preoperative hypertension treatment. Most of the previous studies paid little attention to hypertension. They only investigated whether the patients received preoperative medication for hypertension or not, and concluded hypertension is not a risk factor. Only few authors investigated the real value of pre-operative blood pressure. Hypertension is one of the most common disease especially in old patients, but it is well known that there are many untreated hypertension patients and poorly managed hypertension patients in spite of the medication. Pre-operative hypertension were speculated to be the important reason for the abnormal blood pressure increase after extubation. According to these results, we recommend that blood pressure be evaluated prior to spine surgery and that antihypertensive treatment be initiated when hypertension is identified.



## ASSESSMENT OF THE ANYBODY FULL BODY MUSCULOSKELETAL MODEL IN COMPUTING SPINE LOADS AT LUMBAR LEVEL: COMPARISON WITH *IN VIVO* VALUES OBTAINED DURING EXERCISE TASKS

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**Introduction:** Musculoskeletal models provide a valuable insight to characterize the relation between human motion and internal biomechanical loads. Through an inverse dynamic approach, this modeling technique allows to compute the intersegmental forces acting during the execution of specific imposed body motion and under the action of known external loads. When focusing on the characterization of human spine, musculoskeletal modeling can be accounted to non-invasively evaluate the lumbar loads during physiological activities (e.g. training, ergonomics and rehabilitation) and pathological scenarios (e.g. spine deformities and surgical fixation strategies). To this purpose, model validation, which is commonly performed by comparing the intersegmental forces computed by the model with corresponding measurements obtained *in vivo*, becomes essential. In the panorama of available modeling software, AnyBody software is a commercial tool that provides a full body musculoskeletal model, used by several researchers worldwide. One previous conference contribution attempted to evaluate the suitability of the AnyBody model in computing the L4L5 load [1]. However, that work held several limitations and a comprehensive validation is to be considered as lacking. The present study was thus aimed at validating the appropriateness of the AnyBody model in computing lumbar spine loads at L4L5 level in physiological conditions.

**Methods:** One male subject in good physical condition was enrolled to accurately replicate twelve exercise tasks during which Wilke et al. evaluated *in vivo* the L4L5 disc pressure [2]. Weight and height of the volunteer matched those of the subject assessed by Wilke et al. Motion capture data were acquired during the execution of the tasks and then imported into AnyBody to set the model kinematics. The intersegmental axial load at L4L5 level was calculated during each task and the corresponding L4L5 disc pressure was derived accounting for the disc area. The computed pressures were compared with the *in vivo* measurements. The relationship between disc pressure and body motion angles reported by Wilke et al. when assessing 'flexion-extension', 'lateral bending' and 'axial rotation', was evaluated as well.

**Results:** Positive agreement between the calculated values and the *in vivo* measurements was generally confirmed during all

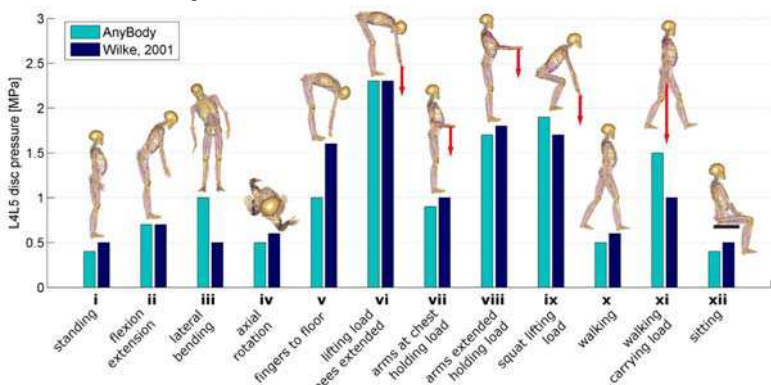


Figure 1. Pressure values calculated with AnyBody model (in light blue) and measured *in vivo* by (Wilke, 2001) (in dark blue) in the specific task. The red arrows depict the 10 kg load applied to each hand during 'straight legs lifting load', 'arms at chest holding load', 'arms extended holding load' and 'squat lifting load' tasks, and the 20 kg load applied to the solely right hand during 'walking carrying load' task.

tasks (Figure 1). Significant very strong correlation (0.89) was pointed out. The regression line, which describes the relation between the compared pressures, showed slope and intercept values equal to 42° and 0.1 MPa. When assessing the relationship between disc pressure and body motion angles, comparable values were exhibited during 'flexion-extension' and 'axial rotation' whereas differences were found in 'lateral bending' when the angle between the thoracolumbar junction and the pelvis exceeded  $\pm 15^\circ$ .

**Discussion:** The results of the present work demonstrate the suitability of the AnyBody model in computing lumbar spine loads. Specific caution needs to be taken only when considering postures characterized

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- [2] Wilke HJ, Neef P, Hinz B, Seidel H, Claes L (2001) Intradiscal pressure together with anthropometric data—a data set for the validation of models. Clin Biomech 16 Suppl 1:S111-26.

## HOW EFFECTIVE IS MIS-TLIF IN THE SURGICAL TREATMENT OF LUMBAR DEGENERATIVE DISEASES?: A COMPARATIVE STUDY WITH OPEN PLIF PROCEDURE

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**INTRODUCTION:** Minimally invasive surgery (MIS) - Transforaminal lumbar interbody fusion (TLIF) technique has the growing popularity, though its efficacy remains to be clarified. The goal of the current study was to compare the clinical results of the MIS-TLIF with those of open PLIF (posterior lumbar interbody fusion) in the treatment of lumbar degenerative diseases. It was investigated how effective the MIS-TLIF was over the open PLIF.

**METHODS:** Consecutive 89 patients undergoing single-level spinal arthrodesis for a diagnosis of degenerative spondylolisthesis (DS) and foraminal stenosis (FS) from 2011 to 2014 were reviewed with a minimum F/U of 1 year (1 - 5 years). There were 47 males and 42 females with a mean age of 71 years (47-88 years). All patients were operated by 2 senior spine surgeons. Patients were categorized into 2 groups; MIS-TLIF (46 pts.) operated by a surgeon and open PLIF (43 pts.) operated by the other one. All patients underwent the decompressive procedure before the arthrodesis. MIS-TLIF was performed after microscopic decompression through a unilateral approach. Open PLIF was associated with posterolateral fusion. All decompressive procedures were followed by pedicle screw instrumentation. Local bone graft with HA granules were used. There was no statistically significant difference in age and type of neurological impairment between 2 groups. Outcome measurements were visual analogue scale (VAS) for low back pain, lower limb pain and numbness, Roland-Morris Disability Questionnaire (RDQ), and Japanese Orthopaedic Association Back Pain Evaluation Questionnaire (JOABPEQ). Fusion status was evaluated using X-ray CT by the independent observer. Mann-Whitney U test was used for statistical analysis. All statistical analyses were performed using SPSS for Windows Version 17.0 and the p-value was set at 0.05.

**Results:** There was no statistically significant difference between 2 groups in the improvement of each VAS value and the RDQ scores. There was also no statistically significant difference between 2 groups in the improvement of JOABPEQ domains, except the domain of the low back pain. This domain means the lumbar spine functional scores related to low back pain in JOABPEQ, and the improvement of scores was significantly higher in MIS-TLIF group than in open PLIF one ( $P < 0.001$ ). Intervertebral bone union was obtained in 92% in MIS-TLIF group and 94% in open PLIF one. There was no statistically significant difference between 2 groups in terms of fusion rate.

**Discussion:** The study demonstrated that MIS-TLIF provided the equivalent clinical results to open PLIF in the treatment of lumbar DS and FS. However, MIS-TLIF showed the better improvement in the domain of lumbar spine dysfunction caused by low back pain. This might be because MIS-TLIF is less invasive to back muscles than open PLIF. MIS-TLIF can be a recommendable surgical procedure in the treatment of lumbar DS and FS.

## COMPARISON OF MICROENDOSCOPIC DISCECTOMY WITH TRANSFORMIMAL PERCUTANEOUS ENDOSCOPIC DISCECTOMY IN LUMBAR DISC HERNIATION: RESULTS OF A RANDOMIZED CONTROLLED TRIAL

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**Introduction:** Lumbar disc herniation (LDH) is a common cause of low back and leg pain. Microendoscopic discectomy (MED) and transformimal percutaneous endoscopic discectomy (TPED) have been approved to be two minimally invasive surgical approaches to treat LDH. However, there was still no comparison study to confirm which technique, MED or TPED, is more effective or minimally invasive.

**Methods:** We performed a prospective controlled randomized study of 87 patients with low back and leg pain caused by LDH nonresponsive to conservative treatment who underwent MED or TPED with more than 12-month follow-up period. Visual analogue scale (VAS) and Oswestry disability index (ODI) were evaluated. Multifidus muscle injury and atrophy were evaluated by creatinine kinase (CK) levels, T2 signal intensity ratio of multifidus to psoas muscle and cross-sectional area (CSA) using MRI. Other studied variables were the duration of the procedure, wound size, hemorrhage, and times of C-arm perspective.

**Results:** There were smaller wound size and less intraoperative hemorrhage in TPED group than in MED group ( $P < 0.001$ ), however there was more times of C-arm perspective in TPED group ( $P < 0.001$ ). The mean CK level was higher in the MED group on days 1 and 3 postoperatively ( $P < 0.001$ ). The back and leg pain VAS and ODI decreased over time after surgery at every follow-up time point. At 3-week and 6-week follow-ups, LBP VAS and ODI were significantly lower in the TPED group ( $P < 0.001$ ). The increased percentage change in the T2 ratio at operative side 6 weeks postoperatively was larger in the MED group ( $P < 0.001$ ). The decreased percentage change in the lean multifidus CSA and the increased percentage change in the T2 ratio at operative side 1 year postoperatively were larger in the MED group ( $P < 0.001$ ).

**Discussion:** This present study concluded that the TPED had a little less muscle injury and atrophy, and more better clinical outcome than the MED in early time follow-up, however both techniques had similar clinical effect in long time follow-up. And the reasons why TPED showed better clinical effect about the LBP relief than MED in relatively-short period after the operation can be generally divided in two part. First, TPED does less damage to multifidus than MED, as patients in MED group had higher serum CK level at the 1<sup>st</sup> and 3<sup>rd</sup> day postoperatively and higher T2 signal intensity ratio of gross multifidus to psoas, which reflected tissue edema at 6<sup>th</sup> week postoperatively. Second, radiofrequency ablation used in TPED may be another reason, as previous studies reported radiofrequency ablation can improve the physical function and relief of LBP in patients with chronic discogenic back pain. At 1 year follow-up postoperatively, the multifidus muscle showed significantly more atrophy in MED group than that in TPED group, however there is no significant difference in clinical effect between both groups. One important defect of TPED should not be ignored that was more C-arm perspective times intraoperatively leading to more radiation exposure.

## VARIATION IN PROCEDURAL UTILIZATION FOR LUMBAR SPINE DISORDERS IN FEE-FOR-SERVICE VS SALARIED HEALTHCARE SYSTEMS IN THE UNITED STATES

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**Background:** The phenomenon of provider inducement for procedural care has been recognized in a number of clinical contexts. There is a growing concern that spine care practitioners may preferentially choose more costly or invasive procedures in a fee-for-service system, irrespective of the underlying lumbar disorder being treated. This study sought to use TRICARE claims data as a natural experiment to determine whether: 1) Rates of fusion-based procedures were higher in the fee-for-service (Purchased Care) setting as opposed to the salaried Department of Defense (DoD) setting (Direct Care); and 2) If preference for fusion-based procedures varied by indication for surgery.

**Methods:** Patients surgically treated for lumbar disc herniation, spinal stenosis and spondylolisthesis (2006-2014) were identified. Patients were divided into two groups based on whether the surgery was performed in the fee-for-service setting or at DoD facility. Differences in the rates of fusion-based procedures, discectomy and decompression between both care settings were assessed using logistic regression techniques to adjust for differences in case-mix and surgical indication.

**Results:** There were 28,344 patients in the entire study, 21,290 treated in Purchased Care and 7,054 treated in Direct Care. Fusion-based procedures, particularly interbody fusion, were significantly more likely to be performed in the Purchased Care setting ( $p < 0.001$ ). After adjustment for case-mix and surgical indication, patients with disc herniations and spinal stenosis remained significantly more likely to receive an interbody fusion procedure in the Purchased Care setting. No difference in the use of interbody fusion as compared to posterolateral fusion was appreciated for patients with spondylolisthesis.

**Conclusions:** The preferential use of interbody fusion procedures was significantly higher in the Purchased Care setting, irrespective of the underlying diagnosis. These findings should be considered as health systems look to address the new financial incentives associated with healthcare reform.

## THE EFFECT OF 1- OR 2- LEVEL POSTERIOR LUMBAR INTERBODY FUSION ON GLOBAL SAGITTAL BALANCE

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**Introduction:** Sagittal imbalance is associated with poor clinical outcomes in patients with degenerative lumbar disease. Many studies have reported on the effect of various types of lumbar fusion surgeries on regional and global sagittal balance. It was reported that a lateral lumbar interbody fusion could improve regional sagittal profiles, although several studies reported that it could not change global sagittal alignment. However, there is no consensus on the impact of posterior lumbar interbody fusion (PLIF) on local and global sagittal balance. The purpose of this study is to reveal the effect of 1-level or 2-level PLIF on global sagittal balance.

**Methods:** This study included 88 patients who underwent a 1-level or 2-level PLIF for spinal stenosis. All patients were followed up for >2 years. Clinical outcomes included a visual analog scale, Oswestry Disability Index, and EuroQol 5-dimension questionnaire (EQ-5D). Radiological parameters included, lumbar lordosis, sacral slope, pelvic tilt, pelvic incidence, thoracic kyphosis, C7–S1 sagittal vertical axis (SVA), and segmental angle. Fusion, loosening, and subsidence rates were also evaluated. Patients were divided into two groups according to their preoperative C7–S1 SVA (Group N: SVA ≤ 5 cm vs. Group I: SVA > 5 cm) and their clinical and radiological outcomes were compared.

**Results:** All clinical outcomes and radiological parameters improved postoperatively. Preoperative demographic and clinical data showed no difference except in the anxiety/depression domain (2.7 for group N and 2.2 for group I,  $p = 0.016$ ) of EQ-5D. However, no differences were found in postoperative clinical outcomes. In group N, lumbar lordosis and thoracic kyphosis increased, and pelvic tilt decreased postoperatively. However, no difference was found in the C7–S1 SVA and segmental angle. In contrast, all sagittal profiles showed an improvement in group I postoperatively. C7-S1 SVA decreased from 9.5cm to 3.8cm ( $p < 0.001$ ) in group I.

**Discussion:** Although many studies showed restoration of regional sagittal balance by various fusion method such as transforaminal or lateral interbody fusion, they were unlikely to frequently change the global sagittal balance. However, our study showed a definite improvement in global sagittal balance after 1- or 2-level PLIF surgery. There are several explanations that support our results. First, the patient could extend the back by decompressive surgery. Second, an increased segmental angle by a lordotic cage could increase lumbar lordosis, which lead to a restoration of global sagittal balance. Third, surgical technique might be important. Cages were inserted into the disc space anteriorly as much as possible, and a compression maneuver between screw heads was performed to restore segmental lordosis.

In conclusion, global sagittal alignment as well as spinopelvic parameters were improved by short-level lumbar fusion in patients with spinal stenosis. The degree of improvement was higher if their preoperative C7–S1 SVA was >5 cm. Clinical, functional outcomes, and quality of life improved postoperatively regardless of preoperative sagittal alignment. However, further study is required to evaluate which parameters could impact the restoration of global sagittal balance.

## SURGICAL OUTCOMES OF PEDICLE SCREW WITH CORTICAL BONE TRAJECTORY COMPARED WITH CONVENTIONAL TRAJECTORY WITH LUMBAR SPINAL STENOSIS - A 1-YEAR FOLLOW-UP STUDY

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### Introduction

Cortical bone trajectory (CBT) is a new trajectory for pedicle screw insertion in the lumbar spine. Some studies have reported on the efficacy of CBT compared with that of conventional pedicle screw techniques. The CBT technique, in which the screw insertion point and trajectory are different from that in conventional pedicle screwing, may be less invasive regarding the amount of surgical exposure. However, it is still unknown if the CBT technique is clinically less invasive for patients with lumbar spinal stenosis (LSS). The aim of this study was to clarify the invasiveness of the CBT technique compared with that of conventional pedicle screw insertion for patients with LSS.

### Methods

In total, 67 patients (33 men, 37 women) were enrolled in this retrospective study and divided into the following two groups: conventional pedicle screw insertion (control, n=35), and CBT technique (CBT, n=32). Bone grafts were performed with morselized local bone fusion with or without hydroxyapatite granules. The number of fusion and decompression levels, operative time, estimated blood loss, fusion methods including posterolateral fusion and transforaminal interbody fusion (TLIF), laboratory data including white blood cell counts, the amount of creatine phosphokinase and C-reactive protein levels 1 week after surgery were examined. The rates of pseudarthrosis and screw loosening were evaluated using computed tomography with at least 1 year of follow-up. Clinical outcomes were assessed using the visual analog scale (VAS) for low back and leg pain and Japanese Orthopedic Association Back Pain Evaluation Questionnaire (JOABPEQ). These items were compared between the control and CBT groups in statistical significance.

### Results

There were no significant differences in age, sex, preoperative VAS and JOABPEQ subdomain scores, number of decompression levels, operative time, laboratory data, fusion rates, and rates of screw loosening between the control and CBT groups. The number of fusion levels was less in the CBT group than in the control group (number of fusion levels / case: CBT,  $1.9 \pm 0.9$ ; control,  $2.6 \pm 1.1$ ,  $P=0.01$  by Mann-Whitney U-test), while the number of TLIF levels in the CBT group was more than in the control group (number of TLIF / case: CBT,  $0.70 \pm 0.12$ ; control,  $0.54 \pm 0.12$ ,  $P=0.34$  by non-paired t-test). Multivariate regression analysis after adjustment for age, sex, the number of decompression, fusion, and TLIF levels revealed that estimated blood loss in the CBT group was statistically less than in the control group ( $\beta$ -coefficient:  $-0.37$ ,  $P=0.001$ ), and JOABPEQ lumbar spine function subdomain score in of the CBT group was significantly higher than in the control group ( $\beta$ -coefficient:  $-0.52$ ,  $P=0.001$ ).

### Discussion

We found that the CBT technique resulted in less blood loss and higher acquired points in JOABPEQ score than conventional pedicle screw insertion. These results suggest that using the CBT technique for patients with LSS could result in less invasion and higher QOL than conventional pedicle screw insertion.

## TWO YEAR FOLLOW-UP AFTER PERCUTANEOUS INTERSPINOUS PROCESS DEVICE FOR LUMBAR SPINAL STENOSIS IN A PROSPECTIVE CASE-SERIE OF PATIENTS WITH SEVERE CO-MORBIDITIES

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**Introduction:** Degenerative lumbar spinal stenosis is a common pathology in the elderly population where comorbidity is common and therefore a treatment method with low risks as well as low cost and possibly also better results than open decompression are wanted. To analyse the clinical outcome more than 2 years of follow-up of patients treated with Aperius PerCLID. To present the clinical experience, re-operation rate, complications and discuss the indications of Aperius.

**Methods:** Forty patients underwent surgery for the onset of neurogenic intermittent claudication (NIC) with Aperius. All the patients had more than 6 months of symptom duration of NIC due to spinal stenosis on MRI. The patients had pseudo-claudication symptoms exacerbated by prolonged standing or by activities in the upright posture, and short walking distance. All patients filled in questionnaires; EQ5D, Oswestry Disability Index (ODI), SF-36, and EQ5D-VAS score for leg pain and low back pain. The patients also answered questions regarding their walking distance and if they were using any walking aids at base-line and at follow-up. The patients filled in the surveys at base-line, at the out-patient clinic before meeting the orthopaedic surgeon, and at the follow-up visits 2 weeks, 3 and 6 months and 1 and 2 years postoperatively. The patients were examined clinically by an orthopaedic surgeon and radiologically with plain X-ray or MRI if so required.

**Results:** Patients treated with Aperius had in 43% good outcome results and there was a 32% statistically improvement of the physical functions at one year follow-up. There were no other statistically significant symptom improvements in this patient cohort at one year follow-up. The secondary outcomes, when the observation time was extended up to 42 months, showed several significant improvements of the patients' symptoms. There was a 45% ( $p < 0.005$ ) significant improvement of VAS for back pain and 61% ( $p < 0.000$ ) of VAS for leg pain. There was also a 55% ( $p < 0.014$ ) significant improvement of quality of life according to EQ5D. The outcomes of the spine functions according to ODI and the physical component score (PCS) according to SF36 showed statistically significant improvements with 16% ( $p < 0.023$ ) and 42% ( $p < 0.002$ ) respectively. For the latter a value of 50 is normal PCS and therefore 37 points in our series is poor outcome although there is an improvement. There was also a significant improvement of the walking distance at a maximum of 500m with 24% ( $p < 0.05$ ).

**Conclusions and discussion:** Patients treated with Aperius were significantly physical better at one year follow-up. These results underline the importance of meticulous patient selection, before deciding to operate an individual with an interspinous implant. The elderly and patients with high co-morbidity may benefit from this type of surgery, giving them some relief of symptoms, at least temporary. Although we have had a high revision rate at one year follow up we think that this type of surgery is well applicable as a method in the spine surgeon's arsenal when patient selection is done with utmost care.

**PATIENT REPORTED OUTCOMES FOLLOWING SPINAL SURGERY FOR DEGENERATIVE DISC DISEASE, DISC HERNIATION, SPONDYLOLISTHESIS AND SPINAL STENOSIS.**

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**Introduction.** To compare satisfaction, back and leg pain, disability and quality of life outcomes at one-year follow-up after elective spine surgery, based on pre-surgical diagnosis.

**Methods.** There were 18 Canadian Spine Outcomes and Research Network sites representing 14 cities from 8 provinces used to derive the sample; 1531 patients who consented and then proceeded to thoracolumbar spine surgery between October 2008 and September 2015. One-way ANOVA analysis was used to compare outcomes by diagnosis. Patient reported outcome measures were patient satisfaction and change in: leg pain, disability score, and health-related quality of life (SF-12, EQ5D) from baseline to 1 year post surgery. Four pre-surgical diagnoses were evaluated: degenerative disc disease (DDD) (n=88), disc herniation (n=429), spondylolisthesis (n=377) and spinal stenosis (n=637).

**Results.** There were no significant differences in change in mental component score (SF12) or EQ5D by diagnosis. Those who had surgery for degenerative disc disease had the least improvement in back pain, leg pain, disability scores and physical component scores:

- Back Pain change (-2.68): significantly less improvement than surgery for spondylolisthesis (-3.98,  $p<0.01$ ) and stenosis (-3.55,  $p<0.04$ ).
- Leg Pain change (-2.61): significantly less improvement than surgery for disc herniation (-4.11,  $p<0.0001$ ), spondylolisthesis (-4.38,  $p<0.0001$ ) and stenosis (3.98,  $p<0.001$ ).
- Disability Score change (-15.98): significantly less improvement than surgery for disc herniation (-25.47,  $p<0.0001$ ) and spondylolisthesis (-21.82,  $p<0.04$ ).
- Physical Component Score change (7.82): significantly less improvement than surgery for disc herniation (12.35,  $p<0.001$ ).

There were no significant differences in satisfaction rates between those who had surgery for degenerative disc disease vs disc herniation and vs stenosis. Those with spondylolisthesis were significantly more satisfied with surgery than all other diagnoses ( $p<0.01$ ).

**Discussion.** Clinically significant improvements in patient reported outcomes were achieved across all diagnoses at 1 year post surgery; however, those with degenerative disc disease had the least amount of improvement.



## COMPARATIVE STUDY OF 1-YEAR CLINICAL OUTCOMES USING ROBOT-ASSISTED PEDICLE SCREW FIXATION AND FREEHAND TECHNIQUE IN POSTERIOR LUMBAR INTERBODY FUSION: A PROSPECTIVE, RANDOMIZED CONTROLLED TRIAL

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**Introduction:** The clinical efficacy for robot-assisted pedicle screw fixation remains unclear, compared to the conventional freehand technique for lumbar spinal fusion surgery. The purpose of this study was to compare the clinical outcomes of surgery with robot-assisted posterior interbody fusion compared to that with freehand posterior interbody fusion in patients with degenerative spinal disease.

**Methods:** 78 participants with degenerative spinal disease were randomly allocated (1:1) to the minimally invasive (MIS), posterior lumbar interbody fusion (Robot-PLIF) or conventional, freehand, open approach, posterior lumbar interbody fusion (Freehand-PLIF). The primary endpoint was the baseline adjusted-Oswestry Disability Index (ODI) score at 1 year after surgery. Secondary endpoints included ODI score, Visual Analog Scale (VAS) score for back/leg pain, general health status at all follow-up assessments, and radiological outcomes including fusion status and decrease of adjacent segment disc height at 1 year after surgery.

**Results:** The baseline adjusted-ODI scores in both groups at 1 year after surgery were not different. At 1 year after surgery, the mean baseline-adjusted ODI scores (95% confidence interval [CI]) in the Robot-PLIF and Freehand-PLIF groups were 20.29 (15.1–25.47) and 21.74 (16.77–26.70), respectively ( $P = 0.688$ ). The overall changes in the ODI ( $P = 0.682$ ) and VAS for back ( $P = 0.606$ ) and leg pain ( $P = 0.640$ ) over the 1-year period were not significantly different between the groups. However, the ODI scores and VAS scores for back and leg pain significantly decreased with time after surgery in both groups ( $P < 0.001$  for all 3 variables). Whereas there was no significant difference in fusion status between the groups ( $P = 0.103$ ), the decrease in disc height at the proximal adjacent segment was significantly less in the Robot-PLIF group than in the Freehand-PLIF group ( $P = 0.039$ ).

**Discussion:** 1-year surgical outcomes including VAS, ODI, and SF-36 did not differ between the both groups. The disc height in the proximal adjacent segment was significantly less decreased in the Robot-PLIF group, compared to the Freehand-PLIF group.

## WHAT IS THE APPROPRIATE TIMING OF PATIENT-RATED FOLLOW-UP AFTER SURGERY FOR DEGENERATIVE DISORDERS OF THE LUMBAR SPINE?

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### Introduction

Patient-rated measures have become the gold standard for assessing spine surgery outcomes. However, the frequency and length of follow-up is not standardized due to a lack of information on the dynamics/evolution of the course of change. Journals and study protocols often demand a minimum 2-year follow-up, but the indiscriminate application of this principle may not be warranted. We examined the course of change in patient outcomes up to 5 years postoperatively.

### Methods

The data from 3'334 consecutive patients (1'789 women, 1'545 men; aged 61±15 years) undergoing first-time surgery between 1.1.2005 and 31.12.2010 for differing lumbar degenerative disorders were evaluated, using data from our in-house Spine Outcomes registry, linked to Spine Tango. The multidimensional Core Outcome Measures Index (COMI) was completed by 3'124 (94%) patients preoperatively, and 3'164 (95%) at 3 months' follow-up, 3'153 (95%) at 1 year, 3'112 (93%) at 2 years, and 2'897 (87%) at 5 years follow-up. 2'502 (75%) completed COMI at all five timepoints.

### Results

COMI decreased significantly from pre-op to 3 months' follow-up (3.7-points), and from 3 months' to 12 months' follow-up (0.4-points), then levelled off up to 5 years' follow-up (0.04-0.05 point-change). The course of change up to 12 months differed slightly depending on pathology/whether fusion was done. Individual patient COMI change-scores from pre-op to 3 months' follow-up showed a significant correlation with those from pre-op to 12 months' (r=0.65;p<0.0001), 24 months' (r=0.57;p<0.0001), and 5 years' (r=0.51;p<0.0001) follow-up. Similarly, the change scores from prep to 12 months' follow-up correlated with the change scores from pre-op to 24 months' (r=0.74;p<0.0001) and 5 years' follow-up (r=0.65;p<0.0001). Similar results were observed when analysing individual achievement of the minimum clinically important change (MCIC) score: the proportion of patients achieving this rose from 68.6% at 3 months to 72.5% at 12 months, and then stayed at approximately the same level up to 5 years' postoperatively (73.2% at 24 months and 72.8% at 5 years).

### Discussion

Stable group mean COMI scores were seen from 1-year postoperatively onwards. These findings should be taken into consideration when planning the followup schedule in clinical studies involving this patient population. As the early post-operative results appear to herald the longer-term outcome, a 'wait and see policy' in patients with a poor initial outcome is not advocated. Analysis of reasons for the failure to achieve a good result should begin at 3 months' postoperatively. This may avoid unnecessary suffering on the part of the patient.

## NELL-1 COMBINED WITH BONE MARROW ASPIRATE CONCENTRATE IN A POLYELECTROLYTE COMPLEX BASED CONSTRUCT ENHANCES POSTEROLATERAL SPINAL FUSION IN RABBITS

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**Introduction:** Neural epidermal growth factor-like protein-1(NELL-1) is a novel osteogenic growth factor in bone regeneration. However, the role of NELL-1 in bone regeneration is still being explored. NELL-1 specifically functions at the late stage during bone marrow mesenchymal stem cells (BMSCs) differentiation, which promotes chondroprogenitor cells to osteogenesis, and may not have as much effect during the early stages of osteogenesis, which involves BMSCs proliferation and migration to defect site. The addition of platelet derived growth factors(PDGFs) may enhance bone formation by recruiting adequate BMSCs. At the same time, bone marrow aspirate could be a source of BMSCs. We hypothesize that combination growth factor therapy in vivo, namely either addition of PDGF or bone marrow aspirate, could enhance the osteogenicity of NELL-1 in a rabbit posterolateral spinal fusion model.

**Methods:** Rabbit BMSCs were loaded into the middle channel of a three-dimensional chemotaxis slide. Time lapse images were taken every 15 minutes for 20 hours. The directness of the migration of cells was determined by Rayleigh test ( $p < 0.05$  indicates directed migration). Protein release profiling were evaluated by immersing PEC beads coated with growth factors in phosphate buffered saline(PBS) at 4 °C. Growth factor content was determined by fluorometric assay. The bioactivity of NELL-1 was measured by alkaline phosphate(ALP) assay with rabbit BMSC and the bioactivity of PDGF was measured by crystal violet staining with NIH 3T3 cell. Data were analyzed by the Student t test ( $P < 0.05$  indicates statistically significant). Results were expressed as means  $\pm$  standard errors. All animal related procedures were approved by the institutional ethics committee prior to animal surgery. Rabbits underwent L4-L5 inter-transverse fusion. 2mL of bone marrow aspirate from the iliac crest was centrifuged to decrease the total volume to 200 $\mu$ L. Heparin based polyelectrolyte complex(PEC) was used as the growth factor delivery carrier. Polycaprolactone tri-calcium phosphate scaffold was packed with growth factor coated PEC. Four groups of implants were evaluated as follows:(1)200 $\mu$ g NELL-1 with 200 $\mu$ L bone marrow aspirate concentrate (BMC);(2)200 $\mu$ g NELL-1 with 12.5 $\mu$ g PDGF;(3)200 $\mu$ L BMC;(4) autologous graft. New bone formation was evaluated by X-ray computed tomography at 8 weeks after surgery.

**Results:** NELL-1 could not induce directed migration of rabbit BMSCs at 125 $\mu$ g/mL, while PDGF can attract fibroblasts at 30ng/mL. Both PDGF and NELL-1 were released in a controlled manner within 14 days (PDGF:24.8 $\pm$ 3.5%, NELL-1:15.6 $\pm$ 2.2%). NELL-1 increased ALP level on day 14 while PDGF failed to stimulate the growth of NIH 3T3 cells after day 3. PEC+NELL-1+BMC group demonstrated significant fusion rate, while PEC+NELL-1+PDGF showed minor bone formation.

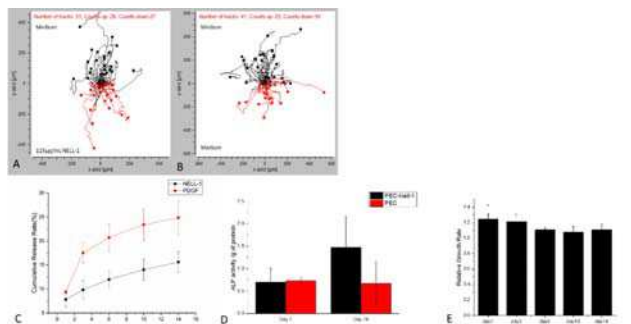


Figure1. Chemotactic property and controlled released profiling of growth factors. Rabbit BMSC migration tracking(A). Down: 125 $\mu$ g/mL NELL-1, up: medium. Rayleigh test  $P = 0.184 > 0.05$ , suggested that NELL-1 could not attract BMSC at the above concentration. Medium control(B). Cumulative NELL-1 and PDGF eluted from PEC quantified in vitro using a fluorescent assay(C). Alkaline phosphate level after 7 days and 14 days of rabbit BMSC under treatment of PEC loaded with or without NELL-1(D). Relative growth of NIH 3T3 cells under treatment of PDGF released from PEC at day 1, 3, 6, 10, 14(E).

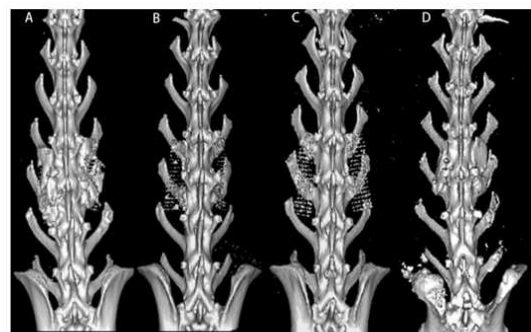


Figure2. Representative CT images of the bone formation after 8 weeks of implantation. PEC+NELL-1+BMC(A), PEC+NELL-1+PDGF(B), PEC+BMC(C), Autologous graft(D). Notice robust bone formation in PEC+NELL-1+BMC, while PEC+NELL-1+PDGF and PEC+BMC showed minute bone formation.

**Discussion:** NELL-1 delivered with BMC enhances posterolateral spinal fusion in rabbits. Compared with the conventional stem cell therapy, BMC bypasses isolating and differentiating of BMSCs. It concentrates the BMSCs via a 10-minute centrifugation which in turn will shorten the surgery time. BMC provides not only BMSCs but also the matrix containing protein components that promote bone formation. This study demonstrates the potentially therapeutic strategy of NELL-1 and BMC for spinal fusion and confirms the versatility of PEC based on heparin affinity for delivering growth factors with heparin binding domains including NELL-1 and PDGFs.

## PREOPERATIVE KNOWLEDGE TEST FEEDBACK INTERVENTION (KTFI) INCREASES PATIENTS' KNOWLEDGE LEVEL - A RANDOMIZED CONTROLLED TRIAL IN 100 SPINAL STENOSIS PATIENTS

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### Introduction

Surgery for spinal stenosis will likely increase in the future with ageing of the population. For an informed consent, the patient has to master a broad understanding of the risks, benefits and likely outcomes of different treatment options. Previous studies have shown that traditional preoperative patient education does not meet patients' expectations. Empowering patient education aims at increasing patients' knowledge level, and it has been shown to reduce preoperative anxiety, improve patients' decision-making abilities, hasten recovery, and increase postoperative quality of life in surgical patients. The aim of our study was to assess the impact of a specific preoperative patient education method (Knowledge Test Feedback Intervention, KTFI) on the knowledge level of spinal stenosis patients.

### Methods

100 spinal stenosis patients undergoing lumbar decompression with or without fusion were randomized into intervention group (IG, n=50) or control group (CG, n=50) using the minimization method. Our intervention was based on the concept of empowering knowledge covering all aspects of the surgical pathway (bio-physiological, functional, experiential, social, financial, ethical). The KTFI consisted of a knowledge test specifically developed for this study, and a telephone discourse based on the test results. The knowledge test had 27 "true-false-do not know" items, and the percentage of correct answers constituted the test result. The telephone discourse was conducted on an average 9 days before surgery according to the principle of empowering discourse: the patient had an active role in regulating the depth of discussion, and in reflecting the significance of the different issues to his/her life. To blind the patients, the CG had a general telephone discourse on their health history. Both groups additionally received routine patient education according to the standards of the hospital. The knowledge test was performed at baseline, at admission to hospital and at discharge, as well as at 3 and 6 months after surgery to measure the patients' knowledge level.

### Results

The study groups were balanced regarding the background factors. At baseline, no difference in knowledge level existed between the study groups. After the intervention (baseline to admission), the knowledge level of IG increased significantly from 49.6% to 79.9% (change 30.3%; 95% CI 24.5,36.0) whereas no change was detected in CG. A minor improvement in the knowledge level was detected in CG during the hospitalization (admission to discharge) (change 5.7%; 95% CI -0.1,11.6). The knowledge level remained stable in both groups throughout follow-up, and the difference between the groups was significant at all time points.

### Discussion

The KTFI was effective in increasing spinal stenosis patients' preoperative knowledge level compared to routine patient education. Our results are in line with previous studies where enhanced patient education methods have been used in other surgical disciplines. A need for low-technology interventions exists as all ageing patients do not use e-learning technology. Whether the increased knowledge level will be reflected in e.g. improved treatment outcomes remains a focus of further study.

## BOOT CAMP PROGRAMS FOR LUMBAR SPINAL STENOSIS: A RANDOMIZED CONTROLLED TRIAL COMPARING OUTCOMES FOLLOWING A COMPREHENSIVE VERSUS A SELF-DIRECTED NON-SURGICAL APPROACH

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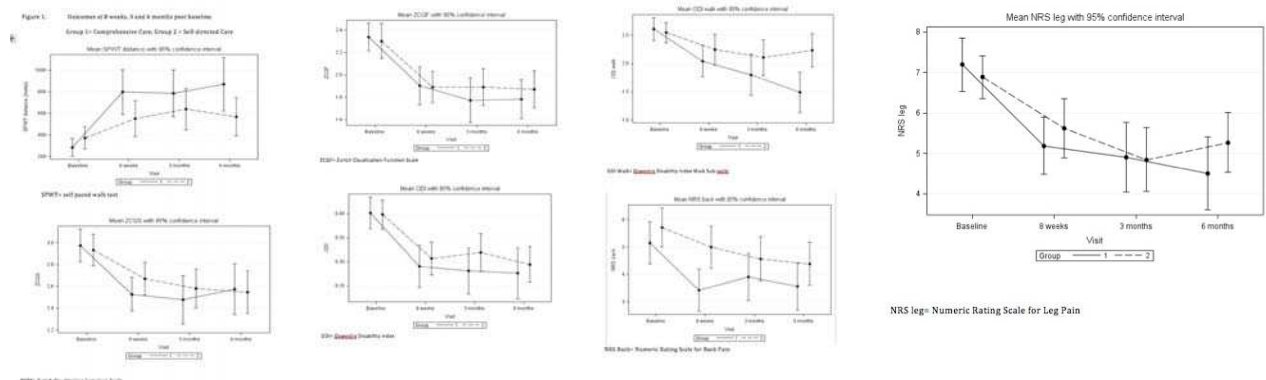
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**Introduction:** Neurogenic claudication due to degenerative lumbar spinal stenosis is a leading cause of pain, disability and loss of independence in older adults. Reduced walking ability is the dominant functional limitation in this population. There is an exponential rise in the number of people suffering from neurogenic claudication due to the aging population. Effective non-surgical approaches are unknown. The study objective is to compare outcomes following comprehensive care to self-directed care.

**Methods:** Eligible consenting participants with neurogenic claudication due to lumbar spinal stenosis and limited walking ability (<30 minutes) were randomized to a 6-week comprehensive program that included twice weekly manual therapy or self-directed care following a single educational session. Both groups received a pedometer and an exercise manual and video with instructions on daily home exercises and self-management strategies to be followed for life. Follow-up assessments were performed at 8 weeks, 3 months and 6 months. The primary outcome was the between group mean difference in walking distance from baseline to 6 months using the self-paced walking test assessed by a blinded assessor. Secondary outcomes included the mean difference in the functional and symptom scales of the Zurich Claudication Questionnaire, the Oswestry Disability Index (ODI), the ODI walking subscale, and the Numeric Pain Scale (NPS) for low back and leg pain. Intention-to-treat analysis was performed for all outcomes.

**Results:** Fifty-one participants were randomized to the comprehensive and 53 to the self-directed group. The adjusted mean difference in walking distance in the comprehensive group versus the self-directed group at 8 weeks was 345.4 metres (m) (95% confidence interval (CI), 150.0 to 540.7), at 3 months, 304.1 m (95% CI, 77.9 to 530.3) and at 6 months, 421.0 m (95%CI, 181.4 to 660.6). At 6 months, 79% and 67% of participants in the comprehensive group achieved at least 30% and 50% improvement in walking distance respectively compared to 64% and 53% of participants respectively in the self-directed group. At 6 months all secondary outcomes showed significant improvement from baseline in both groups (except ODI walk in the self directed group) with the comprehensive group demonstrating significantly greater improvement in the ODI walk scale, -0.8 (95% CI, -1.3 to -0.4) and the NPS for leg pain, -1.2 (95% CI, -2.4 to -0.1) compared to the self-directed group.

**Discussion:** Both boot camp programs showed significant improvement in walking distance at each follow-up period with the comprehensive program demonstrating superior improvement. The superior benefits of the comprehensive program were sustained at 3 and 6 months even after the active intervention was terminated. The additional time and attention participants received in the comprehensive group may account for early benefits but unlikely impacted the benefits at 6 months. The boot camp programs are training programs designed to give participants the knowledge, skills and self-confidence to maximize their functional activity for life with an emphasis on walking ability. It appears that manual therapy combined with one-on-one instruction on daily exercises and self-management strategies can provide better outcomes than a self-directed approach.



## EFFECTIVENESS OF DECOMPRESSION SURGERY FOR LUMBAR SPINAL STENOSIS IN PATIENTS AGED 80 YEARS AND OLDER

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### INTRODUCTION:

Recently, the incidence of lumbar surgery in elderly patients is increasing. The purpose of this study was to clarify the effectiveness of decompression surgery for lumbar spinal stenosis in patients aged 80 years and older.

### METHODS:

This study included 246 patients with lumbar spinal stenosis who were at least 60 years old. All patients received decompression surgery without fusion. The follow-up period was 1 year. Surgical outcomes were evaluated by numerical rating scales (NRS: 0–10) for low back pain, leg pain, leg numbness, satisfaction rate, and the Japanese Orthopaedic Association Back Pain Evaluation Questionnaire (JOABPEQ). The participants were divided into three groups according to their age: the 60s group (aged 60–69 years), 70s group (aged 70–79 years), and 80s group (aged ≥ 80 years). The data from these three groups were then compared. Statistical analysis was performed using the Kruskal-Wallis test, Wilcoxon test, and Chi-squared test. A *p* value less than 0.05 was considered significant.

### RESULTS:

There were 89 patients in the 60s group, 128 patients in the 70s group, and 29 patients in the 80s group. There were no significant differences between the three groups in preoperative NRS values and JOABPEQ scores. One year after surgery, there were no significant differences between the three groups in NRS values and satisfaction with the surgical outcome. The effectiveness of decompression surgery as assessed by the JOABPEQ regarding improvement in subscale of walking ability was 81.6% in the 60s group, 57.1% in the 70s group, and 53.9% in the 80s group; improvement in walking ability was significantly lesser in the 70s and 80s groups compared with the 60s group. There were no significant differences between the three groups in the other subscales of the JOABPEQ.

### DISCUSSION:

The study results showed that the effectiveness of decompression surgery for lumbar spinal stenosis patients in the 80s group was comparable to that in the 60s and 70s groups. The 60s group was only superior to the 70s and the 80s groups regarding postoperative improvement in walking ability.

## CLINICAL EFFICACY OF MINIMALLY INVASIVE DIRECT LATERAL INTERBODY FUSION FOR ADULT SPINAL DEFORMITY

Young-Hoon Kim, Jae-Won Lee, Kee-Yong Ha, [Sang-Il Kim](#)

### Introduction

Trans-psoas DLIF is recently being popular as a minimally invasive approach for the various degenerative spine diseases including adult spinal deformity (ASD), since it is known to be effective for correction of coronal deformity and indirect decompression. However, there is a paucity of studies evaluating the efficacy of this technique for ASD comparing with the conventional posterior spinal fusion. Therefore, the aim of this study is to evaluate the radiological and clinical results of minimally invasive direct lateral interbody fusion (DLIF) for adult spinal deformity comparing with the open posterior spine fusion

### Methods

Patients who underwent corrective surgery for the lumbar/ thoracolumbar ASD were reviewed from 2002 to 2014 in a single institute. Patients with coronal Cobb's angle (CA)  $\geq 10^\circ$ , age  $\geq 50$  years, treated with mentioned surgical methods, at least 2 years follow-up, no lack of data were included. The patients with 3 column osteotomy was excluded. Fortytwo patients who underwent DLIF combined posterior spinal fusion (DP group) and 35 patients who underwent posterior spinal fusion only (P group) were finally enrolled. Efficacy in deformity correction was evaluated for coronal and sagittal radiological parameters, and clinical outcomes such as VAS, ODI, SRS-23, were compared. In addition, as a subgroup analysis, efficacy of DLIF for indirect decompression and deformity correction was assessed using the radiological data from the patients who underwent staged operation in DP group

### Results

There was no significant difference in demographic data except age and follow-up. Clinical outcomes such as VAS, ODI, SRS-23 were improved after surgery in both groups without any significant difference between the groups. Radiological parameters implicating sagittal correction such as postoperative pelvic incidence – lumbar lordosis (PI – LL), postoperative - preoperative sagittal vertical axis ( $\Delta$ SVA), postoperative LL – preoperative LL ( $\Delta$ LL), pre- and post-operative T1 pelvic angle, pelvic tilt, sacral slope, LL did not show any significant difference between two groups. Coronal parameters such as postoperative – preoperative Cobb's angle ( $\Delta$ CA), coronal imbalance also did not show any significant difference. In terms of indirect decompression, foramen height (8%, preoperative 18.2 mm, postoperative 19.8 mm) and spinal canal cross sectional area (9.5 %, preoperative 114.3 mm<sup>2</sup>, postoperative 126.3 mm<sup>2</sup>) were increased after DLIF. However, the increase rate was lower than that of the other reports.

### Discussion

DLIF combined with open posterior spinal fusion for ASD did not present any favorable deformity correction or clinical outcomes. Moreover, sole indirect decompression using minimally invasive DLIF without direct decompression may result in inadequate decompression considering the relative low rate of indirect decompression effects in ASD surgery.

## LOWER EXTREMITIES MOTOR FUNCTION OF THE L2 NERVE ROOT TRANSECTION CASES IN TOTAL SPONDYLECTOMY

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**Introduction:** During total spondylectomy (TS), the nerve root is often transected to perform the surgery safely. At our institution, the L2 and upper nerve roots are transected, and the L3 and lower nerve roots are preserved. However, since transection of the L2 root also affects the branch to the femoral nerve, the effect on femoral nerve motor dysfunction is uncertain.

**Aim:** This study aimed to investigate the relationship between L2 root transection and postoperative leg motor and sensory function.

**Patients and Methods:** Thirteen patients (7 men, 6 women; mean age: 47 years) who underwent TS with transection of the bilateral L2 roots were included. The motor function of the lower extremities was determined using a modified Frankel classification, and Manual Muscle Testing (MMT) of the iliopsoas (IP) and quadriceps femoris (QF) muscles was performed preoperatively, at 1-week and 1-month post-operation, and on the last follow-up day. The results from the weaker side were used when MMT showed a laterality difference. We also evaluated the amount of time until the patient could start leaving the bed, and postoperative sensory dysfunction.

**Results:** The preoperative MMT score for the IP was 4 in 3 patients, and 5 in 10 patients. The MMT score for the QF was 4 in 1 patient, and 5 in 12 patients. The Frankel classification was E in 10 patients, and D3 in 3 patients. At 1-week post-op, the MMT for the IP muscles decreased to 2 (compared with pre-op) for 1 patient, and QF also decreased 2 for another 1 patient. For the remaining 11 patients, IP and QF was 4 or 5. At 1-month post-op, MMT for the IP and QF muscles improved to above 4 in all patients. On the last follow-up day, decreased MMT of the IP remained in 1 patient, and MMT of the QF improved in all patients. The Frankel classification was D3 in 6 patients, D2 in 5 patients, and C in 3 patients at 1-week post-op, and D3 in 2 patients and E in 11 patients on the last follow-up day. No patient had gait disturbance. The mean time until the patient could start leaving the bed was 8.5 days (range: 4 - 12 days), except for 2 patients. Of the 2 patients, one had surgical site infection and another had deep vein thrombosis. 9 patients had mild numbness in the anterior surface of thigh or groin.

**Discussion and Conclusion:** Although muscle strength of the IP and QF muscles was slightly affected by transection of the L2 roots, it should be noted that walking function remained intact and recovered over time. Transection of the L2 roots appears to be an acceptable procedure in TES.



**THE EFFECT OF PARITY ON AGE-RELATED DEGENERATIVE CHANGES IN SAGITTAL BALANCE**

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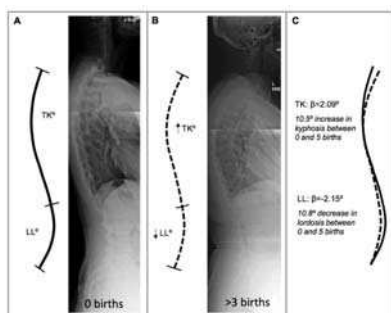
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**Introduction:** Age-related spinal instability and sagittal imbalance are more prevalent in females than males. Examples of which include adult idiopathic scoliosis, hyperkyphosis, and degenerative spondylolisthesis. Increased risk for these conditions in females may be associated with the elevated mechanical loading and ligamentous laxity that occurs during pregnancy and childbirth. For instance, parity, the number times a female has given birth, is positively associated with risk of degenerative spondylolisthesis. Understanding how parity affects sagittal alignment may improve our understanding of disease mechanisms and inform patient care.

**Methods:** A sample of 233 females from the general population was obtained from TwinsUK register. The inclusion criteria were twin participants without spine trauma or spine surgery at the time of enrollment. Parity information was provided via questionnaires. Sagittal balance measurements (cervical lordosis, CL; thoracic kyphosis, TK; lumbar lordosis, LL; pelvic incidence, PI) were collected from standing lateral radiographs using Spineview software. The difference between PI and LL (PI-LL) is predictive of malalignment and was calculated for each subject. Lumbar degeneration (average Pfirrmann grade) and lumbar vertebral BMD were collected from separate studies on the same subjects. Statistical analyses included 1) univariate regression analyses for each independent variable (CL, TK, LL, PI, degeneration, BMD) with parity and 2) backward stepwise multivariate linear regression of each sagittal balance measurement (CL, TK, LL and PI) with parity while including all other variables as potential covariates (listed in Table 1). Variables were tested for normality and collinearity. b coefficients are reported for parity and represent degree change in sagittal balance measures per additional birth. All analyses included robust standard error estimation and clustered twin pairs.

**Results:** Parity data were available for 208 females (64.4 ± 7.4 years) and ranged from 0 to 5 births (0: n=37; 1: n=15; 2: n=95; 3: n=55; 4: n=9; 5: n=3). In univariate analysis, parity did not have an independent relationship with disc degeneration, lumbar BMD, or any of the individual sagittal balance parameters (p>0.05 for all). From multivariate analyses, parity associated with an increase in TK (b=2.09°, p=0.01), a decrease in LL (b=-2.15°, p<0.001), and an increase in PI (b=2.5°, p<0.001; Table 1). Consequently, PI-LL was positively associated with parity independently (b=2.2°, p<0.01). PI-LL was on average 7.0 ± 2.5° greater in multiparous (>2 births) subjects than in nulliparous subjects (p<0.01; Figure 1).

**Conclusion:** This analysis demonstrates parity is positively associated with deterioration of sagittal balance. Interestingly, in addition to TK increasing and LL decreasing with parity, PI increased by 2.5° per birth. Combined, these changes lead to a significant difference between PI and LL (PI-LL) with increasing parity. The difference between PI and LL ("PI-LL mismatch") is characteristic of sagittal imbalance, and >10° is considered severe. Historically, PI has been assumed to be a fixed measure; however, this change with parity may indicate a compound effect of increased loading plus ligamentous laxity on the sacroiliac joint during pregnancy. Given our current observations, we expect the influence of parity on sagittal balance in a symptomatic population may be stronger.



**Figure 1:** A and B have radiographs of example female subjects with 0 births and >3 births. Both are near the average PI-LL difference for those separate parity groups. In addition, A and B have schematics of sagittal alignment, that are then overlapped for comparison in C, showing differences between β coefficients for TK and LL, ranging from the minimum (0) to the maximum (5) number of births in our analysis.

Multivariate Regression of Spinopelvic Measurements

	Thoracic Kyphosis (°) (r <sup>2</sup> =0.45)			Lumbar Lordosis (°) (r <sup>2</sup> =0.64)			Pelvic Incidence (°) (r <sup>2</sup> =0.50)		
	β	RSE	p	β	RSE	p	β	RSE	p
<b>Parity (births)</b>	<b>2.09</b>	<b>0.82</b>	<b>0.01</b>	<b>-2.15</b>	<b>0.59</b>	<b>&lt;0.001</b>	<b>2.53</b>	<b>0.68</b>	<b>&lt;0.001</b>
Age (years)									
BMI (kg/m <sup>2</sup> )									
Cervical lordosis (°)	0.25	0.04	<0.001						
Thoracic Kyphosis (°)				-0.46	0.05	<0.001	0.34	0.06	<0.001
Lumbar Lordosis (°)	0.74	0.07	<0.001				0.85	0.06	<0.001
Pelvic Incidence (°)	-0.37	0.07	<0.001						
Lumbar degeneration (avg Pfirrmann)	2.57	1.06	0.02	-2.9	0.76	<0.001			
Lumbar BMD (g/cm <sup>2</sup> )									

**Table 1:** Results from multivariate regression analysis for TK, LL, and PI with parity and additional covariates. All of the variables on the left were included in the backward stepwise regression and those that associated with dependent variable were retained in the resulting multivariate model.

## IMPORTANCE OF TAILORING SURGICAL STRATEGIES TO PREOPERATIVE PELVIC INCIDENCE (PI) IN ADULT SPINAL DEFORMITY: A COMPARATIVE ANALYSIS OF 138 PATIENTS WITH HIGH PI AND LOW PI

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**Introduction.** Sagittal malalignment drives pain and disability in adults with spinal deformity (ASD). Restoration of global sagittal balance hinges on reestablishing normal lumbopelvic alignment [pelvic incidence (PI) - lumbar lordosis (LL)  $<10^{\circ}$ ]. By extension, patients with high PI necessitate greater LL to achieve lumbopelvic harmony. The purpose of this study is to compare patients with ASD based on variation in pre-operative PI.

**Methods.** Consecutive patients with ASD who underwent thoracolumbar fusion for ASD (2003-2013) at a single institution were retrospectively reviewed. Inclusion criteria: posterior instrumentation from pelvis to L1 or above and minimum 2-year follow-up. Two sub-groups were isolated and compared based on degree of pre-operative PI: "Low-PI" (PI  $\geq 1$  standard deviation *below* the mean) and "High-PI" (PI  $\geq 1$  standard deviation *above* the mean). Peri-operative spinal deformity parameters, operative data, complications, and HRQoLs (ODI, SRS-22, SF-36, VAS back/leg pain) were assessed for each group and compared using ANOVA and Kruskal-Wallis tests. Associations between achievement of lumbopelvic restoration (PI-LL  $<10^{\circ}$ ) and surgical strategies [i.e location of upper-instrumented vertebra (UIV: upper thoracic vs. lower thoracic), type of interbody fusion, posterior only approach, 3 column osteotomy] were evaluated with binomial logistic regression analysis.

**Results.** Four hundred fifty-eight patients who underwent operation had an average PI of  $54.8 \pm 12.8$ . Of this group, 64 had Low-PI (PI  $<42^{\circ}$ ; mean PI  $35.1^{\circ} \pm 5.6^{\circ}$ ) and 74 had High-PI (PI  $>67.6^{\circ}$ ; mean PI:  $74.3^{\circ} \pm 6.1^{\circ}$ ). Average follow-up was  $35.4 \pm 22.9$  months. Baseline demographic data was similar between groups. High-PI had more severe pre-operative sagittal deformities (4cm greater SVA,  $23^{\circ}$  greater PI-LL,  $18^{\circ}$  greater PT). Operative strategies were similar for both groups in regards to 3-column osteotomies, UIV, interbody fusions, and average number of posterior levels fused.

After operation, both groups had significant improvements in all HRQoL scores. Complications and peri-operative HRQoL data were similar between groups. Operation resulted in similar improvements (percentage and absolute) in all radiographic parameters between groups, except for percent improvement in High-PI's PI-LL. In turn, sagittal alignment was satisfactorily restored in Low-PI (Average SVA 2.1cm, PI-LL  $-5^{\circ}$ , PT  $13^{\circ}$ ), while High-PI remained sagittally imbalanced (Average SVA 6.8cm, PI-LL  $18^{\circ}$ , PT  $30^{\circ}$ ). Logistic regression revealed that restoration of PI-LL to  $<10^{\circ}$  was significantly less likely in High-PI than Low-PI (Odds ratio: 0.265, 95% CI: 0.129-0.545,  $p=0.000$ ). While no surgical strategies were predictors of achieving appropriate sagittal balance for Low-PI, an upper thoracic UIV was found to be a predictor of achieving PI-LL  $<10^{\circ}$  in High-PI (Odds ratio: 3.516, 95% CI: 1.090-11.341,  $p=0.035$ ).

**Discussion.** Patients with high PI represent a unique subset of ASD. Compared to patients with Low-PI, High-PI patients at time of operation had more severe sagittal plane deformity and remained sagittally malaligned post-operatively, as lumbopelvic parameters were commonly not restored. One factor that increased the odds of achieving normal lumbopelvic alignment in High-PI patients was using the upper thoracic spine for the UIV. As such, surgical strategies should be tailored to preoperative PI in order to achieve appropriate lumbopelvic and global sagittal alignment in adults with spinal deformity.

## AN ANALYSIS OF RADIOGRAPHIC PARAMETERS COMPARISON BETWEEN LUMBAR SPINE LATERICUMBENT AND FULL-LENGTH LATERAL STANDING RADIOGRAPHS

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**Introduction:** The sagittal spinal parameters can be measured in the spine lateral radiographs, whatever it's taken by the latericumbent position or the full-length lateral radiographs in upright position. Nowadays, more and more studies have paid more attention to the spine sagittal balance. The sagittal lumbar-pelvis parameter measurement is widely used in many studies. Unfortunately, the sagittal alignment is different from various positions. The difference and correlation of lumbar-pelvis parameters between the most popular position, latericumbent position and upright standing position, are still unclear. This study aims to investigate the difference of sagittal parameters in spine lateral radiographs between latericumbent and upright positions, identify the correlation of standing lumbar lordosis (LL) and latericumbent lumbar-pelvis parameters, and establish a linear fitting formula.

**Methods:** The sagittal alignment of 157 continuous patients was assessed using Surgimap software from two kinds of lateral radiographs, to acquire the following parameters: lumbar lordosis (LL), pelvic incidence (PI), pelvic tilt (PT), sacral slope (SS), L4-L5 intervertebral angle (IVA4-5), L4-L5 intervertebral height index (IHI4-5), and PI-LL. The statistical analysis was calculated by SPSS 19.0 software. The Kolmogorov-Smirnov Test, Pair t-tests, Pearson correlation analyses, and Multivariate linear regression analysis were used to analyze the data.

**Results:** We found there were significantly statistical difference in LL, SS, PT, IVA4-5, and PI-LL, except for PI and IHI4-5 in the two positions. The result showed a significant relativity between standing LL and latericumbent LL, PI, and SS. Thus, a predictive formula of standing LL was obtained with latericumbent LL, PI, and SS as predictors.

**Discussion:** Not all of the sagittal parameters obtained from two positions are identical. When making surgery plans before lumbar spine surgery, spinal surgeons should give sufficient consideration to differences between the two views. We can predict standing LL with the formula when we couldn't get whole-spine lateral standing radiographs.

## SPINO-PELVIC SAGITTAL IMBALANCE AS A RISK FACTOR FOR ADJACENT SEGMENT DISEASE AFTER SINGLE-SEGMENT PLIF

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**Introduction:** The importance of spino-pelvic balance and its implications for clinical outcomes after spinal arthrodesis have been shown by recent studies. However, little is known about the relationship between adjacent segment disease (ASD) after lumbar arthrodesis and spino-pelvic alignment. The purpose of this study was to clarify the relationship between spino-pelvic radiographic parameters and symptomatic ASD after L4/5 single-level posterior lumbar interbody fusion (PLIF).

**Methods:** This was a retrospective 1:5 matched case-control study. Twenty patients who had undergone revision surgery for symptomatic ASD after L4/5 PLIF and did have standing radiographs of the whole spine before primary and revision surgeries were enrolled from 2005 to 2012. As a control group, 100 age, sex, and pathology-matched patients who had undergone L4/5 PLIF in the same period, had no signs of symptomatic ASD for more than 3 years, and could have whole spine radiographs at pre-operation and last follow-up were selected. Mean age at the time of primary surgery was 68.9 years in the ASD group and 66.7 years in the Control group. Several radiographic spino-pelvic parameters were measured as follows: sagittal vertical axis (SVA), thoracic kyphosis (TK), sacral slope (SS), pelvic tilt (PT), pelvic incidence (PI), lumbar lordosis (LL) and segmental lordosis at L4/5 (SL) in sagittal view, and C7-the central sacral vertical line (C7-CSVL) in coronal view. Radiological parameters were compared between the groups.

**Results:** No significant change was found between pre- and post-operative radiographic parameters in each group. In terms of pre-operative radiographic parameters, the ASD group showed significantly lower LL (40.7° vs. 47.2°,  $P < 0.01$ ) and higher PT (27° vs. 22.9°,  $P < 0.05$ ) than the Control group. SVA  $\geq 50$  mm was observed in 10 of 20 patients (50%) in the ASD group and in 21 of 100 patients (21%;  $P < 0.01$ ) in the Control group. PI-LL  $\geq 10^\circ$  was seen in 15 of 20 patients (75%) in the ASD group and in 40 of 100 patients (40%;  $P < 0.01$ ) in the Control group on pre-operative radiographs. Postoperatively, the ASD group showed significantly lower TK (22.5° vs. 30.9°,  $P < 0.01$ ) and lower LL (39.2° vs. 48.1°,  $P < 0.05$ ) than the Control group. PI-LL  $\geq 10^\circ$  was seen in 15 of 20 patients (75%) in the ASD group and in 43 of 100 patients (43%;  $P < 0.01$ ) in the Control group.

**Discussion:** Pre-operative global sagittal imbalance (SVA  $> 50$  mm and higher PT) and pre- and postoperative lower LL and PI-LL mismatch were significantly associated with ASD. Therefore, even with a single-level PLIF, appropriate SL and LL should be obtained at surgery to improve spino-pelvic sagittal imbalance. The results also suggested that the achievement of the appropriate LL and PI-LL prevents ASD after L4/5 PLIF.

## THE INCIDENCE OF PLEURAL FLUID AND ITS ASSOCIATED RISK FACTORS FOLLOWING POSTERIOR CORRECTIVE SPINAL FUSION IN PATIENTS WITH ADOLESCENT IDIOPATHIC SCOLIOSIS

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**Introduction:** Subclinical pleural fluid (PF) is often observed following posterior corrective spinal fusion (PCSF) in adolescent idiopathic scoliosis (AIS) patients. However, few reports have been published regarding the incidence, characteristics, and associated risk factors.

**Aim:** To determine the incidence of PF and its associated risk factors following PCSF in patients with AIS, and make surgeon easy to rule out other potential causes of PF.

**Material and Methods:** A total of 76 AIS patients who underwent PCSF and followed-up for a minimum of 1 year were enrolled in this study. The volume of PF in each thorax was detected with thoracolumbar CT images taken preoperatively, at 1 week and 3 months follow-up. The patients were divided into two groups: Group A included patients who developed PF 1 week after surgery, and Group B included patients who never developed PF during the course of the study. In addition, patient demographics included comorbidities, operation factors, serum albumin levels, scoliotic parameters, occurrence of malposition of pedicle screw insertion, and complications were collected and associated risk factors for PF accumulation were analyzed with univariate (paired t-test and Fisher's exact test) and multivariate logistic regression analyses.

**Results:** There were 71 female and 5 male patients (mean age, 16.2 years). All cases had a right convex curve in thoracic spine. The mean number of fused levels was 10.0. Other causes of PF were not observed. Group A and B consisted of 54 patients (71%) and 22 patients (29%), respectively. The distribution was almost same in patients with Lenke type 1 to 3 curves (71% in 58 cases), and those with Lenke 5 and 6 curves (72% in 18 cases). In Group A, PF accumulated bilaterally in 36 cases, only in the right thorax in 13 cases, and only in the left thorax in 5 cases. There was significant difference between the depth of PF in the right and left sides ( $p < 0.001$ ). All patients were asymptomatic for PF, except 2 patients experienced prolonged fever (over 38 degrees C) over 3 days postoperatively. All but 1 case had no evidence of PF at 3 month follow-up. In univariate analysis, the number of fused levels ( $p = 0.021$ ), the amount of autotransfusion during operation ( $p = 0.023$ ), and intraoperative bleeding ( $p = 0.04$ ) in Group A were significantly larger than those in Group B. However, multivariate analysis identified 11 or more fused levels as a significant independent risk factor for PF accumulation (odds ratio: 3.88, 95% confidence interval: 1.31-11.47), without any potential interaction. Same results were identified in subanalysis including patients with only Lenke type 1 to 3 curves (odds ratio: 4.63, 95% confidence interval: 1.36-15.79). Pedicle screw malposition, the mean coronal curve correction rate and other scoliotic factors were not significantly correlated.

**Conclusion:** PF was observed in 71% of the patients who underwent PCSF for AIS. The right thorax was more commonly involved than the left. A higher number of fused levels (11 or more) was an independent risk factor of PF.

## PHARMACHOMETRICS FOR CHANGING BEHAVIORS INDUCED BY LUMBAR FACETECTOMY AND REPEATED COLD STRESS IN RATS

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### INTRODUCTION:

Nonspecific low back pain is one of the main complaints related to bipedalism in humans. Although medication is effective for nonspecific low back pain, it is controversial which medications are effective. One reason for this controversy is the heterogeneity of patients with nonspecific low back pain. Therefore, a suitable animal model of nonspecific low back pain is needed to evaluate the efficacy of medication. Discogenic low back pain is thought to be one cause of nonspecific low back pain. According to Lotz, three factors are important in the pathogenesis and treatment of discogenic low back pain: inflammation, innervation, and hypermobility. Psychosocial factors can also increase low back pain. We have developed and reported a rat model of low back pain induced by lumbar facetectomy to meet the conditions as mentioned before. In this model, the repeated cold stress increased the magnitude of the behavioral changes in our previous study. The purpose of the present study was to compare the efficacy of medications used to treat nonspecific low back pain utilizing our animal model.

### METHODS:

All rats underwent bilateral L4–5 facetectomy and repeated cold stress loading. Fifty rats were divided into 5 groups (n = 10 in each group): 1) control group—rats given no drugs; 2. acetaminophen group—rats given acetaminophen (100 mg/kg/day); 3) loxoprofen group—rats given loxoprofen sodium hydrate (5 mg/kg/day); 4) duloxetine group—rats given duloxetine (15 mg/kg/day); and 5) pregabalin group—rats given pregabalin (10 mg/kg/day). Repetitive oral administration of each drug was applied for 3 weeks except for the control group from 7 weeks after the operation. The CatWalk system and the von Frey test were used to evaluate the painkilling effect of each drug at 9 and 10 weeks postoperatively.

### RESULTS:

The CatWalk system showed no significant differences in gait parameters in the acetaminophen and loxoprofen groups compared with the control group. In the duloxetine group, there were no significant differences at 9 weeks postoperatively; however, significant differences in swing time and number of steps were observed 10 weeks postoperatively compared with the control group. In the pregabalin group, swing speed of the front paw, stride length, and average speed were significantly higher, and the number of steps, stand time, step cycle, and duty cycle were significantly lower compared with the control group. There were no significant differences in the von Frey test in the acetaminophen, loxoprofen and duloxetine groups, while the withdrawal threshold increased more in the pregabalin group.

### DISCUSSION:

Our evaluation of the efficacy of medications used clinically for patients with nonspecific low back pain showed that only pregabalin improved the behavioral changes in our rat model. Acetaminophen, loxoprofen and duloxetine were not effective in our low back pain model. Collectively, these results suggest that behavioral changes observed in this model may result from innervation of the degenerative intervertebral disc but not inflammation or psychological distress. Innervation of the degenerative intervertebral disc may play an important role in mechanisms causing nonspecific low back pain.

## GAIT ANALYSIS OF LUMBAR SPINAL STENOSIS USING A WIRELESS INERTIAL MEASUREMENT UNIT

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### Introduction

Previous quantitative gait analyses using walk tests in patients with lumbar spinal stenosis (LSS) have been limited by the length of the measurable walkway. The analysis of intermittent claudication on flat ground has previously been impossible due to this limitation. Miniature, wireless inertial sensors have solved this problem. In this study, we used a novel wireless inertial measurement unit (IMU) to analyze the gait characteristics of pre- and postoperative patients with LSS.

### Methods

Eighteen patients (7 males and 11 females, mean age 72 years) who had undergone lumbar surgery for LSS were enrolled. A six-minute walking test, comprised of shuttling between 30 m straight walkways, was performed before surgery and 12 weeks after surgery. The IMU was mounted on the spinous process of the first thoracic vertebra, and data were transmitted to a personal computer via Bluetooth. Patients were encouraged to maintain their maximum walking speed and reach their maximum walking distance. Three-dimensional (Euler angles: pitch, roll, and yaw; see Figure) accelerations and angular velocities were measured and analyzed using a Kalman filter. The paired *t*-test and Spearman's rank correlation coefficient were used for statistical analysis, and  $p < 0.05$  was considered statistically significant.

### Results

The maximum walking distance (pre-op:  $281.5 \pm 136.3$  m, post-op:  $356.6 \pm 88.0$  m,  $p = 0.01$ ) and the step length (pre-op:  $0.48 \pm 0.12$  m, post-op:  $0.55 \pm 0.11$  m,  $p = 0.01$ ) significantly increased after surgery. The postural sway range of pitch rotation (anterior–posterior) significantly decreased (pre-op:  $3.24 \pm 1.42$  degree, post-op:  $2.55 \pm 1.14$  m,  $p = 0.01$ ) after surgery. The post-op change of the sway range of pitch rotation was negatively correlated with the amount of change in both cadence (pre-op:  $114.1 \pm 14.3$  steps/min, post-op:  $115.71 \pm 12.2$  steps/min) and step length ( $R = -0.589$ ,  $p = 0.01$ ,  $R = -0.543$ ,  $p = 0.02$ , respectively).

### Discussion

The results of this study reveal post-op improvements in maximum walking distance, step length, and anterior–posterior postural sway. Additionally, improvements in postural sway are correlated with improvements in both step length and cadence. These improvements came after the surgical treatment for LSS and thus may be the characteristic gait improvements in this condition. This wireless IMU is useful for quantitative gait analysis in patients with LSS due to its small size, low cost, and ability to transmit data up to 100 m during a flat-ground walking test.

The use of a wireless IMU is valuable for the quantitative gait analysis of LSS. Our results show that the gait characteristics of patients with LSS are short step length and large anterior-posterior postural sway.

## LUMBAR SPINE SHAPE AS A BIOMARKER OF LUMBAR DISC DEGENERATION: A PRELIMINARY ANALYSIS

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**Introduction:** Low back pain is the top global cause of years lived with disability. Lumbar disc degeneration (LDD) is a condition, which has been found to be significantly associated ( $p < 0.001$ ) with non-specific low back pain (NSLBP), affecting 30% of the UK population annually. Current treatment approaches with a psychosocial focus result in, at best, moderate treatment effects for LDD patients, which makes holistic research necessary in order to understand this condition and target management. The intrinsic shape of the lumbar spine has been previously characterised (1) and it appears that individuals retain a unique spinal signature which is independent of the position they assume. This preliminary analysis aims to characterise the lumbar spine curvature in an asymptomatic group of subjects with and without LDD in order to examine the effects of LDD on the intrinsic lumbar spine shape.

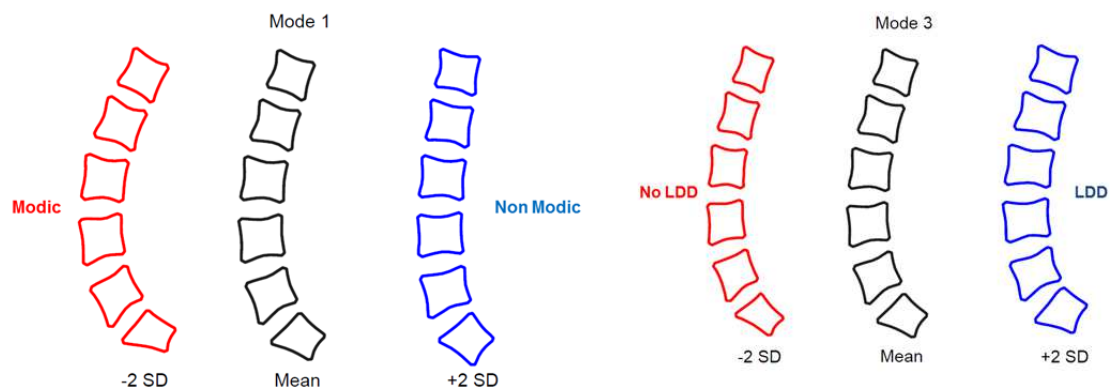
**Methods:** 31 healthy, asymptomatic volunteers (18 males, 13 females, mean 52 years (SD 11)) were recruited. 3T MRI was used to acquire T2 weighted sagittal lumbar spine images (L1-L5/S1). LDD was determined by one, blinded, consultant radiologist (AL) using modified Pfirrmann grading. An LDD sum score (L1-L5/S1) quantified the degree of degeneration in each subject. Modic or vertebral end plate changes were also identified due to their highly significant association with LDD. Statistical Shape Modelling (SSM) was used to model lumbar spine morphology. SSM identified variations in lumbar spine shape as different 'modes' of variation with images receiving a score for each mode, quantifying deviation from the mean. The relationships between lumbar spine shape, LDD and Modic changes were examined using Pearson correlations and Mann Whitney U tests.

**Results:** SSM identified 7 modes of variation in spinal shape that accounted for 91% of the overall variance. Greater LDD sum scores were associated with vertebrae with larger AP diameter and more anteriorly tilted S1 vertebrae ( $P=0.03$ ), scoring higher Mode 3 scores (10% variance). Subjects with LDD scores  $\geq 6$  were also more likely to have smaller L4-S1 disc spaces ( $P=0.02$ ) as identified by a significant difference in Mode 7 scores (2% variance). Participants with Modic changes had a curvier or more lordotic lumbar spines ( $P=0.02$ ), scoring significantly lower in shape Mode 1 (55% variance). They also had a more evenly distributed lumbar curve ( $P=0.048$ ), scoring lower in Mode 2 (12% variance).

**Discussion:** Preliminary findings have identified an association between the degree of disc degeneration and both the diameter of the lumbar vertebrae and the disc space height in asymptomatic subjects. An association between Modic changes and lordosis in the absence of pain was also demonstrated. Since compensatory kyphosis of the lumbar spine is commonly observed in patients with LDD and recurrent pain, further examination using patient data will be required.

**Conclusion:** Preliminary analysis within an asymptomatic population confirms that intrinsic lumbar spine shape is different in those with and without LDD.

**Funding:** This study was supported by a travel fellowship awarded to JAD by the Society of Back Pain Research. JAD is funded by an Arthritis Research U.K AHP Fellowship.



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## SUPERIOR CORTICAL SCREW IN LUMBAR SPINE: A BIOMECHANICAL AND MICRO-STRUCTURE BASED STUDY IN OSTEOPOROTIC HUMAN VERTEBRAE

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**Introduction:** Osteoporosis reduces the bone-screw purchase, potentially decreasing screw pullout strength and other biomechanical properties. Clinically, there are various entry points used for pedicle screws. Modification of pedicle screw insertion to improve screw stabilization may help to compensate for the detrimental effects of decreased vertebral bone mineral density. The study try to verify the pullout strength of superior cortical screw (SCS) of osteoporotic lumbar spine was higher than Magerl' method by means of biomechanical test and microarchitecture analysis.

**Methods:** In our study, two modes of screw insertion were performed in 13 cadaveric lumbar vertebrae: Magerl' method in the left pedicle, and SCS method in the right (its entry point located vertically 3 mm above Magerl' point). Before screw fixations, the pedicle and its corresponding anterior vertebral body part were divided into six levels equally from superior to inferior by micro-CT and tested for microarchitecture properties, such as BMD, BV/TV, Tb.N, Tb.Sp and Tb.Th. Furthermore, pedicle was assessed separately, which was divided into 3 levels horizontally and tested, as well. And after screw fixations, microarchitecture properties of the bone surrounding screws were also analyzed. Finally, the screw pullout strength was tested biomechanically.

**Results:** BMD, BV/TV, Tb.N, Tb.Sp and Tb.Th were significantly different between the upper and the middle thirds of the pedicle and its corresponding anterior vertebral body ( $p < 0.05$ ). And BMD, BV/TV, Tb.N, Tb.Sp in the upper two thirds varied every 2 millimeters in thickness ( $p < 0.05$ ). As for pedicle only, BMD, BV/TV, Tb.N, Tb.Sp and Tb.Th were also statistically different between the upper and the middle thirds ( $p < 0.05$ ). Biomechanical test showed pullout strength was increased 22.4% by SCS, comparing with Magerl' method ( $p < 0.05$ ). Furthermore, the pullout strength was statistically correlated to BMD ( $p < 0.01$ ), BV/TV ( $p < 0.01$ ) and Tb.Th ( $p < 0.01$ ).

**Conclusions:** The bone structure is denser in the upper one-third of the pedicle and its corresponding anterior vertebral body part, which contributes to the elevated pullout strength of pedicle screw. Superior cortical screw for screw insertion may be another alternative technique in posterior lumbar instrumentation, especially in osteoporotic patients.

## THE MECHANISM OF THORACOLUMBAR BURST FRACTURE MAY BE RELATED TO THE BASIVERTEBRAL FORAMEN

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**Introduction** The basivertebral foramen (BF), locating in the middle posterior wall of the vertebral body, may induce local weakness and contribute to the formation of the retropulsed bone fragment (RBF) in thoracolumbar burst fracture (TLBF). The objective of this study is to clarify the relationship between the basivertebral foramen (BF) and the retropulsed bone fragment (RBF) in thoracolumbar burst fracture (TLBF) and explain the mechanism of RBF using radiology, microarchitecture of vertebral and biomechanical cadaveric experiment.

**Methods:** 74 patients suffering from burst fractures with RBFs were studied using CT reconstruction imaging, and related parameters were measured (length, height, width of RBF and vertebral body) . Ten cadaveric spine were selected and Micro-CT scans were then used to divide each vertebral body into three layers (Superior, Middle, Inferior), each of which was further divided into 9 regions (R1 – R9). Microarchitecture parameters were calculated, including bone volume fraction (BV/TV), bone mineral density (BMD), trabecular connectivity (Conn.D), and trabecular number (Tb.N) and thickness (Tb.Th). Differences were analyzed between regions. Burst fractures were simulated on cadaveric spines in order to test their relationship between RBFs and BF.

**Results:** The length and height of RBFs ranged from one-third to half of vertebral body length and height, and RBF width was usually one-third of vertebral body width. BV/TV, Conn.D, Tb.N, Tb.Th, and BMD were often lowest in the MR2 and MR5 regions, which correspond to regions most affected by burst fracture. SR2 and SR5 tended to be the most vulnerable regions of the superior layer. In simulated burst fractures, the fracture line of RBF went across the vertex or upper surface of the BF.

**Discussion:** The most vulnerable regions in the vertebral body lie within or just superior to the basivertebral foramen. The central MR2 region in particular could become a potential risk of fracture and RBF formation. This work focuses on clarifying the mechanism of the formation of RBF in TLBF fragments. And it will be of great significance in estimating nerve injury, vertebral canal occlusion, fracture stability, and longitudinal ligament rupture. Then it can guide our choice of surgical methods.

## THE CHANGES OF SAGITTAL SPINO-PELVIC MORPHOLOGY IN LONG-TIME LOADING CHINESE PERSONS COMPARED WITH THE NON-LOADING

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**Introduction :** A few studies have been showed there were obvious variations of spino-pelvic parameters between populations with different ethnicity background. However, as a large agricultural country, studies about the sagittal spino-pelvic alignment of Chinese persons after long-term loading have not yet been found. The primary objective of this study is to evaluate the changes of sagittal spino-pelvic morphology between long-time loading and non-loading of Chinese persons.

**Methods:** We retrospectively reviewed 263 patients from 2012 to 2015 in outpatient and hospitalization department of SRRSH hospital who suffered from back pain and performed long-standing lateral X-ray. 85 of them were farmers with a long-time loading history over 20 years (Group Loading), while others were office workers who denied long-term loading history (Group Non-loading). Two researchers measured the parameters independently as followings and analyzed the results: thoracic kyphosis (TK), lumbar lordosis(LL), T9 sagittal offset, T1 sagittal offset, sacral slope(SS), pelvic incidence(PI) ,pelvic tilt(PT), C7 tilt, spino-pelvic angle(SPA), and sagittal vertical axis (SVA).

**Results:** Group Loading included 37 males and 48 females with the average age  $62.8\pm 8.8$  years, average body mass index(BMI)  $22.6\pm 4.4$  and bone mineral density(BMD)  $1.04\pm 0.25$  (g/cm). Group Non-loading included 71 males and 107 females with the average age  $59.2\pm 10.7$  years average BMI  $23.9\pm 3.1$  and BMD  $1.15\pm 0.24$  (g/cm). The mean value of spino-pelvic parameters in group Loading were  $38.8\pm 17.1^\circ$  for TK,  $39.9\pm 29.3^\circ$  for LL,  $11.9\pm 5.7^\circ$  for T9 sagittal offset,  $4.0\pm 5.9^\circ$  for T1 sagittal offset,  $26.2\pm 12.0^\circ$  for SS,  $46.1\pm 11.6^\circ$  for PI,  $22.0\pm 12.4^\circ$  for PT,  $93.4\pm 8.0^\circ$  for C7 tilt,  $113.6\pm 14.5^\circ$  for SPA, and  $39.9\pm 60.0$ mm for SVA, while these in group Non-loading were  $33.4\pm 18.5^\circ$  for TK,  $36.0\pm 23.4^\circ$  for LL,  $10.4\pm 5.4^\circ$  for T9 sagittal offset,  $2.6\pm 5.2^\circ$  for T1 sagittal offset,  $27.4\pm 10.4^\circ$  for SS,  $47.1\pm 12.2^\circ$  for PI,  $20.1\pm 12.6^\circ$  for PT,  $93.1\pm 6.6^\circ$  for C7 tilt,  $114.8\pm 14.6^\circ$  for SPA, and for  $42.3\pm 58.4$ mm SVA, respectively. The comparison of gender, age and weight between two group were not significant ( $p>0.05$ ). The comparison of spino-pelvic parameters showed that the TK and T9 sagittal offset in group Loading were significant higher than the group Non-loading in all ages ( $p<0.05$ ), and PT in female was significant higher in the age of 40-50 ( $p<0.05$ ), while the LL in male value was significant lower in the age of 40-50 ( $p<0.05$ ). T1 sagittal offset had a tendency to be higher in group Loading while the SS, SVA value had a tendency to be lower on the contrary. The comparison of PI, C7 tilt, SPA value was not significant between the two groups ( $p>0.05$ ).

**Discussion:** Long-term loading tends to increase the risk of pathological thoracic kyphosis and lumbar lordosis loss. At the meanwhile, the spine and pelvis can compensate with pelvic retroversion and lumbar lordosis loss to maintain the stability of sagittal spino-pelvic

## AN INCREASED CHANGE IN THE POSTERIOR PELVIC INCLINATION FROM THE SUPINE TO STANDING POSITION IN ELDERLY OSTEOARTHRITIS OF THE HIP IS ASSOCIATED WITH THE SAGITTAL SPINO-PELVIC ALIGNMENT

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### Introduction

Although an increased change in the posterior pelvic inclination from the supine to standing position in elderly hip osteoarthritis (HOA) may be associated with aging and sagittal spino-pelvic alignment (SSPA), there is little evidence to support this view. The object of this study was to determine the association between the postural pelvic posterior inclination and the SSPA.

### Methods

A total of 324 patients (55 men and 269 women: average age 65 years old) treated by total hip arthroplasty due to HOA were evaluated. The SSPA parameters analyzed in the present study were the sagittal vertical axis (SVA), lumbar lordosis (LL), lumbar range of motion (DLL), sacral slope (SS), pelvic incidence (PI), and pelvic tilt (PT). The posterior pelvic inclination angle (PIA) in the supine position and the change in the PIA from the supine to the standing position ( $\Delta$ PIA) were measured using antero-posterior pelvic radiographs. Positive and negative PIA were defined as  $\Delta$ PIA over and under  $10^\circ$ , respectively.

The values of these parameters were compared among 10-year groups. The levels of the SRS-Schwab classification modifiers were used to investigate the degree of sagittal malalignment. The findings of PI-LL  $> 20^\circ$ , SVA  $> 9.5$  cm and PT  $> 30^\circ$  were considered to indicate marked sagittal alignment based on the SRS-Schwab classification.

The significance of differences among the age groups were evaluated using an analysis of variance (ANOVA) with the Bonferroni's correction. A value of  $P < 0.05$  was considered to be significant.

	Positive PIA (n=31)	Negative PIA (n=92)	P value
SVA	88mm	65mm	$P < 0.05$
TK	$29^\circ$	$33^\circ$	$P = 0.17$
LL	$24^\circ$	$40^\circ$	$P < 0.001$
SS	$26^\circ$	$33^\circ$	$P < 0.05$
PT	$34^\circ$	$18^\circ$	$P < 0.001$
PI	$59^\circ$	$53^\circ$	$P = 0.15$
PI-LL $> 20^\circ$	64%	27%	$P < 0.001$
SVA $> 9.5$ cm	45%	22%	$P < 0.05$
PT $> 30^\circ$	55%	10%	$P < 0.001$

**Results** The percentage of patients with positive PIA was 13% for the whole patient population, 3% in those in 50s or younger, 8% in those in their 60s and 36% in those in their 70s or older. Among the subjects in their 70s or older, the positive PIA group (n=31) showed significantly lower LL and higher SVA than the negative PIA group (n=92) (Figure). With regard to the sagittal modifiers in the SRS-Schwab classifications of their 70s or older, the PI-LL and PT levels of the positive PIA group were significantly worse than those in the negative PIA group ( $P < 0.01$ ).

### Discussion

An increased change in the posterior pelvic inclination from the supine to standing position in HOA patients is associated with aging and sagittal spino-pelvic malalignment, which may be referred to as secondary hip-spine syndrome. Patients in their 70s with sagittal

spino-pelvic malalignment should have both their supine and standing posture evaluated by hip X-ray before total hip arthroplasty to ensure accurate implantation.

## KINEMATIC AND KINETIC INDICES FOR LUMBAR SPINE STABILITY IN SUBJECTS WITH RECURRENT LOW BACK PAIN

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**Introduction:** The purpose of this study was to evaluate the relationship between normalized kinematic and kinetic stability indices for spinal regions during non-dominant leg standing with eyes-open and eyes-closed conditions between subjects with recurrent low back pain (LBP) and control subjects.

**Methods:** Forty-two subjects participated in the study, including 22 subjects with LBP (12 male, 10 female) and 20 control subjects (12 male, 8 female). The kinematic stability index for the spinal regions (core spine model, lumbar spine, lower thorax, and upper thorax) and the kinetic stability index (utilizing force plate) were measured. All participants were asked to maintain non-dominant leg standing for 25 seconds, with the dominant hip and knee flexed approximately 90 degrees.

**Results:** For the kinematic index for stability, the visual condition ( $F=30.06$ ,  $p=0.0001$ ) and spinal region ( $F=10.82$ ,  $p=0.002$ ) were statistically significant. The post hoc test results indicated a significant difference in the lumbar spine compared with the upper and lower thorax and the core spine model. The kinetic stability index during the eyes-closed condition significantly decreased in the LBP group ( $t=-3.24$ ,  $p=0.002$ ).

**Discussion:** The subjects with recurrent LBP demonstrated higher lumbar spine stability in the eyes-open condition. This higher stability of the lumbar spine might be due to a possible pain avoiding strategy from the standing limb. The LBP group also demonstrated significantly decreased kinetic stability during the eyes-closed condition. The subjects with recurrent LBP rely on visual input due to decreased proprioception from lumbar spine injuries while minimizing normalized kinetic changes from the ground. Clinicians need to consider both kinetic and kinematic indices while considering visual condition for lumbar spine stability in subjects with recurrent LBP.

**Keywords:** lumbar spine; stability; recurrent low back pain; vision; kinetic; kinematic.

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## IN VITRO EXPERIMENT ANALYZING THE INFLUENCE OF THE RIB CAGE ON HUMAN THORACIC SPINE STABILITY BY STEPWISE REDUCTION OF THE SINGLE STRUCTURES

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**Introduction:** The rib cage is considered to stabilize the thoracic spine. However, the effect of surgical interventions concerning the rib cage, e.g. in scoliosis treatment, or traumata like rib and sternal fractures is still little known. The purpose of the study was to determine the contribution of the rib cage and its single structures to human thoracic spine stability. Additionally, data of the mechanical properties were generated with intent to validate finite element models of the human thoracic spine including the rib cage.

**Methods:** Six fresh frozen human thoracic spine specimens (C7-L1, 56 years in average, range 50-65) including the intact rib cage with intercostal muscles were tested quasi-statically in a custom-built spine tester and monitored with an optical motion tracking system. While applying 2 Nm pure moments in flexion/extension (FE), lateral bending (LB), and axial rotation (AR), the relative motions of the functional spinal units of the thoracic spine (T1-T12) were studied (1) in intact condition, (2) after removing the intercostal muscles, (3) after median sternotomy, (4) after removing the anterior part of the rib cage up to rib stumps, (5) after removing the right sixth to eighth rib heads to simulate a scoliosis correction, and finally (8) in the isolated spine after removing all rib heads. Statistical analysis was performed using Shapiro-Wilk-test for normality ( $p > 0.1$ ), t-test of significance ( $p < 0.05$ ), and Holm-Bonferroni method to control the familywise error rate.

**Results:** The range of motion (ROM) increased largely in all three loading planes (FE: + 60%, LB: + 58%, AR: + 130%) in the isolated spine compared to the intact condition (FE:  $11 \pm 4^\circ$ , LB:  $15 \pm 4^\circ$ , AR:  $20 \pm 7^\circ$ ). Removing the anterior part of the rib cage already induced a significant ( $p < 0.05$ ) increase of the ROM in the three loading planes (FE: + 52%, LB: + 42%, AR: + 94%). The intercostal muscles had a significant influence on thoracic spine stability in LB (+ 22%) and in AR (+ 23%). The sternotomy caused a significant increase of the ROM in FE (+ 12%) and in AR (+ 22%) compared to its previous condition. Removing the right sixth to eighth rib heads resulted in a slight, symmetric increase of the ROM. Coupled motions were detected mainly in lateral bending with secondary axial rotation in the opposite direction and slightly in axial rotation with secondary lateral bending in the same direction.

**Discussion:** The rib cage has a significant influence on human thoracic spine stability, e.g. in axial rotation by a factor of approximately 2. Therefore, the thoracic spine should be tested with regard to all rib cage structures in vitro. Because of coupled motions, the ranges of motion of the functional spinal units could not be measured and should be analyzed separately in a monosegmental test setup with entire ribs and its sternal portion. Median sternotomy, which is performed in cardiac surgeries, as well as removing the rib heads for scoliosis correction, showed a significant influence on thoracic spine stability and should be clinically considered.

**Conflict of interest statement:** The institution of the authors has received funding from the German Research Foundation (DFG), Project WI 1352/20-1.

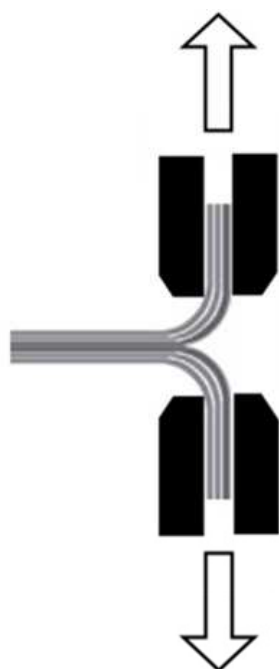
## THE EFFECT OF COMPRESSIVE LOADING ON THE DELAMINATION STRENGTH OF THE ANNULUS FIBROSUS

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**Introduction:** The intervertebral disc (IVD) is designed to withstand compressive loads due to hydrostatic pressure within the nucleus pulposus and the strong laminate structure of the annulus fibrosus. When under compression, however, the IVD bulges outward such that high stresses are generated within and between the annulus layers, possibly leading to microscopic damage. This study aimed to assess damage to the adhesive bond, or interlamellar matrix, of the annulus following compressive loading.

**Methods:** Twenty three bovine tail functional spine units (FSU) were obtained from a common source and frozen at -20°C until testing. Each FSU was dissected to leave only osteoligamentous structures and randomly assigned to one of three conditions for two hours: 0N, 250N, and 1000N. The bovine tail endplate area is approximately one third the size of the human lumbar endplate and therefore 250N and 1000N are similar magnitudes to what the lumbar spine would experience during upright standing and moderate lifting, respectively. All FSUs were mounted in custom aluminum cups and secured with dental plaster. Following compressive loading, multilayer annulus samples (6 layers thick) were dissected from each FSU. Samples were initially manually delaminated between the innermost two layers to create a T-peel sample (Figure 1). Samples were then fully delaminated at 0.5mm/sec (UStretch, Cellscale, Waterloo, ON). Peel strength and stiffness were calculated for each sample and statistically compared between the three loading conditions.



**Results:** Peel strength did not differ between the three loading conditions ( $p > 0.05$ ). For peel stiffness, although not significant, a trend towards reduced stiffness was observed in both the 250N and 1000N conditions compared to the unloaded control ( $p = 0.065$ ,  $0.069$ , respectively; approximate 23% drop in stiffness in both loading conditions) with no differences observed in stiffness between the 250N and 1000N conditions ( $p = 0.90$ ).

**Discussion:** The tensile strength of the interlamellar matrix is less than that of individual layers of the [1,2] and therefore is more susceptible to damage. It's plausible that the interlamellar matrix could become damaged when the IVD is compressed due to the tensile strain that the annulus experiences. This study found that physiological compressive loads do not appear to affect interlamellar peel strength when exposures are short term (i.e. two hours). However, the trend towards decreased stiffness is noteworthy. It is possible that these physiological loads are altering the mechanical properties of the interlamellar matrix, which, in time, may negatively affect its strength. However, it is also possible, given that no differences were observed between the 250N and 1000N loading conditions, that this reflects an effect of creep and residual deformation in the interlamellar matrix that may be present regardless of the magnitude of loading. In order to test this, a future condition where the loaded IVD is allowed to recover unloaded for a period of time before peel testing would be necessary.

**Figure 1:** T-peel test. Tabs created via manual delamination were clamped in order to fully delaminate each sample at 0.5mm/sec. Arrows indicate direction of tension to propagate delamination.

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## THE EFFECT OF SHORT DURATION LOW BACK VIBRATION ON PAIN DEVELOPED DURING PROLONGED STANDING

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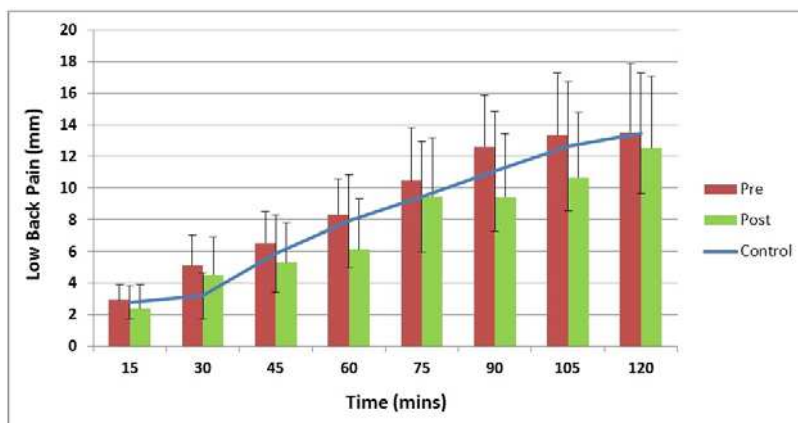
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**Introduction:** Standing-induced low back pain (LBP) is becoming more common in the workplace and has been shown to develop in periods of standing as short as two hours. Vibration, using a massage belt, is often prescribed as a method of pain management over drug alternatives. The purpose of this study was to determine if vibration applied to the low back could alleviate LBP developed during prolonged standing.

**Methods:** Two separate collections (part I and II) were performed. The first included 18 participants and the second included 15 additional participants. In part I, the aim was to ascertain the effect of vibration applied after a prolonged period of standing. Participants stood for 2.5 hours while performing standardized tasks. After two hours, which has been shown to induce LBP in previously asymptomatic, healthy individuals [1,2], vibration was applied over the lumbar region of the back via a vibration massage belt (53Hz vibration) for three-minute durations at both the 2-hour and 2-hours 15 minute time points. In part II, the aim was to ascertain the effect of vibration applied intermittently over two hours of standing. During a control day, no vibration was applied during the two hours of standing; on an experimental day, vibration was applied via the vibration belt in three-minute durations every 15 minutes for two hours. During all data collections, perceived LBP was collected via a 100mm visual analogue scale every 15 minutes. Force plate data were also collected to determine centre of pressure changes.

**Results:** LBP during all data collections significantly increased over time ( $p < 0.01$ ). In part I, both vibration exposures decreased LBP immediately after vibration; however pain returned within 15 minutes post-vibration. In part II, vibration also significantly decreased LBP immediately following each vibration exposure ( $p = 0.039$ ); however, when compared to the LBP developed on the control day, no differences in total LBP development were observed ( $p = 0.69$ ) (Figure 1). For both part I and II, decreases in anterior-posterior and medial-lateral centre of pressure movement were observed during each bout of vibration.

**Discussion:** Vibration is becoming increasingly popular as a pain management modality. This study aimed to determine vibration's effect on reducing LBP development during prolonged standing. While immediate relief was reported after each bout of vibration, both as a treatment strategy following the development of standing-induced LBP (part I) and as a preventative strategy intermittently applied during prolonged standing (part II), this reduction in LBP was not sustained. This was evident in the lack of difference in reported LBP on the control day compared to the vibration day in part II. In fact, LBP was generally higher just prior to each vibration bout than what was reported on the control day. Therefore, while vibration may provide immediate relief of LBP while standing, the cumulative effects may actually result in greater LBP when compared to standing in the absence of vibration.



**Figure 1:** Average ratings of perceived LBP (using 100mm scale) over time on the control day as well as pre and post vibration exposure. Standard error bars are shown.

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## RESONANCE FREQUENCY ANALYSIS OF PEDICLE SCREW STABILITY: A CADAVERIC STUDY WITH MICRO-CT

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**INTRODUCTION :** Pull-out strength (PO) and peak-torque (Tpeak) are used to evaluate implant stability<sup>1</sup>. Resonance frequency analysis (RFA) is a non-invasive technique for evaluating implant stability in dentistry<sup>2</sup>. The aim of this study was to use RFA to analyze pedicle screw stability and examine its relationship with micro-CT parameters.

**METHODS:** Four different densities of model-bones and 62 cadaveric vertebrae were tested. PO, Tpeak, and RFA (ISQ: obtained by Osstell, Göteborg, Sweden) were applied. For model-bones only, screw removal and re-insertion were repeated four times to consider the effects of 'loosening'. Micro-CT of vertebrae was performed twice, before and after insertion (Fig. 1a-c). Cancellous bone areas of pedicle screws were extracted (Fig. 1d, e). Micro-architectural parameters of this area were measured. Pedicle diameter and length measurements as macro-morphological characters were performed (Fig. 1c). Pearson's correlation coefficient (R) was used to evaluate the relationships among three test forces and the relationship between the test forces and micro-CT parameters. Stepwise forward multiple regression analysis was performed to evaluate whether the combination of micro-architectural and macro-morphological parameters would improve prediction of the test forces.

**RESULTS:** Model-bones: A strong positive correlation existed between PO and Tpeak (Fig. 2a). ISQ showed moderate positive correlations with PO and Tpeak (Fig. 2b, d). With 'loosening', all test forces decreased. ISQ was preserved in high-density material, unlike PO and Tpeak (Fig. 2c, e).

Fig. 1

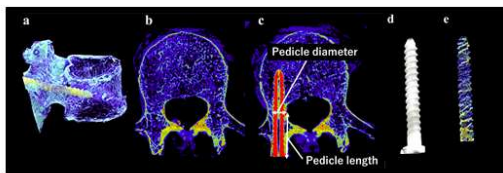


Fig. 2

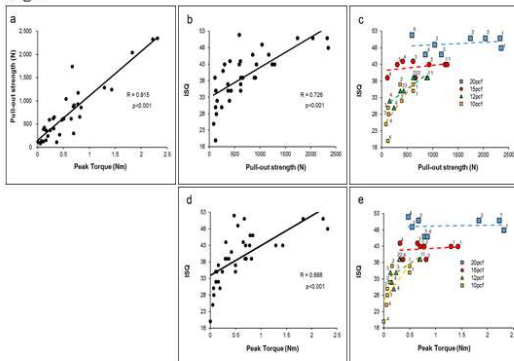


Fig. 2c, e: Regression lines were described for each material. Plot numbers show the times of screw removal and re-insertion. Figures 2c and 2e show the same scatter plots as Figures 2b and 2d. Plot shapes and colors were changed for every density (10, 12, 15, and 20 pcf).

Vertebrae: A strong positive correlation existed between PO and Tpeak ( $R=0.779$ ). ISQ showed moderate positive correlations with PO ( $R=0.324$ ) and Tpeak ( $R=0.349$ ), like model-bones. PO and Tpeak had negative correlations with pedicle diameter (PO:  $R=-0.302$ , Tpeak:  $R=-0.277$ ). ISQ had moderate negative correlations with pedicle length ( $R=-0.393$ ). PO and Tpeak showed moderate correlations with BS/TV (PO:  $R=0.689$ , Tpeak:  $R=0.681$ ). Predictions of PO and Tpeak improved when BS/TV was combined with pedicle diameter (PO vs. BS/TV+diameter:  $R=0.774$ , Tpeak vs. BS/TV+diameter:  $R=0.721$ ). ISQ showed a moderate correlation with N.Nd/TV ( $R=0.533$ ). Prediction of ISQ improved when N.Nd/TV was combined with pedicle length (ISQ vs. N.Nd/TV+length:  $R=0.690$ ).

**DISCUSSION:** PO reflects the installation strength of the parallel axis along the screw insertion path<sup>3</sup>, and Tpeak was a similar test force to PO in this study. ISQ reflects that of the vertical axis along the path<sup>4</sup>. ISQ may be related to the resistance of the broader material structure outside the screw pitch than PO and Tpeak. This might yield the following characters: material density more strongly influenced ISQ than PO and Tpeak. PO and Tpeak correlated negatively with pedicle diameter through minute structural changes between screw pitch. ISQ correlated negatively with pedicle length through the effect of 'lever arm'<sup>5</sup>. PO and Tpeak showed moderate correlations with BS/TV: bone surface density, similar to bone mineral density. ISQ correlated more strongly with N.Nd/TV: bone quality.

**CONCLUSION:** We have offered the first report that pedicle screw stability can be measured by RFA. PO and Tpeak correlates with bone density, while ISQ correlates with bone quality. Three test forces can be predicted by combining macro-morphological and micro-architectural parameters.

## POSTURAL INFLUENCE ON LUMBOSACRAL SAGITTAL ALIGNMENT - WHAT IS THE “IDEAL” FUSION ALIGNMENT?

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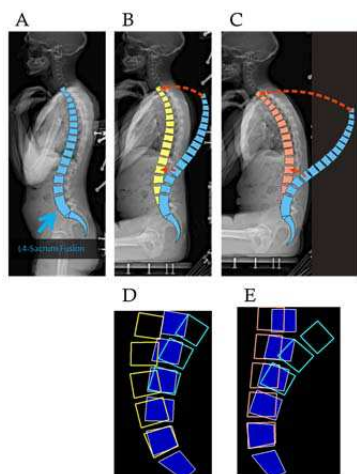
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**Introduction:** L4-Sacrum is the most prevalent site of spinal fusions for painful degenerative conditions in adults. Lumbopelvic alignment in the standing posture is recommended as the ideal fusion alignment to avoid postoperative complications; even though, adults are spending increasing amount of time in sedentary activities involving sitting. In this study, we asked: (1) how do different sitting postures alter the lumbosacral spinal alignment, and (2) what impact will this have on the biomechanics of proximal lumbar segments adjacent to fusion?

**Methods:** Postural influence on lumbosacral sagittal alignment was assessed by analyzing full-length radiographs of 11 asymptomatic volunteers taken in three postures: (i) standing, (ii) erect-sitting, and (iii) slumped-sitting. Next, for each subject, we calculated what would happen to the alignment of the lumbar (L1-S1) spine, in the absence of compensation, in erect- and slumped-sitting postures if the L4-S1 vertebrae were fixed to simulate L4-S1 fusion in the standing alignment (**Figure 1A,B,C**). Finally, we calculated the change in L1-L4 alignment that will be necessary if the subject were to fully compensate to restore the L1 vertebra to its pre-fusion angular alignment (**Figure 1D,E**). Similar calculations were also made for the second scenario where the simulated L4-S1 fusion was performed in the erect-sitting alignment and the subject attempted standing and slumped-sitting postures.



**Results:** Transitioning from standing to erect-sitting decreased L4-S1 lordosis (29° to 17°,  $p < 0.001$ ); whereas, transition from erect-sitting to slumped-sitting changed L1-L4 curvature from 15.6° lordosis to 2.5° kyphosis ( $p < 0.001$ ). Simulation of L4-S1 fusion performed in the standing alignment required significantly greater flexion of L1-L4 segments as compared to pre-fusion to accommodate the erect- and slumped-sitting postures (**Table 1**). Simulated fusion across L4-S1 performed in erect-sitting alignment required increased extension and flexion of L1-L4 segments to accommodate standing and slumped-sitting postures, respectively (**Table 2**).

**Discussion:** The measured postural influence on lumbar curvature and the biomechanical analysis suggest the importance of preoperatively assessing flexion and extension ranges of motion in the patient's upper (L1-L4) lumbar segments in order to arrive at a patient-specific decision regarding the ideal L4-S1 fusion alignment. The increased demand on junctional segments to accommodate post-fusion standing and sitting postures may contribute to their mechanical breakdown.

**Figure 1.** Postural mismatch in different sitting postures caused by simulated L4-S1 fusion performed in the standing posture. **(A)** Standing posture. **(B)** Erect-sitting posture. **(C)** Slumped-sitting posture. **(D,E)** Alignment of the post-fusion lumbar spine compensated (Dark Blue) to maintain the same L1 slope as in the erect- and slumped-seated postures before L4-S1 fusion.

**Table 1. Changes in Alignment of L1-L4 Segments During Postural Transition Before and After L4-S1 Fusion in Standing Alignment**

Postural Transition	Before Simulated L4-S1 Fusion	After Simulated L4-S1 Fusion	P value
Standing to Erect-Sitting	2° flexion	13° flexion	$P < 0.01$
Standing to Slumped-Sitting	20° flexion	36° flexion	$P < 0.01$

**Table 2. Changes in Alignment of L1-L4 Segments During Postural Transition Before and After L4-S1 Fusion in Erect-Sitting Alignment**

Postural Transition	Before Simulated L4-S1 Fusion	After Simulated L4-S1 Fusion	P value
Erect-Sitting to Standing	2° extension	13° extension	$P < 0.01$
Erect-Sitting to Slumped-Sitting	18° flexion	23° flexion	$P = 0.096$

## TARGETING THE LOW BACK IMPROVES RETURN TO PLAY IN ATHELETES WITH FUNCTIONAL HAMSTRING DISORDERS

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Hamstring muscle injuries (HMI) are among the most common time-loss sports injuries and the most common sports injury in football (1). Clinical presentation of athletes with (HMI) include pain, weakness, and increased fatigability locally as well as loss of motor control in the lumbopelvic region (2). However, treatment targeting the lumbopelvic region among athletes with HMI is not often implemented. The objective of the current study was to compare two rehabilitative treatment programs, one including targeting treatment to the lumbopelvic region on clinical findings and return to play among elite football players. A second aim was to analyze clinical predictors of return to play.

Sixteen consecutive athletes in the Greek Super Football League (ages 21-32 years) diagnosed with acute HMI and functional muscle disorder (FMD) within 5 days of injury were randomly assigned to 1 of 2 rehabilitation groups. Inclusion criteria for all participants consisted of the presence of HMI with no MRI signs of structural hamstring strain, a positive slump test, <3 kg/cm pain pressure threshold (PPT) upon digital algometry to the involved biceps femoris muscle belly (BF), ipsilateral sacroiliac joint (SIJ) and L5 and L4 spinous processes (Digital Algometer, CLA, Bethany Beach, Delaware, USA), and positive isometric hamstring digital muscle strength testing (Digital Muscle Tester, MicroFET2, Hoggan Scientific, Salt Lake City, Utah, USA). These variables were again re-assessed at the conclusion of treatment and used as outcome measures for group comparisons and predictor variables in this randomized clinical trial.

Eight athletes received standard supervised HMI rehabilitative treatment consisting of passive interventions of therapeutic ultrasound, hamstring massage and Nordic progressive hamstring exercises (standard treatment group, ST). The other 8 athletes were assigned to a program of impulsive mechanical manipulation and manual therapy delivered to targets in the lumbar spine, sacroiliac joint and the involved biceps femoris muscle with the Impulse iQ® (Neuromechanical Innovations, Chandler, Arizona, USA) and CORE lumbar stability exercises (mechanical manual therapy group, MMT). Both groups received treatments three times a week for three weeks prior to re-evaluation.

A series of mixed design 2x2 ANOVA's were conducted with time (pre-post) as the within-subjects factor and treatment group (ST vs. MMT) as the between-subjects factor with Bonferroni correction. Days to return to play were compared among groups using an independent t-test, and linear regression analyses were conducted to predict days to return to play from the objective clinical outcome variables. Significance was set at  $p < 0.05$  for all analyses. In this randomized lumbopelvic spine was shown to rehabilitation program for improvement in objective measures of FMD and HMI and returning elite football players to sport participation. These results, combined with the findings that L5 and SIJ PPT improvement predict return to play among athletes in the current study suggest that treatment targeting the lumbopelvic spine is an important consideration in HMI rehabilitation among athletes.

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## TIDEMARK AVULSIONS ARE A HIGHLY PREVALENT FORM OF ENDPLATE DAMAGE

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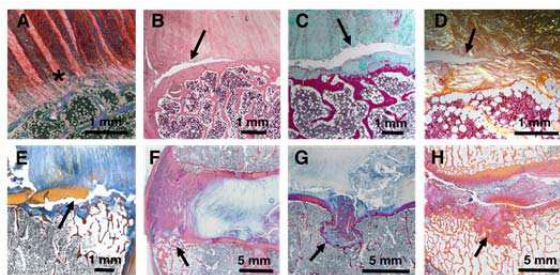
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**Introduction:** Irregularities at the disc-vertebra interface associate with back pain and spinal injury. However, studies of pathophysiology, natural history, and clinical significance are limited by a lack of consensus on terminology and classification. To address this, we are using histology to identify and categorize the major types of endplate irregularities. Histology provides a high-resolution view of tissue features and structures involved, thereby providing the mechanistic underpinnings for clinical classification.

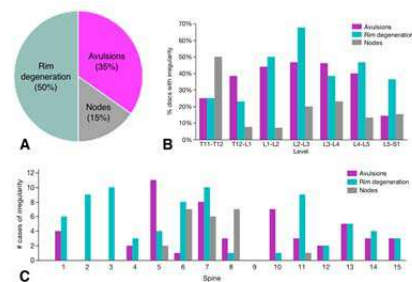
**Methods:** Eighty-nine moderately- to severely-degenerated human lumbar and lower thoracic intervertebral discs were extracted from fifteen cadaver spines (11M/4F, ages 49-67). Discs were fixed, decalcified, and analyzed histologically in the sagittal plane using four stains with and without polarized light: Hematoxylin and Eosin (H&E), Masson trichrome, Mallory-Heidenhain, and Safranin O Fast Green. A preliminary classification scheme of endplate irregularities was generated, and incidence of each type was recorded.

**Results:** Based on location and patho-anatomical features, endplate irregularities were grouped into three main categories: (1) *Avulsion*: tissue separation at the disc-vertebra interface (Fig. 1 B-E), (2) *Rim degeneration*: degeneration of the bone-annulus interface, including bone marrow changes and loss of annular fiber organization (Fig. 1F), and (3) *Nodes*: extrusion of nucleus material and/or ingrowth of fibrocartilage into vertebral bone at the central portion of the disc (Fig. 1 G&H). Two types of nodes were observed: traumatic (herniation of nucleus material through the endplate; Fig. 1G) and degenerative (bony erosion and abnormal fibrocartilage ingrowth; Fig. 1H). Interestingly, 90% of avulsions occurred along the tidemark where outer annulus fibers insert into the calcified cartilage layer (Fig. 1 B-D). Tidemark avulsions occurred in 35 of 89 discs, and of those discs, 14 had multiple avulsions. Eighty-seven percent of all avulsions occurred anteriorly. Avulsions and rim degeneration were more common than nodes (Fig. 2A) and occurred most frequently in the lumbar spine (Fig. 2B), while nodes occurred most frequently in the thoracic spine. Often, similar endplate irregularities were observed in multiple discs of the same spine; for example, 20 of 23 nodes were distributed amongst only 5 of the 15 spines, with 7 nodes occurring in a single spine (Fig. 2C).

**Conclusion:** This study reveals the high prevalence of avulsion injuries at the tidemark between the annulus and calcified cartilage layer. While annulus avulsions are well-documented, the precise failure location of annulus fibers at the tidemark has only been observed in biomechanical studies of excised animal tissue, and has not been previously identified in human spines. One possible reason is that tidemark avulsions are difficult to discern with clinical imaging due to limited image resolution and the closing of small tissue separations when discs are under *in vivo* loading conditions. Interestingly, the majority of avulsions occurred anteriorly. However, traumatic avulsions coincident with disc herniation (not included in our study population) are thought to occur posteriorly, with the inner annulus avulsing the CEP during flexion. We also observed that similar endplate irregularities often occurred in multiple discs of a given spine, motivating further analysis of the unique etiologies of endplate irregularities and patient-specific risk factors.



**Figure 1.** Histology images of (A) intact tidemark denoted by asterisk, (B-D) tidemark avulsions, (E) CEP-bone avulsion, (F) rim degeneration, (G) traumatic node, and (H) degenerative node. Arrows point to endplate irregularities. Sections are stained with (A&B) Hematoxylin and Eosin (H&E) with (A) and without (B) polarized light, (C) Masson trichrome, (D) Safranin O with polarized light, and (E-H) Mallory-Heidenhain.



**Figure 2.** (A) distribution of endplate irregularities by category; (B) distribution of endplate irregularities by disc level; (C) distribution of endplate irregularities by individual, demonstrating a single category of irregularity often occurring multiple times in a given spine.

**MACHINE LEARNING FOR THE ANALYSIS OF MEDICAL IMAGES OF THE SPINE**

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**Introduction.** Artificial neural networks are biologically inspired tools used to approximate complex nonlinear functions with a high number of inputs and either real or discrete output. They are a powerful tool for nonlinear regression and classification problems, and are currently used for a high number of tasks in which a robust automatic performance is needed, e.g. handwriting recognition, face identification and self-driving vehicles (1). It is believed that the so-called deep learning methods (i.e. based on complex multilayer network architectures) will have a potential application field in the automatic processing of medical images, to improve the objectivity of the image analysis and finally to provide a valuable support to the diagnostic process. The aim of this work was to test machine learning techniques, including deep learning methods, in the automatic processing of lumbar x-rays images and MRI scans.

**Methods.** Machine learning methods have been tested for two tasks: the recognition of landmarks in sagittal radiographic images of the lumbar spine and the grading of disc degeneration on T2-weighted MRI lumbar scans. To these aims, large sets of images have been collected: 1007 sagittal x-rays of patients with various spinal disorders including spondylolisthesis, degenerative changes and adult scoliosis, and 2600 MRI scans of patients suffering from degenerative disc disease. Ground truth (the positions of the vertebral corners for the x-rays and Pfirrmann grading (2) for the MRI scans) has been generated by human expert operators. Various neural network architectures (including two-layer dense networks, convolutional networks as well as deeper multi-layer architectures) have been trained and tested for their accuracy in predicting the location of the landmarks and in grading the degeneration of the intervertebral discs. The Tensorflow framework (3) has been employed for the creation, testing and use of the machine learning algorithms.

**Results.** In general, convolutional architectures proved to offer the best compromise between accuracy and resources (memory and CPU time) needed for the network training, which resulted to be in any case highly computationally demanding. The identification of the vertebral corners on sagittal x-rays provided results satisfactory by visual inspection, except for few images (<5%). The automatic Pfirrmann grading agreed with the ground truth for more than 90% of the images. In general, the methods appeared to be very promising but still needed some refinements before being usable in a clinical setting.

**Discussion.** Neural networks as well as other machine learning methods are currently being used in many industrial and research fields, and can therefore be considered consolidated methods for many applications including biomedical image processing. The availability of large datasets (the so-called "big data") in combination with recent methodological advances is nowadays starting to allow exploiting the full potential of artificial intelligence techniques in medical imaging. This preliminary investigation confirmed that the fields of application of such methods will arguably include the automatic processing of medical images of the spine in the next future.

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## BIOMECHANICAL LOADS ON THE LUMBAR SPINE DURING SIMULATED WHEELCHAIR PUSHING

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**Introduction:** Health care workers have a high prevalence of occupational back injuries related to patient handling tasks such as pushing and pulling of patients in attendant-propelled, or manual, wheelchairs. Caregivers often push loads in excess of 100 kg during manual wheelchair pushing. Wheelchair design affects biomechanical load for attendants, but there is no published data to justify the current design of the handles on standard manual wheelchairs. Thus, the objective of this study was to determine how wheelchair pushing influences biomechanical loading to the lumbar spine during simulated wheelchair pushing.

**Methods:** 62 subjects performed simulated wheelchair pushing and turning in a laboratory. An overhead rig allowed for the setup of a mock manual wheelchair, with a handle height of 91 cm, handle width of 46 cm, and rear-facing handles. Linear or rotational resistance provided by an overhead braking system increased incrementally during each pushing or turning trial such that subjects ended each trial with a maximum voluntary exertion (MVE). A dynamic, EMG-assisted biomechanical model estimated spinal loads. In addition, measures of external hand force and net torque were also assessed. Finally, multiple linear regression techniques were employed to develop biomechanically based wheelchair pushing guidelines relating resultant hand force or net torque to spinal load; these force tolerances were compared to psychophysically determined pushing guidelines.

**Results:** The highest compressive spinal loads were found at L3/L4, while peak lateral and anterior/posterior shear loads were found at L5/S1. Compressive and A/P shear spinal loads were significantly higher for males ( $p < 0.01$ ) and were increased by 13.9% and 39.1% respectively during wheelchair turns compared to straight wheelchair push exertions. Maximum strength in terms of resultant hand force was  $295 \pm 72$  N for males and  $206 \pm 53$  N for females, while maximum torque applied for turns was  $70 \pm 20$  Nm and  $51 \pm 19$  Nm. For straight wheelchair push exertions, subjects applied hand force at a mean angle of  $39.8 \pm 15.6$  degrees relative to the horizontal. Results from regressions determined maximum acceptable resultant hand forces during wheelchair pushing and are shown in Table 1; biomechanically determined values were 17-18% lower than the closest psychophysically determined comparisons.

**Discussion:** Wheelchair pushing poses biomechanical risk to the lumbar spine in compression and A/P shear, particularly for males. Current psychophysically-determined maximum acceptable push forces (Snook and Ciriello, 1991) are not protective enough of biomechanical risk. Given that subjects applied hand forces at a high angle relative to horizontal, there is opportunity for improved wheelchair design, particularly in regard to handle height. In particular, higher handle heights might result in a more horizontally applied hand force, which would decrease rolling resistance in wheelchair pushing. Finally, the results of the study should be considered within its limits; the study population was young and inexperienced in patient handling, and subjects were not guaranteed to produce a true MVEs.

**Table 1.** Comparison of biomechanically determined maximum acceptable resultant hand force determined in this study with closest psychophysically based comparison (i.e., 2.1 m push, one push every five minutes, handle height 0.94 m) from Snook and Ciriello (1991)

Percent of Population Protected	Biomechanically Based Hand Force Limit (Resultant Hand Force, N)	Psychophysically Based Hand Force Limit (Horizontal Hand Force, N)
90	226	275
75	291	353
50	363	441
25	435	530
10	501	608

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## BIOMECHANICAL PUSH-PULL LIMITS THAT PROTECT THE LUMBAR SPINE

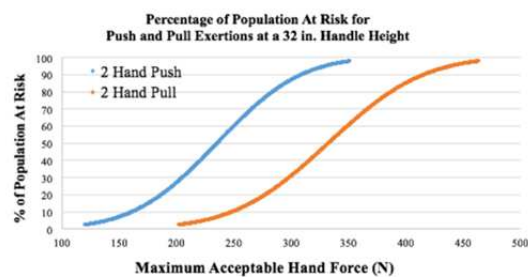
William S. Marras<sup>1</sup>, Eric B. Weston<sup>1</sup>, Jonathon Dufour<sup>1</sup>, Gregory G. Knapik<sup>1</sup>, Safdar Khan<sup>1</sup>, Ehud Mendel<sup>1</sup>

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**Introduction:** Occupationally-related back disorders have been long associated with heavy work involving both lifting as well as pushing and pulling. While numerous biomechanically-based guidelines for lifting activities have been developed over time, no biomechanically-based push-pull guidelines have been developed. As a matter of fact, only psychophysically-based guidelines exist for pushing and pulling (Snook and Ciriello, 1991). However, since much of the disc does not contain nociceptors it is unclear how people could judge the “acceptability” of push-pull activities through psychophysical analyses. Thus, the objective of this study was to assess the level of push-pull hand forces that would result in spine loads exceeding threshold tolerance limits for different push-pull conditions.

**Methods:** 62 subjects (31 male and 31 female) without back pain were recruited as participants in this study. Subjects were asked to push or pull with two hands against instrumented handles that were either 32, 40 or 48 in. in vertical height. The handles were connected to a vertical bridge instrumented with particle brakes. These brakes were programed to gradually increase the bridge resistance until the subject could no longer move the handles. 3D hand forces were monitored continuously via the instrumented handles. In addition, electromyographic (EMG) activity of the 10 power producing torso muscles (rt./lt. erector spinae, latissimus dorsi, rectus abdominus, internal oblique, and external oblique) were monitored continuously throughout each exertion. A 36 camera motion capture system (Optitrac™) was used to document the body position throughout the exertions. Hand force, muscle EMG and body kinematics were used as input to a biologically-assisted biomechanical model to determine 3D spinal forces at each level of the lumbar discs throughout each exertion (Hwang, et al. 2016). The model was calibrated for each subject.

**Figure 1.** Cumulative distribution of hand forces relative to the % the population exceeding A/P shear tolerances during Pushing and Pulling



**Results:** The highest compressive spinal loads were found at L3/L4, while peak lateral and anterior/posterior shear loads were found at L5/S1. When comparing the spinal loads to tissue tolerances (Gallagher and Marras, 2012) the 2 hand push-pull conditions at a 32-inch handle height resulted in the greatest proportion of shear loads exceeding the tissue tolerance limits. Figure 1 shows the relationship between the handle force and spine risk (via A/P shear) for 2 hand pushing and pulling. Similar relationships were derived for the other conditions.

**Discussion:** These results represent the first attempt to derive biomechanically relevant occupational pull limits for a large population of male and female subjects. When comparing these values to psychophysically derived limits our findings were up to 22% lower indicating that people perceive they could exert more force than would be considered protective from a biomechanical prospective. These results can form the basis for industrial guidelines.

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**THICKNESS OF THE LIGAMENTUM FLAVUM IS ASSOCIATED WITH THE TOTAL CONTENT OF ADVANCED GLYCATION END PRODUCTS (AGEs) IN LUMBAR SPINAL STENOSIS PATIENTS**

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**Introduction:** Advanced glycation end products (AGEs) have been known to be a factor in the decrease in bone strength due to crosslinking collagen molecules. Although previous reports have shown the relationship between the degenerative change in intervertebral discs, cartilage and ligament, and AGEs, it remains unclear which findings are clinically affected by AGEs. The purpose of this study was to examine the relationship between AGEs concentration of the ligamentum flavum in the lumbar spine and clinical factors in lumbar spinal stenosis patients.

**Methods:** We enrolled 30 patients (mean AGEs; 69.2±8.9 year-old, 18 females and 12 males) who were underwent surgery for lumbar spinal stenosis from 2013 to 2014. We collected the ligamentum flavum during surgery and measured the total content of AGEs (total AGEs) by neutral fluorescence. We evaluated the relationship between the total AGEs content in the ligamentum flavum and clinical factors such as age, sex, history of diabetes mellitus (DM), the lumbar spine sampling level, the ligamentum flavum thickness in MRI and range of motion of the lumbar spine in X-P.

**Results:** The total AGEs content was 942.5 ± 384.7 ng quinine per mg of collagen in all subjects. The total AGEs was significantly higher in the samples of the patients with DM than in those without DM (1230 vs 855, p = 0.02); it was significantly associated with ligamentum flavum thickness (r =0.41, p = 0.03), whereas, it was not significantly correlated with age, sex, or the level or range of motion of the lumbar spine.

**Discussion:** The result that the total AGEs content was higher in the patients with DM was in accordance with previous reports. We showed that total AGEs content was significantly associated with ligamentum flavum thickness. This finding might suggest that accumulation of AGEs in the ligamentum flavum caused its hypertrophic change. However, the mechanism of AGEs accumulation in the ligamentum flavum remains unknown and warrants further molecular and biological research.



## MEASURING PARTICIPATION IN CHRONIC BACK PAIN PATIENTS - THE 5-ITEM PAIN DISABILITY INDEX

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**Introduction:** Of the three broad outcome domains of body functions and structure, activity, and participation (e.g., engaging in valued social roles) outlined in the World Health Organization's (WHO) International Classification of Functioning, Disability and Health (ICF), it has been argued that participation is the most important to individuals, particularly those with chronic health problems. Yet, participation is not commonly measured in back pain research. The aim of this study was to investigate the construct validity of a modified 5-Item Pain Disability Index (PDI) score as a measure of participation in people with chronic back pain.

**Methods:** Participants with chronic back pain were recruited from a multidisciplinary pain centre in Alberta, Canada. Each was given a questionnaire package containing measures of participation, resilience, anxiety and depression, pain intensity, and pain-related disability, in addition to the PDI. The first 5 items of the PDI deal with social roles involving family responsibilities, recreation, social activities with friends, work and sexual behavior, and comprised the 5-item PDI seeking to measure participation. The last 2 items of the PDI deal with self-care and life support functions, and were excluded. This two-factor structure of the PDI has been supported by previous research (Tait et al., 1990). Construct validity of the 5-item PDI as a measure of participation was examined using Pearson correlations or Point-Biserial correlations to test each hypothesized association.

**Results:** Participants were 69 people with chronic back pain and a mean age of 48.0 years. Forty-three (62.3%) were women. As hypothesized, the PDI was associated with all measures of participation, including the Participation Assessment with Recombined Tools–Objective ( $r = -0.61$ ), Late-Life Function and Disability Instrument: Disability Component (Frequency:  $r = -0.66$ , Limitation:  $r = -0.65$ ), Work and Social Adjustment Scale ( $r = 0.85$ ), a global perceived participation scale ( $r = 0.56$ ), employment status ( $r = -0.30$ ) and the Usual Activity domain of the 15D ( $r = 0.51$ ). The expected correlations observed indicating a moderate or strong association provided supporting evidence for the construct validity of the PDI as a measure of participation. The Oswestry Disability Index and the PDI were also strongly correlated ( $r = 0.71$ ). The PDI was associated to a lesser degree with depressive symptoms and resilience, as measured by the Hospital Anxiety and Depression Scale (HADS) ( $r = 0.25$ ) and the Connor-Davidson Resilience Scale ( $r = -0.28$ ), as would be expected. No statistically significant association was found between the PDI and the HADS Anxiety score.

**Discussion:** It is important that outcome measures of participation are included in back pain research to gauge the effects of painful spinal conditions and interventions on maintaining valued social roles. A simple, concise measure would be very useful for this purpose in clinical and research settings. The results of this study support the construct validity of the 5-item PDI as such a measure of participation in people with chronic back pain.

## ALTERED INTERVERTEBRAL DISC MECHANICS IN VIVO AFTER 60D BED-REST

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### Introduction

Based on data from intervertebral disc (IVD) explants, we must assume that the biomechanical behaviour of the IVD is altered in vivo when it is more hydrated, such as in the morning after overnight rest or after spaceflight. This is thought to influence IVD injury risk [1,2]. However, quantifying IVD mechanics in humans in vivo, and hence the influence of altered IVD hydration states on these mechanics, is difficult. The aim of this work was to examine the mechanical behaviour of the IVD in humans under loading as a function of hyperhydration through prolonged bed-rest.

### Methods

23 male subjects completed 60d bed-rest and were measured at baseline and at the end. A step-wise load-sustained load-load release protocol using the Dynawell L-Spine device was implemented: two T2-weighted scans were taken at rest before loading with then the scan repeated after 10kg, 14kg and then 50% of body mass were applied. Load was then sustained at 50% of body mass for 14 minutes with five further repeated scans. After load release, three follow-up scans at rest were performed. The IVDs (L23 to L5S1) were segmented into 5 subregions anterior to posterior. The five images centred around the spinous process were taken for further analysis. IVD height compressibility at first 50% body mass load (versus rest), height reduction per 10 minutes of sustained load at 50% body mass, height recoil after load release, and sustained height reduction after load release were calculated

### Results

IVD height increased from 8.63mm at baseline to 9.31mm at the end of bed-rest ( $p=0.02$ ). At the end of bed-rest, greater compression of IVD height at the first '50% of body mass' loading level ( $-0.099[0.153]$ mm  $p=0.005$  at end bed-rest versus  $-0.074[0.196]$ mm,  $p=ns$  at baseline) was seen. Furthermore, with sustained load at 50% body mass, faster IVD height reduction ('creep') was observed at end bed-rest ( $6.4[10.3]$ µm/min  $p=0.007$  versus  $3.4[12.9]$ µm/min  $p=ns$  at baseline). Upon load release the IVD height remained compressed at the end of bed-rest ( $-0.099[0.153]$ mm versus before the loading protocol,  $p=0.005$ ) whereas this was not the case at baseline testing ( $-0.074[0.196]$ mm  $p=0.08$ ).

### Discussion

We showed that, in vivo, IVD mechanics are altered in a state of hyperhydration, after prolonged bed-rest. Specifically, the IVD height exhibited greater elastic compressibility with loading and more viscous creep with sustained load. This altered mechanical behaviour will likely increase IVD injury risk.

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## POSTOPERATIVE CHANGE IN SAGITTAL SPINOPELVIC ALIGNMENT AND LOW BACK PAIN AFTER TOTAL HIP ARTHROPLASTY

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### INTRODUCTION:

There have been several reports regarding improvement of low back pain (LBP) after total hip arthroplasty (THA). Recently, many studies have demonstrated sagittal spinopelvic alignment to be correlated with health-related quality of life scores. However, the relationship between LBP and the change in spinopelvic alignment after THA is still unknown. The aim of this study is to identify the prevalence of pre- and postoperative low back pain in patients undergoing THA as well as to assess the influence of spinopelvic parameters on the improvement of low back pain after THA.

### METHODS:

This prospective cohort study involved end-stage hip osteoarthritis patients who underwent THA between 2013 and 2014 at our institution. We collected radiographic and questionnaire data at the preoperative period and after THA. The level of LBP was assessed by VAS score. The sagittal anterior pelvic plane angle (SAPPA) is defined as the angle between the anterior pelvic plane and the vertical plane. A positive value is pelvic retroversion. Radiographic parameters included thoracic kyphosis (TK), lumbar lordosis (LL), pelvic incidence (PI), sacral slope (SS), sagittal vertical axis (SVA), and sagittal anterior pelvic plane angle (SAPPA). LBP of more than 30 mm (VAS score) was defined as LBP (+) group.

### RESULTS:

A total of 45 patients (8 men, 37 women) with an average age of  $60.7 \pm 13.8$  years agreed to participate in the study. The prevalence of preoperative LBP was 56% (24/45) (Table.1). After THA, the prevalence of LBP decreased by 27% (12/45). The mean VAS score for LBP significantly decreased from 39 mm before surgery to 23 mm at after THA. There were no significant changes in lumbar or pelvic alignments including LL, TK, PI-LL, SS, and SAPPA at after THA; however, only SVA significantly increased after THA (26 mm vs. 39 mm,  $P= 0.007$ ). Postoperative TK, LL, SS, SVA, and SAPPA was similar between the LBP (+) and the LBP (-) group. However, postoperative PI-LL mismatch was significantly larger in the LBP (+) group ( $21.6^\circ$  vs.  $7.8^\circ$ ,  $P < 0.001$ ). There was no significant correlation between the change in the SAPPA and the postoperative VAS score for LBP ( $R= -0.031$ ,  $P= 0.839$ ).

### DISCUSSION AND CONCLUSION:

THA did not result in any significant change in the sagittal spinopelvic alignment. Postoperative change in sagittal pelvic rotation did not influence postoperative LBP. Postoperative PI-LL mismatch was the only predictive factor associated with persistent low back pain after THA.

Table 1. Change in low back pain after THA

Preoperative	THA	N, (%)	Postoperative	THA	N, (%)
LBP(+)	group	24 (53%)	LBP(+)	group	9 (20%)
			LBP(-)	group	15 (33%)
LBP(-)	group	21 (47%)	LBP(+)	group	3 (7%)
			LBP(-)	group	18 (40%)

LBP(+): VAS > 30

## RADIOGRAPHIC FACTORS AND DIAGNOSTIC INDICATOR OF THE ONSET OF LUMBOSACRAL FORAMINAL STENOSIS

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**Introduction:** Lumbosacral (L5/S1) foraminal stenosis (LSFS) can now be identified with advanced imaging technology, but imaging findings often do not correspond with the damaged nerve roots, leading to false-positive asymptomatic findings that make diagnosis difficult. The purpose of this study is to evaluate the radiographic factors and elucidate the diagnostic indicator of the onset of radiculopathy caused by LSFS.

**Methods:** Subjects comprised 123 patients (81 men, 42 women) with L5 radiculopathy showing radiographic L5-S1 foraminal vertical stenosis and for whom favorable surgical outcomes (JOA recovery rate  $\geq 50\%$ ) were obtained. Fifty-seven patients (37 men, 20 women; mean age, 69.0 years) underwent L5-S1 foraminal decompression or fusion and were diagnosed with LSFS (FS group). Sixty-six patients (44 men, 22 women; mean age, 71.6 years) had both radiographic L5-S1 foraminal vertical stenosis and L4-5 canal stenosis, underwent L4-5 single level decompression or fusion and were diagnosed with L4-5 canal stenosis (CS group). In FS and CS groups, we evaluated minimum foraminal height on MDCT, and L5-S1 disc height, intervertebral angle, range of motion, L5/S1 tilting angle ( $^{\circ}3$ ), Cobb angle ( $^{\circ}10$ ), anterior or posterior spondylolisthesis ( $^{\circ}2$ mm), LL, SS, PI and L1-sagittal vertical axis (L1-SVA) defined as the horizontal offset from the posterosuperior corner of S1 to the vertebral body of L1 on standing lateral-view X-ray.

**Results:** Between FS and CS groups, no significant difference was seen in minimum foraminal height (FS: 4.1 mm vs. CS: 4.0 mm), L5-S1 disc height (2.3mm vs. 2.3mm), range of motion ( $4.9^{\circ}$  vs.  $4.6^{\circ}$ ), Cobb angle ( $17.1^{\circ}$  vs.  $14.1^{\circ}$ ), L5/S1 tilting angle ( $4.8^{\circ}$  vs.  $5.2^{\circ}$ ), complications of L5 posterior spondylolisthesis (37% vs. 44%) and LL ( $31.6^{\circ}$  vs.  $35.2^{\circ}$ ). The complications of degenerative lumbar scoliosis (53% vs. 30%;  $p < 0.05$ ), L5/S1 wedging (53% vs. 8%;  $p < 0.01$ ) and L1, 2, 3 or 4 posterior spondylolisthesis (56% vs. 18%;  $p < 0.01$ ) were more in FS group. The complication of L3 or 4 anterior spondylolisthesis (14% vs. 42%;  $p < 0.01$ ), PI ( $41.0^{\circ}$  vs.  $45.8^{\circ}$ ;  $p < 0.01$ ) and SS ( $18.7^{\circ}$  vs.  $24.4^{\circ}$ ;  $p < 0.01$ ) were less in FS group, and intervertebral angle ( $8.4^{\circ}$  vs.  $6.6^{\circ}$ ;  $p < 0.05$ ) and negative values of L1-SVA (75% vs. 8%;  $p < 0.01$ ) were greater in FS group. Multiple logistic regression analysis identified 2 significant risk factors for the onset of radiculopathy caused by LSFS, L5/S1 wedging and negative value of L1-SVA. The diagnostic indicator of L5/S1 wedging or negative value of L1-SVA for the onset of radiculopathy caused by LSFS, was diagnostic sensitivity: 93.0% and specificity: 84.8%.

**Discussion:** In the patients with radiographic L5-S1 foraminal vertical stenosis on MDCT, radiographic findings of L5/S1 wedging ( $^{\circ}3$ ) or negative value of L1-SVA should be the diagnostic indicator for the onset of radiculopathy caused by LSFS.

## THE CORRELATION BETWEEN SAGITTAL SPINOPELVIC ALIGNMENT AND DEGREE OF LUMBAR DEGENERATIVE SPONDYLOLISTHESIS

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**Introduction:** The purpose of this study was to analyze patients with degenerative spondylolisthesis (DS), in terms of the correlation between the sagittal spinopelvic parameters and the severity of slip in each lumbar spine, including both anterior and posterior directions.

**Methods:** 104 patients (59 women and 45 men) with low back pain were included in this study. Standing lateral radiographs were taken for each patient using a standardized procedure. Dynamic flexion-extension lateral lumbar films were also taken. The spinopelvic parameters, including pelvic incidence (PI), sacral slope (SS) and pelvic tilt (PT), angle of thoracic kyphosis (TK), angle of lumbar lordosis (LL), and sagittal vertical axis offset (SVA) were measured. The percentage of LL (LLP) was also calculated as following:  $(LL \text{ in lumbar extension position} - LL \text{ in standing position}) \times 100 / (LL \text{ in lumbar extension position} - LL \text{ in flexion position})$ . Additionally, the %Slip was measured at each level between the L1 and L5. The slip direction was presented as plus to the anterior, and minus to the posterior.

**Results:** The PI significantly correlated with the L3 %Slip ( $\rho=0.278$ ,  $p=0.004$ ), L4%Slip ( $\rho=0.641$ ,  $p=0.000$ ), SS ( $\rho=0.614$ ,  $p=0.000$ ), and LL ( $\rho=0.484$ ,  $p=0.000$ ). The SS correlated with the L3%Slip ( $\rho=0.243$ ,  $p=0.013$ ), L4%Slip ( $\rho=0.549$ ,  $p=0.000$ ), L5%Slip ( $\rho=0.233$ ,  $p=0.020$ ), and LL ( $\rho=0.794$ ,  $p=0.000$ ). The LLP correlated slightly with the L4%Slip ( $\rho=0.326$ ,  $p=0.011$ ) and L5%Slip ( $\rho=0.303$ ,  $p=0.022$ ).

**Discussion:** Our results show a significant correlation between spinopelvic parameters and slip severities of the L3 as well as the L4 and L5, including slip to the posterior and anterior directions, suggesting that PI and/or SS could cause a posterior slip as well as an anterior slip at those levels. Moreover, our results suggest that the high LL, which was near to maximum extension position in the lumbar spine, could be a risk to develop DS.

## VALIDATION OF NEW TECHNIQUE FOR ASSESSING THE MUSCLE ACTIVITY OF THE PSOAS MAJOR USING DIFFUSION-WEIGHTED MAGNETIC RESONANCE IMAGING

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### Introduction:

The psoas major (PM) is a deep muscle that acts on hip flexion and lumbar lordosis. Since the PM is located in the deepest portion of the trunk muscles, an invasive method, such as fine-wire electromyography (EMG), is needed to measure its muscle activity. However, it has recently been reported that deep muscle activity can be measured noninvasively using diffusion-weighted magnetic resonance imaging (DW-MRI) (Yanagisawa et al., 2015). The purpose of this study was to examine the validity for assessing PM muscle activity using DW-MRI, and to clarify the activity pattern of the PM during trunk muscle exercises.

### Methods:

Seven healthy men participated in this study. Activation of the PM on the right side was evaluated by fine-wire EMG and DW-MRI during and following 3 types of front bridge exercises: hand-knee, elbow-knee, and elbow-toe with a right arm and left leg lift. For the EMG measurement, the fine-wire electrode was inserted into the right PM under the guidance of ultrasound imaging. The EMG signals of the PM were recorded during each exercise in real time. The EMG activity for the PM was normalized as a percentage of the activity during maximum voluntary contraction (%MVC). The axial diffusion-weighted images of the trunk were obtained before, and immediately after, each trunk exercise. All participants performed one exercise per day, and carried out all exercises at intervals of one day or more. The MRI-slice position was set at the midpoint of the L3-L4 intervertebral disk as a point of reference. The b-value was set to 700 s/mm<sup>2</sup>. The apparent diffusion coefficient (ADC) values after exercise, relative to those before exercise, were calculated as the percent change in ADC values for the PM. The relationship between the average of the %MVC and the average of the percent change in ADC values for each exercise was analyzed using Pearson's correlation coefficient (r). Additionally, the Tukey-Kramer HSD test was used to compare the %MVC and percent change in ADC values among the exercises.

### Results:

There was positive correlation between the average %MVC and average percent change in ADC values ( $r=0.99$ ). The percent change in the PM ADC value after the elbow-toe, elbow-knee, and hand-knee exercises was  $14.6 \pm 3.2\%$ ,  $7.3 \pm 4.7\%$ , and  $0.5 \pm 3.5\%$  (mean  $\pm$  SD), respectively. These values showed significant differences between exercises, sequentially. The PM %MVC during the elbow-toe, elbow-knee, and hand-knee exercises was  $18.1 \pm 4.6\%$  MVC,  $12.5 \pm 4.8\%$  MVC, and  $8.4 \pm 9.1\%$  MVC, respectively. In addition, the EMG amplitudes of the PM during the elbow-toe exercise were significantly higher than those during the hand-knee exercise.

### Discussion:

These results suggest that ADC values measured noninvasively using MR-DWI may be useful as an activity index for the PM. The elbow-toe exercise produced the highest activation of the PM among the 3 types of front bridge exercises. Since the base of support is longer for the elbow-toe than for the other exercises, more torque in the hip flexion is needed in order to maintain the posture.

## BIOMECHANICAL ADVANTAGES OF ROBOT-ASSISTED PEDICLE SCREW FIXATION IN POSTERIOR LUMBAR INTERBODY FUSION COMPARED TO FREE-HAND TECHNIQUE IN A PROSPECTIVE RANDOMIZED CONTROLLED TRIAL – PERSPECTIVE FOR PATIENT-SPECIFIC FINITE ELEMENT ANALYSIS

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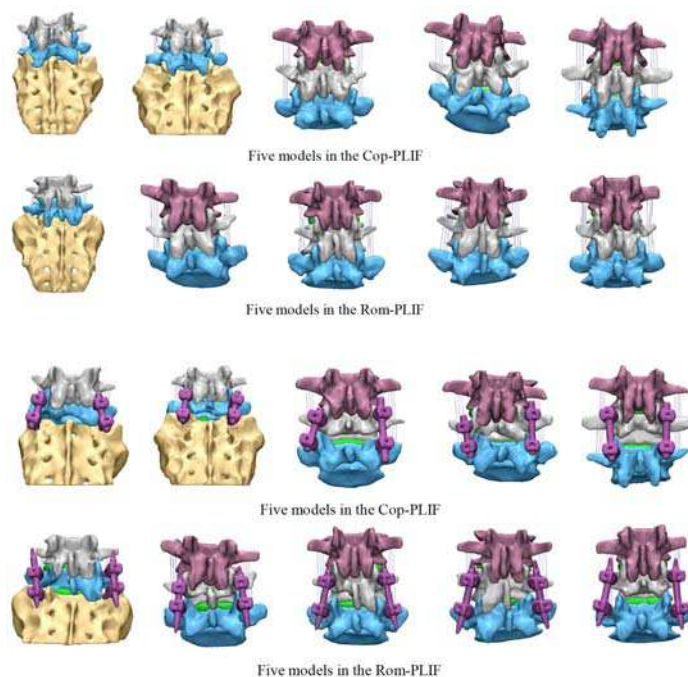
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**Introduction:** There have been conflicting results regarding the surgical outcome of lumbar fusion surgery using two different techniques between robot-assisted pedicle screw fixation and conventional free-hand technique. In addition, there have been no studies about biomechanical issues between the both techniques. Therefore, the purpose of this study was to investigate biomechanical properties in terms of stress at adjacent segments using robot-assisted pedicle screw insertion technique (robot-assisted minimally invasive posterior lumbar interbody fusion, Rom-PLIF) and free-hand technique (conventional, free-hand, open approach, posterior lumbar interbody fusion, Cop-PLIF) for instrumented lumbar fusion surgery, using post-hoc analysis for patient-specific finite element model.

**Methods:** Patients were randomly assigned to undergo an instrumented PLIF procedure using a Rom-PLIF (37 patients) or a Cop-PLIF (41), respectively. Five patients in each group were selected by a simple random sampling method after operation, and 10 preoperative and postoperative lumbar spines were modeled from preoperative high-resolution computed tomography (CT) of 10 patients using the same method for a validated lumbar spine model. Under 4 pure moments of 7.5 Nm, the changes in intradiscal pressure and facet joint contact force at the proximal adjacent segment following fusion surgery were analyzed and compared to preoperative states.

**Results:** Representativeness of random samples was verified. Both groups showed significant increases in postoperative intradiscal pressure at the proximal adjacent segment under 4 moments, compared to the preoperative state. The Cop-PLIF models demonstrated significantly higher percent increments of intradiscal pressure at proximal adjacent segments under extension, lateral bending, and torsion moments than the Rom-PLIF models ( $P = 0.032$ ,  $P = 0.008$ , and  $P = 0.016$ , respectively). Furthermore, the percent increment of facet contact force was significantly higher in the Cop-PLIF models under extension and torsion moments than in the Rom-PLIF models ( $P = 0.016$  under both extension and torsion moments).

**Discussion:** The present study showed the clinical application of subject-specific FE analysis in the spine. Even though there was biomechanical superiority of the robot-assisted insertions in terms of alleviation of stress increments at adjacent segments after fusion, the cautious interpretation is needed because of small sample size.



## CO-ACTIVATION OF TRUNK MUSCLES DURING HIP EXTENSION MOVEMENTS

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### INTRODUCTION:

Active prone hip extension (APHE) is used to both, evaluate and treat patients with hip and lumbar disorders. Patients with low back pain often show improper coordination of the hip and trunk muscles during APHE. Few studies have reported the muscle activity of the trunk and lower extremities during active hip extension. Therefore, the purpose of this study was to clarify the interaction of activity patterns between the trunk and lower limb muscles during active hip extension.

### METHODS:

Eleven healthy men participated in the study. Electromyographic (EMG) signals were measured during the following 3 types of active hip extension exercises: APHE, APHE with a 3-kg weight, and APHE at maximum speed. Each hip extension was performed from the hip in the neutral position to 10 degrees of hip extension. The subjects were instructed to raise their leg with the knee extended in 1 sec, except under the maximum speed condition. Surface electrodes were attached to the bilateral internal oblique (IO), external oblique (EO), rectus abdominis (RA), erector spinae (ES), and lumbar multifidus (MF) muscles. With regard to the upper and lower gluteus maximus (Gmax) and biceps femoris (BF) muscles, electrodes were attached only to the right side. The root mean square (RMS) were calculated from the beginning of the hip extension to the end of the movement, and normalized as a percentage of the activity compared to the maximum voluntary contraction for each muscle (%MVC). To compare the activity levels among trunk muscles during APHE, a one-way ANOVA was employed. In addition, muscle activity differences among the tasks in each muscle were compared using repeated measure ANOVA. The alpha level was set at 0.05.

### RESULTS:

The activity of the left IO muscle (mean  $\pm$  SD: 5.7  $\pm$  2.8 %MVC) was significantly greater than that of the other abdominal muscles during APHE. The activities of the bilateral IO and U-Gmax and L-Gmax significantly increased during APHE at maximum speed compared with APHE at normal speed. The activities of the left IO, left MF, bilateral ES, and L-Gmax significantly increased during APHE with a 3-kg weight compared with APHE without.

### DISCUSSION:

This study showed that a higher activity of the contralateral IO muscle was observed during APHE. APHE leads to right pelvic rotation. It is possible that the contralateral IO activates in order to stabilize the pelvic position against the leg movement. Moreover, faster APHE motion increased abdominal muscle activity, particularly the IO muscle. Because faster movement might cause a larger disturbance to the pelvic-lumbo region, the IO required more muscle activity to stabilize the region.



## DIASTASIS RECTI AND TRUNK MUSCLE FUNCTION IN WOMEN AT ONE-YEAR POSTPARTUM

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**Introduction:** Approximately 50% of women demonstrate a separation of the abdominal muscles at the linea alba, known as diastasis recti (DR), after childbirth [1]. DR appears to persist beyond the postpartum year in a large proportion of women [2]. However, the impact DR has on physical and functional abilities has not been clearly established and is not well understood. The main purpose of this study was to test whether or not women who present with DR at 12-14 months postpartum demonstrate limitations in trunk muscle strength and/or endurance, report higher levels of low back pain and/or dysfunction, or demonstrate a combination of impairments and functional deficits. We also aimed to determine whether the severity of physical impairments and/or their reported symptoms were associated with the amount of separation measured at the linea alba.

**Methods:** A cross-sectional, observational study of primiparous women (n=40) between 12 and 14 months post-partum was conducted. Ultrasound imaging was used to stratify women into cases (n=18) or controls (n=22). Participants were considered cases (DR) if they presented with an inter-rectus distance (IRD)  $\geq 2.2$ cm at two or more measurement sites. Maximal isometric trunk torque generating capacity was measured (Newton-meters) for flexion, extension, and rotation. Trunk endurance was measured (time (seconds) to failure) for trunk flexion, extension, and lateral flexion endurance tasks. Ability to perform a sit-up (0-3 points) and performance on the Sitting-Rising Test (0-10 points), were scored based on the best performance of three trials of each task. Finally, low back pain disability was assessed using the Roland Morris Low Back Pain Questionnaire (0-24 points) and low back, upper back, pelvic, and abdominal pain were scored using separate numerical rating scales (NRSs; 0-100). Women with and without DR were compared using independent t-tests for all normally distributed demographic and outcome variables, whereas the Kruskal-Wallis test was used for isometric extension torque. Pearson's product-moment correlation coefficients and Spearman rank correlation coefficients were used to determine if there were associations between IRD and variables in which significant differences were found between cohorts. An  $\alpha = 0.05$  was used for all tests.

**Results:** Baby's weight at birth was the only demographic variable that was significantly different between the two cohorts: women with DR at one-year postpartum had delivered heavier babies ( $p = 0.009$ ). Women with DR demonstrated lower trunk muscle rotation torque ( $p = 0.004$ ) and lower on sit-up test scores ( $p = 0.024$ ). No other measures were different between the cohorts. The correlation analyses revealed that IRD was positively associated with the weight of the baby at birth ( $r = 0.466$ ,  $p < 0.05$ ) and that IRD was negatively associated with trunk rotation torque ( $r = -0.367$ ,  $p < 0.05$ ) and ability to perform a sit-up ( $r = -0.514$ ,  $p < 0.01$ ).

**Discussion:** The presence of DR in primiparous women at one-year postpartum appears to have an impact on trunk rotation strength and ability to perform a sit-up. However, these impairments do not seem to be associated with self-reported low back pain or dysfunction when measured at one-year postpartum.

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## SPINAL TISSUE LOADING CREATED BY DIFFERENT METHODS OF SPINAL MANIPULATIVE THERAPY (SMT) APPLICATION

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**INTRODUCTION:** Spinal manipulative therapy (SMT) is a common manual intervention for low back pain involving the application of a dynamic, high-velocity, low-amplitude thrust resulting in a mechanical deformation of the spine and surrounding soft tissues. As is the case with medication, the therapeutic effect of SMT may be modified by parameters such as dosage, application site and method of application. Although there are many distinct methods by which to apply SMT, it is not known if different forms of SMT application create different loads on spinal tissues. Should the method of SMT application modulate spinal tissue loading, quantifying this relation may help explain the varied clinical outcomes of SMT in terms of effect and safety.

**Objective:** To quantify loads created in porcine cadaveric spinal tissues arising from three different forms of SMT application.

**Methods:** SMT was applied to the L3/L4 facet joint of 12 porcine cadavers using three SMT techniques: a clinical device that applies forces through a hand-held instrument (INST), a manual technique of applying SMT clinically (MAN) and a research device that applies parameters of manual SMT through a servo-controlled linear actuator motor (SERVO). The resulting vertebral kinematics from each method of SMT application were tracked optically via indwelling bone pins. The L3/L4 segment was then removed, mounted in a parallel robotic platform having a 6-axis load cell and the resulting kinematics from each SMT replayed robotically. Forces experienced by spinal structures were measured and the process repeated following dissection of posterior ligaments (supra- and interspinous ligaments), posterior joint structures (bilateral facet joints, capsules and ligamentum flavum) and the anterior joint structures (intervertebral disc, anterior and posterior longitudinal ligaments).

**Results:** The results show that load distribution within spinal tissues differs significantly as a function of the SMT application method. Generally, SMT application with INST created forces significantly smaller than MAN and SERVO ( $p < 0.05$ ) while MAN and SERVO created greater forces in different directions. Specifically, MAN and SERVO created comparable anteroposterior forces in the intact specimen. Additionally, although MAN created greater anteroposterior forces on anterior joint structures (intervertebral disc, anterior and posterior longitudinal ligaments) compared to SERVO ( $p < 0.05$ ), sequential dissection of spinal structures revealed that anterior joint structures generally experienced greater forces during SMT application with SERVO ( $p < 0.05$ ).

**DISCUSSION:** Given that all SMTs were applied at the same anatomical location, differences in loading distribution are likely related to differences in SMT force-time profile characteristics. Indeed, each method of SMT application was unique in terms of various application characteristics including: preload phase, peak force, time to peak force, contact surface area, total pressure, loading rate. Based on these results, and given our previous work that demonstrated that SMT creates forces that are unique from passive movements, it is possible that different SMT application techniques could be capable of eliciting unique outcomes in terms of effect and safety. These results may partially explain the variation in SMT outcomes observed in clinical trials.

## EFFECT OF LUMBAR DISC FUSION ON ADJACENT SEGMENT DISC DEFORMATION: AN IN-VIVO PATIENT ANALYSIS PRE AND POST FUSION SURGERY

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### INTRODUCTION

Up to 80% of patients develop adjacent segment degeneration (ASD) as early as one year after lumbar fusion, with an estimated 17-36% of patients requiring reoperation due to symptomatic ASD within 5-10 years. Changes in kinematics at the adjacent segment after a spinal fusion have been assumed a biomechanical factor causing ASD. However, evidence of how spinal fusion changes the adjacent segment motion in-vivo is lacking. This study investigated adjacent segment disc deformation under weightbearing conditions before and after fusion surgeries in lumbar patients.

### METHODS

Two patients with disk degenerative disease at L4-S1 were examined for this pilot study. Before undergoing a fusion surgery, each subject was MRI scanned for construction of 3D anatomic models of lumbar vertebrae (Fig. 1). The subjects were then imaged using a dual fluoroscopic imaging system at weightbearing, standing condition (Fig. 2) and then they underwent a fusion surgery at the L4-S1 segments via an anterior approach. The subjects were imaged again after one year of the fusion surgery for post-op analysis. Deformations of the adjacent disc of L3-4 at the standing position before and after the fusion surgery were calculated using the changes in geometry between the endplates of L3 and L4 segments, using the MRI disc as the reference. We specifically compared the adjacent disc deformation at anterior, mid and posterior positions before and after the fusion surgery.

### RESULTS

Our data shows that a fusion surgery causes an increase in compression deformation at the anterior region of the adjacent disc of L3-4 of both patients (Fig. 3). Before surgery, weightbearing standing position caused compressive deformation of 23% and -5% for the two patients, respectively at anterior position of the adjacent disc. One year after surgery, the compressive deformations were 61% and 15% for the two subjects respectively. The surgery caused 38% and 10% increase in compressive deformation for the two patients respectively at the anterior position of the adjacent disc. Similar patterns were observed at the center position of the adjacent disc but with a less magnitude compared to the anterior portion. At the posterior position, the fusion caused decreases in compressive deformation compared to pre-operative conditions.

### DISCUSSION

This study investigated adjacent disc deformation before and after fusion of L4-S1 under a weightbearing standing loading condition. Our data indicates that a fusion surgery increases the compressive deformation at the anterior and center positions of the disc but a decrease in the posterior position of the disc. The anterior approach of fusion increased the fusion height of the fused segments at the anterior position, causing increased stresses onto the adjacent segment discs. Furthermore, lumbar fusion results in higher disc deformation at adjacent segment discs and these deformation changes might be correlated to post-operative degeneration of the adjacent segment discs. Future studies should include large number of patients, evaluate post-operative disc quality changes using advanced MRI techniques like T2 mapping and T1rho sequences and correlate disc deformation changes with disc degeneration measured using MRI techniques.

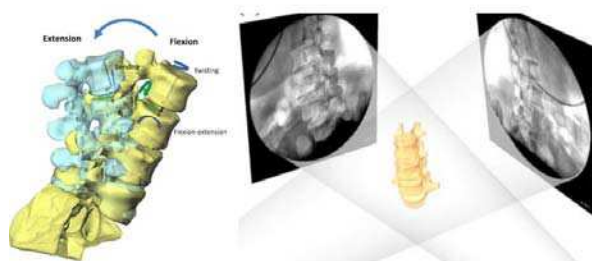


Fig 1: Constructed 3D anatomic model of lumbar vertebrae using MRI scans



Fig 2: Dual fluoroscopic imaging system for in vivo testing of weightbearing standing position.

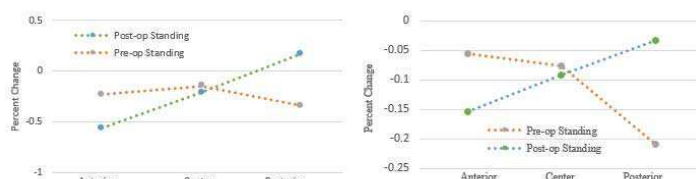


Fig 3: Changes in compression deformation in pre and post fusion surgery

## THE ROLE OF L5-S1 INTERVERTEBRAL DISC SHAPE IN THE PROGRESSION OF A BILATERAL SPONDYLOLYTIC DEFECT AT L5 TO SPONDYLOLISTHESIS: A BIOMECHANICAL INVESTIGATION USING FINITE ELEMENT ANALYSIS

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### INTRODUCTION

Through changes in sacral slope (SS), sacro-pelvic alignment influences the L5-S1 intervertebral disc shape, which may create a biomechanical environment that results in the development of a spondylolytic defect in the L5 vertebra and spondylolisthesis. Since spondylolysis and associated spondylolisthesis are mainly assessed on radiographic images, underlying forces responsible for the progression of the vertebral slippage remain unclear. Using computed tomography (CT) data from lumbosacral spine and nonlinear finite element (FE) modelling, the main aim of this biomechanical study was to examine the role of L5-S1 intervertebral disc shape in the progression of a bilateral spondylolytic defect at L5 to spondylolisthesis.

### METHODS

High resolution lumbosacral CT data from an anonymised healthy male subject (26 yo) were segmented in image processing software Avizo Standard to build a geometrically accurate 3D model of an intact lumbosacral spine (L1-S1). Changes made to sacral slope resulted in observable changes in L5-S1 disc shape. The segmented CT data were manipulated to generate three more models representing: a bilateral spondylolytic defect at L5; a bilateral spondylolytic defect at L5 with SS+10 degrees; a bilateral spondylolytic defect at L5 with SS-10 degrees. The solid models were then imported into FE software Strand7 for pre-processing, running nonlinear solves, and post-processing of the results. The models were loaded in sagittal, coronal, and transverse planes with pure moments of 10Nm. Calibration of material properties was conducted in a separate pilot study.

### RESULTS

A L5 lytic defect significantly increased L5-S1 range of motion (ROM) and mid-discal plane shear and normal stresses from the baseline intact state levels (figure 1). When compared with normal SS lytic model, SS+10 lytic model exhibited greater ROM and disc shear stresses, and posterior normal stress concentration in both flexion and extension. A SS-10 lytic model exhibited greater ROM and disc shear stresses, and anterior normal stress concentration in flexion and extension compared with a normal SS lytic model. Independent of SS, a L5 lytic defect resulted in offloading of the L5-S1 facet joint capsules during flexion and extension.

### DISCUSSION

A spondylolytic defect in the L5 vertebra significantly increased kinematics, and shear and normal stresses in the L5-S1 disc compared with the intact state, which may predispose the disc to accelerated degeneration. Assuming the same mid disc height in the sagittal plane, increasing SS had a "wedging effect" on the L5-S1 disc which induced additional directional instabilities at this level. A L5 lytic defect in SS+10 model exhibited greater flexion instability and abnormal posterior annulus stress concentrations (but no extension instability) when compared with a normal SS lytic model. The SS-10 model exhibited a "flattening" of the L5-S1 disc, which demonstrated extension instabilities and abnormal loading of the anterior annulus. Although other factors such as disc degeneration may be implicated in the progression of vertebral slippage, the findings from this study suggest different pathomechanisms may exist for the progression of a L5 lytic defect to spondylolisthesis in cases of atypical disc shapes.

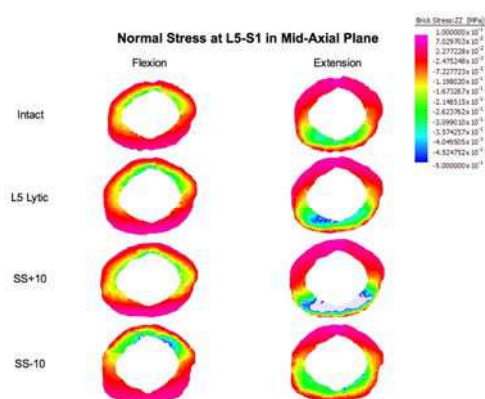


Figure 1: L5-S1 mid-disc normal stress distribution

## A COMPUTED TOMOGRAPHY ANALYSIS OF S2 ALAR-ILIAC AND ILIAC SCREWS: COMPARISON USING HOUNSFIELD UNIT VALUE ALONG SCREW PATHWAY

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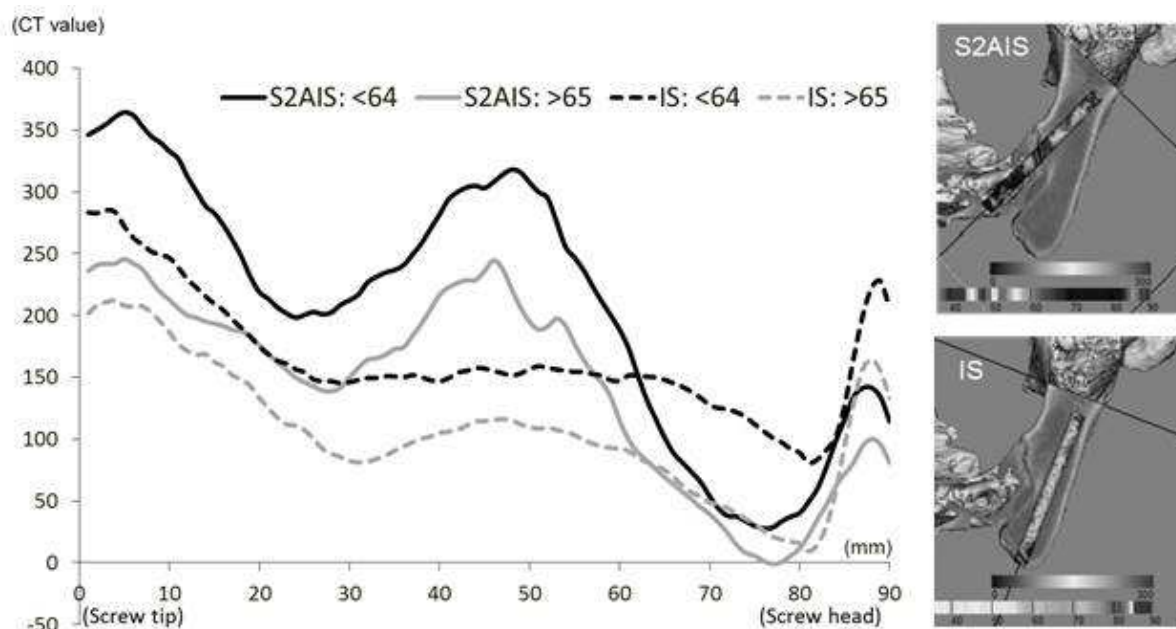
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**Introduction:** S2 alar-iliac and iliac screws are now commonly used in iliosacral fixation. The importance of vertebral bone density in screw fixation has been the subject of several studies evaluating screw stability and predicting lumbar vertebrae strength. A number of studies have been conducted regarding bone density variations in the cervical and thoracolumbar spine. However, such variations in bone density in the pathways of the iliosacral implant have not been well-documented. The purpose of this study was to investigate the bone density along screw pathway of the S2 alar-iliac and iliac screws using computed tomography (CT) values (in Hounsfield units) and to compare these values by age and sex.

**Material and methods:** Abdominal CT scan data were obtained from 33 adults (14 males, 19 females; mean age, 64 years). The CT value was recorded with simulated placement of S2 alar-iliac and iliac screws using the ZedView VEGA (LEXI Co., Ltd., Tokyo, Japan). The CT value was measured to a depth of 90 mm at 1-mm intervals in all screw insertion areas, and the mean CT value was calculated at each site. The CT values of S2 alar-iliac and iliac screws were compared between the young ( $\leq 64$  years old) and the elderly ( $\geq 65$  years old) and between men and women.

**Results:** The CT values of the iliac screws tended to increase at the site where the screw tip reached the cortex, and the CT values of the S2 alar-iliac screws showed the same tendency. In addition, the CT values of the S2 alar-iliac screws were significantly higher than those of the iliac screws at about 40 mm from the screw penetration point, which is the sacroiliac joint. The CT values of both screws in the young were significantly higher than in the elderly (figure). There were no significant differences in findings between men and women.

**Discussion:** Recent studies have demonstrated that CT examinations using automatic exposure control are able to measure regional cancellous bone mineral density accurately. Some papers have further reported that the screw insertion torque is significantly dependent on the bone density, making the CT value around the implant a useful index for determining bone density. This simulation system is useful for preoperative planning because the CT value of the screw insertion area can be visualized and quantified in real time. The results of this study revealed that S2 alar iliac screws have a pathway with a higher CT value and better fixability than iliac screws. The difference in the bone densities by screw pathway should be considered when selecting and placing screw implants for iliosacral fixation.



## NUCLEUS IMPLANT GEOMETRY SIGNIFICANTLY INFLUENCES BENDING STIFFNESS OF THE HUMAN LUMBAR MOTION SEGMENT: A FINITE ELEMENT MODELLING STUDY

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### INTRODUCTION

Nucleus arthroplasty systems are a promising treatment option for early stages of symptomatic intervertebral disc (IVD) degeneration. The synergistic interaction between the implant, remnant nucleus, annulus, and endplates is responsible for stiffness restoration of the motion segment, and is believed to be of critical importance for the clinical success of the implant. The main objective of this finite element modelling study was to systematically assess the effect of variation in the implant geometry on the bending stiffness of the human lumbar spine for an *in situ* curing non-hydrogel silicone based nucleus replacement implant contained within an inflatable balloon (Kunovus LLC, Delaware).

### METHODS

High resolution computed tomography scans of lumbar spine of an anonymised healthy male subject (26 yo) were segmented in image processing software Avizo Standard to build a 3D model of an intact lumbar spine (L1-L5). The solid model was imported into FE software Strand7 for pre-processing, running nonlinear solves, and post-processing of the results. The intact FE model was further manipulated to generate eight more models representing different grades of nucleotomy and implant filling in the L3-L4 IVD (Figure1). A separate pilot study was conducted to calibrate material properties for the IVD tissues and primary ligaments.

### RESULTS

At the index level, both partial and complete nucleotomy significantly increased annular bulge during flexion and extension loading as measured in the mid sagittal plane (greatest increase during Fx in the complete nucleotomy model was 0.63 mm). Compared with the baseline intact state, a complete nucleotomy at L3-L4 significantly increased mean annular stress (+38%), decreased mean stress in the innermost endplate region (-65%), and increased mean axial strain in the capsular ligaments (+7%) at peak flexural load. The anterior and posterior annular bulges were restored to the intact state levels in all the completely filled implant models similarly, but large deviations were observed in the partially filled implant models. In the completely filled implant models, mean annular stresses were below the intact state levels (-5%, for 100% IMP model at peak flexural load) but mean stresses in the innermost endplate region were consistently above the intact state levels (+9%, for 100% IMP model at peak flexural load).

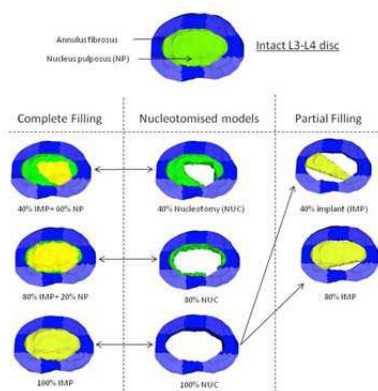


Figure 1: Transverse view of the L3-L4 intervertebral disc in different finite element models of lumbar spine

### DISCUSSION

The present study focused solely on the restoration of bending stiffness of an IVD with different grades of volume fill of a non-hydrogel silicone based nucleus replacement implant. The results of this study present a conservative estimate of the increase in annular bulge as no damage to the annulus was modelled in the nucleotomised or implant filled states. Nucleotomy, whether partial or complete, significantly increased annular bulge and stresses in flexion and extension. These biomechanical changes may cause structural damages to the annulus in the form of delamination of annulus layers, fissure formation and inward buckling of the lamellae, all of which may accelerate annular degeneration. Whilst partial filling of the implant may result in lower implant-endplate interface stresses, annular bulge was restored to normal intact state levels only in the completely filled implant models.

## CORTICAL BONE VS TRADITIONAL TRAJECTORY PEDICLE SCREWS: A COMBINED COMPRESSION AND FLEXION BIOMECHANICAL ANALYSIS

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### Background

Rigid posterior fixation of the lumbar spine may be difficult, particularly in the setting of osteoporosis. Traditional trajectory (TT) pedicle screws follow a lateral-to-medial path and are relatively neutral in the cephalad-to-caudad direction. Recently, a new trajectory has been proposed in order to maximize contact with the cortical bone of the posterior elements. This Cortical Bone Trajectory (CBT) has a more inferomedial starting point and follows a medial-to-lateral and caudad-to-cephalad path.

Previous biomechanical reports have reported favorable peak insertional torque, resistance to pullout, and resistance to toggle in CBT pedicle screws. The purpose of this study was to evaluate CBT vs TT pedicle screws in a combined axial load and sagittal flexion model which may more accurately simulate in vivo loading

### Methods

7 L2-L3 and L4-L5 motion segments were obtained from 7 human cadaveric lumbar spines. One specimen from each cadaver was randomly assigned to undergo instrumentation using CBT pedicle screws. The other specimen from each cadaver underwent instrumentation using TT pedicle screws. The pedicle screws were then connected with a rod and cap screw construct in the standard fashion. A single senior surgeon with experience using both techniques performed all instrumentation.

Each motion segment was then destabilized with bilateral facetectomies and complete removal of the intervertebral disc. Each specimen underwent testing to evaluate construct stiffness. Stiffness was defined as the slope of the loading curve from 5.5 to 7.5 Nm. Specimens then underwent cyclical loading in combined axial compression and sagittal flexion from 200N/2Nm to 750N/7.5Nm at 2 Hz for 50,000 cycles. Cyclical loading was stopped if the specimen was noted to exhibit 15 or more degrees of motion during a cycle. Specimens that survived cyclical loading were then reevaluated for stiffness according to the same protocol.

### Results

There was no difference between the two groups with respect to pre-cyclical stiffness testing: CBT  $2.8 \pm 1.3$  Nm/deg versus TT  $2.1 \pm 0.9$  Nm/deg ( $p = 0.22$ ). 2/7 TT specimens failed during the first 100 cycles of testing and 4/7 TT specimens failed during the first 20,000 cycles. Conversely 0/7 specimens in the CBT group failed during the first 100 cycles and only 1/7 of the specimens in the CBT group failed during the first 20,000 cycles. Only three specimens in each group survived all 50,000 cycles. Post cyclical load testing revealed no difference in stiffness between the CBT group  $6.5 \pm 3.2$  Nm/deg and the TT groups  $4.0 \pm 1.0$  Nm/deg ( $p = 0.55$ ). Subgroup analysis revealed no difference between the L2-L3 and L4-L5 motion segments.

### Conclusion

This is the first study of a single instrumented motion segment that compares CBT to TT pedicle screws in a combined axial compression and sagittal flexion model. The results of this study show no significant difference between the two groups, however, a higher portion of the TT specimens failed early during cyclical loading. From a biomechanical perspective, this study provides additional support in favor of the use of CBT pedicle screws as a valid alternative to TT pedicle screws.

## DIFFERENTIAL PATIENT RESPONSES TO SPINAL MANIPULATIVE THERAPY AND THEIR RELATION TO SPINAL DEGENERATION AND POST-TREATMENT CHANGES IN DISC DIFFUSION

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### Introduction

Our prior prospective non-randomized controlled study revealed that people with low back pain (LBP) who self-reported a >30% improvement in disability after spinal manipulative therapy (SMT) demonstrated significant post-treatment improvements in spinal stiffness, dynamic muscle thickness and disc diffusion, while those not having self-reported improvement did not have these objective changes. The mechanism underlying this differential post-SMT response remains unknown. The objective of the current secondary analysis was to determine if persons with non-specific LBP who respond to SMT have unique lumbar magnetic resonance imaging (MRI) findings compared to SMT non-responders.

### Methods

Thirty-two participants with non-specific LBP received lumbar MRI before and after SMT on Day 1. Resulting images were assessed for facet degeneration, disc degeneration, Modic changes and apparent diffusion coefficient (ADC). SMT was provided again on Day 4 without imaging. SMT responders were classified as having a > 30% reduction in their modified Oswestry disability at Day 7. Baseline MRI findings between responders and non-responders were compared. The associations between SMT responder status and the presence/absence of post-SMT increases in ADC values of discs associated with painful/non-painful segments as determined by palpation were calculated.

### Results

SMT responders tended to have a lower prevalence of severely degenerated facets ( $P = 0.05$ ) and higher baseline ADC values at the L4-5 disc when compared to SMT non-responders ( $P = 0.09$ ). SMT responders were also characterized by significant increases in post-SMT ADC values at discs associated with painful segments identified by palpation ( $P < 0.01$ ). There was no significant between-group difference in disc degeneration or Modic changes.

### Discussion

The less degenerated lumbar MRI findings in SMT responders suggest that SMT response may be mediated by spinal degeneration. Our findings provide novel insight into the underlying nature of the differential response to SMT, possible mechanisms of SMT and the existence of treatment specific forms of LBP.



**CAN A LUMBAR INTERSPINOUS STABILISATION DEVICE PROVIDE ADEQUATE SUPPORT TO ALLOW SPINAL FUSION: A BIOMECHANICAL TEST**

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**Introduction:**

SMS (Q Spine) is a lumbar stabilisation implant placed in the interspinous space and designed to restrict abnormal movement in the lumbar spine. This paper shows the results of biomechanical testing that has been done to use the product as an “adjunct to fusion” instead of an interspinous plate of which there are several on the market and pedicle screws which have a complication rate. The concept is that when an anterior interbody cage has been placed (PLIF/TLIF/ALIF/LLIF) the implant can be placed between the spinous processes, tightened and then bone graft can be placed along the lateral gutters to ensure a successful fusion.

**Methods:**

Testing was carried out as per the ASTM standard F2624 and F1717 at BWF Esslingen labs (DIN EN ISO/IEC 17025 : 2005). It was decided as per the test protocol to modify the test rig to show a more realistic situation using a TLIF PEEK cage as anterior column support with SMS at the back as an adjunct to the cage. (Diagram 1) This was because the original ASTM standards were designed for pedicle screw constructs and we felt it would be more appropriate to test the product with its intended use. The test rig was set up to test 3 SMS Implants with the aim being to see if the device was strong enough to withstand physiological loads and test the mode of failure.

**Results:**

Setup for compression bending fatigue test, using UHMWPE blocks and metal structure to represent an adult lumbar spinous process 5M cycles

Specimen number	F (N)
SMS 13 - 1	471
SMS 13 -2	422
SMS 13 -3	536
Mean value	476 std deviation 57

These figures represent the failure mode of the band slipping through the gate. This was the likeliest failure mode based on our knowledge of the implant. This compares with Spinous process strength in a human lumbar spine of 339N. (18) The static compression bending tests below show the load to failure of the PEEK implant which has a safety value of over 3 times the normal load before a spinous process fracture would occur.

Test set up for static compression bending test

Specimen Nr	Maximum load F (N)
1	1125
2	1023
3	1067
Mean Value	1072 std deviation 51



**Discussion:**

We already know that the SMS implant works as a lumbar stabilisation system where a disc is present. Overall we have shown that using SMS with a cage would be stronger than the normal loads that would be expected on a human spine. The construct will be stiff enough with an anterior cage to stabilise the spine and allow fusion to take place with the addition of bone graft down the postero-lateral gutters. The SMS implant is not as stiff as an Interspinous titanium plate and is not rigidly attached to the spinous process which should eliminate post-operative spinous process fractures.

**ANATOMICAL STUDY OF PSOAS MAJOR MUSCLE ON SAGITTAL MRI**

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**[Background]**

It is said that psoas major muscle does not work as flexor of the lower extremity at 0-45 degrees of the hip joint, but the actual function of this muscle is not clear. Anatomically, psoas major arises from the Th12~L5 vertebral bodies and transverse processes and is attached to the lesser trochanter of the femur. Although there have been many reports about the area of the psoas major on axial MRI, there have been none about its sagittal alignment muscle. We evaluated the influence of the psoas major muscle on pelvic alignment by performing sagittal MRI.

**[Methods]**

In this pilot study, we retrospectively reviewed 56 female patients aged 24 to 92 years ( ; mean age was 54.9) who underwent conventional pelvic MRI from 2010 through 2015. We measured 1)sacral slope (SS), 2)pelvic tilt (PT), 3)pelvic incidence (PI) with sagittal MRI. Anatomically psoas major arises from the Th12~L5 vertebral bodies and is attached to the lesser trochanter of the femur, changing direction over the iliopubic eminence. We paid attention to the anatomy and we measured 4) angle of psoas major muscle to the vertex of the iliopubic eminence on sagittal MRI(PMM angle). When we assume that psoas major acts like a pulley system on iliopubic eminence, . the direction of force of the psoas major muscle is divided into a forward component and an upward component on sagittal plane. The forward component depends on the distance between the lesser trochanter and the pulley. We measured 5)distance of the forward component(LPD). WeThen we analyzed the relations among age, SS, PT, PI, PMM angle and LPD.

**[Result]**

The mean SS was  $36.2\pm 8.3^\circ$ , the mean PT was  $13.3\pm 8.3^\circ$ , the mean PI was  $49.5\pm 10.6^\circ$ , PMM angle was  $117.5\pm 4.4^\circ$ , and the mean LPD was  $48.3\pm 8.1$ mm. There was correlation between age and SS, PT, LPD, between LPD and PT, and between PMM angle and SS, PI, LPD.

**[Discussion]**

The psoas major muscle might act as flexor of the lower extremity at 0 degrees flexion of the hip joint because the psoas major muscle seems to act as pulley system on iliopubic eminence. This study demonstrates that the forward component of the force of the psoas major muscle is getting smaller as the pelvis is tilted backward with aging. We think that it is one of the causes of walking difficulty in the elderly.

## INTERSPINOUS PROCESS IMPLANTS CAUSES WEAR OF THE SPINOUS PROCESSES IN PATIENTS TREATED FOR SPINA STENOSIS – AN EXPERIMENTAL BIOMECHANICAL STUDY WITH COMPARISON TO CLINICAL CASES

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**Introduction:** There are few biomechanical studies on Interspinous Process Implants (IPD) however none investigate the amount of wear on spinous processes. Therefore the objective of the present study was to investigate the effect of repetitive loading of the IPD Aperius on the spinous processes in a biomechanical porcine model. For comparison, three patients treated surgically with the same device have been followed for one to two years clinically and with image analyses (X-rays, MRI, CT-scans).

**Methods:** Four lumbar spines from 6 months old porcine were divided into seven segments, which received IPD. The segments were exposed to 20.000 cyclical loads. Afterwards the deformation (wear) of the segments was registered. The wear of the spinous processes was measured in mm on a following CT-scan. Additionally, the wear of the ex-vivo was compared to the wear of the spinous processes investigated by CT-scans or X-ray in three patients treated surgically with the same interspinous implant.

**Results:** The mean maximal deformation of porcine specimens was 1.79 mm (SD 0.25) with the largest deformation occurring in the first quarter of the loading (< 5000 cycles). The mean wear of the spinous processes after loading was 6.57 mm. A similar level of wear (mean 12.7 mm) of the spinous processes was detected in the patients.

**Conclusions and Discussion:** The Aperius IPD creates significant wear on the spinous processes in an experimental biomechanical study. Similar wear of the spinous processes are also present in patients treated with the same device post-operatively. How these findings influence the short and long term result of this implant device remains to be investigated in further biomechanical as well as clinical studies. For future development of this type of devices a proper selection of materials and design is essential to minimize wear effects on the spinous processes and thereby increase the possibilities for the devices to function as suggested.

## LUMBAR LORDOSIS OF SPINAL STENOSIS PATIENTS DURING INTRAOPERATIVE PRONE POSITIONING

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**Introduction:** To evaluate the effect of spondylolisthesis on lumbar lordosis on the OSI (Jackson; Orthopaedic Systems Inc.) frame. Restoration of lumbar lordosis is important for maintaining sagittal balance. Physiologic lumbar lordosis has to be gained by intraoperative prone positioning with a hip extension and posterior instrumentation technique. There are some debates about changing lumbar lordosis on the OSI frame after an intraoperative prone position. We evaluated the effect of spondylolisthesis on lumbar lordosis after an intraoperative prone position.

**Methods:** Sixty-seven patients, who underwent spinal fusion at the department of orthopaedic surgery of our hospital between May 2007 and February 2012, were included in this study. The study compared lumbar lordosis on preoperative upright, intraoperative prone and postoperative upright lateral X-rays between the simple stenosis (SS) group and spondylolisthesis group. The average age of patients was 67.86 years old. The average preoperative lordosis was 43.5° ( $\pm$  14.9°), average intraoperative lordosis was 48.8° ( $\pm$  13.2°), average postoperative lordosis was 46.5° ( $\pm$  16.1°) and the average change on the frame was 5.3° ( $\pm$  10.6°).

**Results:** Among all patients, 24 patients were diagnosed with simple spinal stenosis, 43 patients with spondylolisthesis (29 degenerative spondylolisthesis and 14 isthmic spondylolisthesis). Between the SS group and spondylolisthesis group, preoperative lordosis, intraoperative lordosis and postoperative lordosis were significantly larger in the spondylolisthesis group. The ratio of patients with increased lordosis on the OSI frame compared to preoperative lordosis was significantly higher in the spondylolisthesis group. The risk of increased lordosis on frame was significantly higher in the spondylolisthesis group (odds ratio, 3.325; 95% confidence interval, 1.101 to 10.039;  $p = 0.033$ ).

**Discussions:** Preservation of lordosis during instrumented lumbar fusion is important in the maintenance of normal sagittal alignment. The patients with degenerative spondylolisthesis or isthmic spondylolisthesis, the removal of a proximal thigh pad will be needed if segmental hyperlordosis is present in the lateral radiograph during level checking. Lumbar lordosis in the spondylolisthesis group with spondylolysis was increased on the OSI frame due to increased segmental lordosis of L5–S1 with anterior rotation of the pelvis. This segmental instability owing to pars defect may contribute to increased lumbar lordosis on the OSI frame in the spondylolisthesis group with spondylolysis. Intraoperative lumbar lordosis on the OSI frame with a prone position was larger in spondylolisthesis patients than in SS patients. Intraoperative lumbar lordosis on the OSI frame with a prone position also produced a larger postoperative lordosis angle after posterior spinal fusion surgery. Increase in lumbar lordosis on the OSI frame should be considered during posterior spinal fusion surgery, especially in spondylolisthesis patients.

## KINEMATIC ANALYSIS OF SPINO-PELVIC-RHYTHM USING A DYNAMIC FLAT PANEL DETECTOR

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### Introduction

Global spinal balance and its relationship to the pelvis have received much more attention since recent studies have shown that sagittal plane alignment correlates closely with disability and quality of life. It is no longer acceptable to perform spine surgery without considering global spinal balance and spinopelvic junction. However, it is well known that sagittal alignment of the human spine and pelvis in a standardized standing position is highly variable in different individuals. Although various formulas are used to predict the postoperative spinopelvic alignment for spinal deformity surgery, these classification and formulas have limitation because no regard is given to dynamic factor. We therefore investigated the variety of spino-pelvic-rhythm in healthy male adults.

### Methods

Fifteen healthy male adults aged  $30.6 \pm 6.2$  (range, 22–43) years old without lumbar disorder volunteered to participate. Imaging with a dynamic Flat Panel Detector (FPD) system was performed under the following imaging conditions: 70 kV, 4 mA, 10 ms, source–detector distance (SDD) 100 cm, and 2 frames/s. Sequential images were captured with the subjects in the standing position with maximal forward bending followed by backward bending for 10s at a constant rate. As a result, 20 lateral radiographs from L1 to femur were obtained. Only knee joint movement was restricted, horizontal front-back movement of pelvis was allowed. Spino-pelvic alignment were evaluated in the following parameters. 1) LL: Lumbar Lordosis, 2) Sacrofemoral angle: the angle formed between the axis of the femur and the line tangent to the upper endplate of S1, 3) SS: Sacral slope, 4) PI: Pelvic Incidence, 5) Movement distance of pelvis: horizontal offset between the vertical line and the posterior edge of S1 endplate. LL and Sacrofemoral angle were plotted in chronological order. For validation of the “Spino-pelvic rhythm”, we investigated the relationship between the LL and Sacrofemoral angle and the lumbar hip ratio (L/H ratio), which was calculated by dividing of the LL by the Sacrofemoral angle.

### Results

The mean changes of LL was  $83.2 \pm 9.5^\circ$ , the changes of sacrofemoral angle was  $25.9 \pm 19.7^\circ$ , SS was  $42.6 \pm 8.9^\circ$ , PI was  $43.2 \pm 7.7^\circ$ , movement distance of pelvis was  $15.7 \pm 3.4$  cm, and L/H ratio was  $3.6 \pm 2.7$ . However, the spino-pelvic rhythm changed over time, because the change of LL was larger than the change of sacrofemoral angle from the middle of the rising motion to the upright position. When compared with the change of LL, individual differences were largely seen in the change of sacrofemoral angle.

### Discussion

These results demonstrated the range of hip joint motion under the physiological condition differed substantially between individuals unlike anatomical motion. Therefore, spino-pelvic rhythm is dependent on the change of sacrofemoral angle.

## PARAVERTEBRAL MUSCLE VOLUME IN PATIENTS WITH LUMBAR DEGENERATIVE SCOLIOSIS

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**Introduction:** Sarcopenia in patients with degenerative lumbar scoliosis (DLS) is frequently found in clinical practice. However, to date the knowledge on paravertebral muscle (PVM) pathology in these patients is limited. Numerous studies have focused on the cross-sectional area of PVM in patients with lumbar spine diseases. After measurement of PVM volume using whole spine CT, we investigated the relationship between the volume and spinal alignment in order to determine the role of PVM volume in patients with DLS.

**Methods:** We recruited 10 patients with DLS (mean age; 70.9 years old, 6 females and 4 males) and 8 patients with lumbar disc herniation without scoliosis (mean age; 62.5 years old, 3 females and 5 males). Whole spine CT was taken and PVM volumes, such as multifidus muscle, longissimus muscle and iliopsoas muscle, were measured from L1 to L5 levels. The muscle volumes were compared between convex and concave sides in patients with DLS. The volume of fat infiltration in PVM was also measured in these patients.

**Results:** There was no difference in the PVM volumes of the right and left sides in patients with lumbar disc herniation. In patients with DLS, the PVM volumes of the concave side were greater than those of the convex side. The Cobb angle was positively associated with the difference in the muscle volumes of the concave and convex sides. There was no difference in the volume of fat infiltration.

**Discussion:** This study enabled PVM volume measurement in 3-dimensional analysis. The current results demonstrated that PVM volume of the convex side was less than that of the concave side and the degree of the scoliosis was correlated with PVM muscle volume. Although it is unknown whether these findings were related to the cause or result, they are new knowledge which will facilitate the understanding of the pathology of DLS.

## NFKB DECOY OLIGODEOXYNUCLEOTIDE INJECTED INTO NORMAL RABBIT INTERVERTEBRAL DISCS REMAINS IN THE DISCS AT LEAST 4 WEEKS AND RESTORED PUNCTURE-INDUCED DEGENERATED RABBIT INTERVERTEBRAL DISCS WITH LONG TERM ANALYSIS

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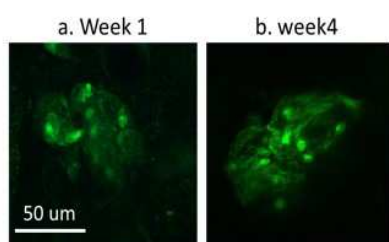
**INTRODUCTION:** Although the intradiscal injection of various pharmacological molecules has been considered for the treatment of discogenic pain, the fate of injected molecules in discs remains unclear [1, 2]. To develop therapeutic drugs with appropriate injection dosage and frequency, the investigation of the distribution and half-life of injected agents in the intervertebral disc (IVD), as well as an efficacy analysis, is essential. The aims of this study were to investigate three different modes of pharmacokinetic analysis of intradiscally-injected NFκB decoy-oligodeoxynucleotide (NFκB-ODN) [fluorescein amidite (FAM)-labeled NFκB-ODN (FAM-ODN), radiolabeled NFκB-ODN and native NFκB-ODN] in normal rabbits and to confirm the long term biological effects of clinical grade NFκB-ODN on degenerated discs in the rabbit needle puncture disc degeneration model [3].

### METHODS:

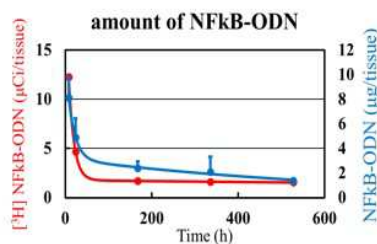
**Distribution studies:** With IACUC approval, under general anesthesia, rabbits received a single 10 μl injection of FAM-ODN (30 μg/disc) into the L2/3, L3/4, L4/5 and L5/6 IVDs (10 rabbits), radiolabeled NFκB-ODN into L3/4 IVDs (5 rabbits) or native NFκB-ODN into L3/4 IVDs (30 rabbits). Injected IVDs were collected at various time points up to 4 weeks. The distribution of FAM-ODN was visualized by confocal microscopy and the remaining amount of injected agents in IVDs was quantified following papain digestion. For the measurement of radiolabeled and native NFκB-ODN, the amount of NFκB-ODN was quantified using whole body autoradiography, and LC/MS/MS, respectively. For the biological effect analysis, clinical grade NFκB-ODN (10, 30, 100 μg/disc, L2/3 and L4/5) was injected 4 weeks after needle puncture in the rabbit disc degeneration model; disc heights were radiographically monitored every other week up to 12 weeks after injection.

### RESULTS and DISCUSSION:

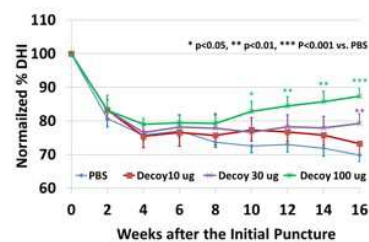
Confocal images after 1 week clearly indicate the nuclear localization of FAM-ODN (Fig.1a). Although the absolute intensity decreased to less than 5% of injected FAM-ODN at 1 week, a similar nuclear localization pattern in NP tissues was observed even 4 weeks after the initial injection (Fig.1b). This long term retention was supported by the results of LC/MS analyses of native NFκB-ODN showing a typical distribution and elimination pattern with a double exponential decay equation,  $y = C1e^{-(t/T1)} + C2e^{-(t/T2)}$  (Fig.2, distribution half-life; 0.5 days, elimination half-life; 25.6 days). Whole body autoradiography revealed the initial elimination was mainly through the kidney and the localization of remaining radioactivity was localized at the injection site from 0 to 28 days. Both fluorescent intensity and quantification of radioactive NFκB-ODN followed an elimination/distribution pattern similar to that of native NFκB-ODN measured by LC/MS. Interestingly, significant recoveries of disc height (30 μg [+11.8%] or 100 μg [+16.2%] of NFκB-ODN) were observed at the later time points of our long-term study (Fig.3, 6-12 weeks after injection, PBS vs. 30 μg, 100 μg,  $p < 0.05$  at 12 weeks); this suggests that the long term retention of NFκB-ODN in the cells may provide prolonged biological effects and supports our contention that a single injection of NFκB-ODN may impart clinically meaningful biological effects. The bioactivity of NFκB-ODN in cells at later time points is under investigation using the NFκB reporter cell line.



**Fig.1:** Confocal microscopy images of nucleus pulposus cells at week 1 (a) and week 4 (b) after injection (x63). Green signal is FAM-ODN.



**Fig.2:** Amount of NFκB-ODN remaining in IVDs post-injection obtained by whole body autoradiography (red) and LC/MS/MS (blue) measurements.



**Fig.3:** Disc height index (DHI) of puncture-induced rabbit degenerated IVDs.

- [1] Walsh AJ et al., Spine. 2004;29(2):156; [2] Akeda et al., Orthop Res Soc. 2005;p0045; [3] Masuda K+, Spine 30(1), 5, 2005

## DISC DEGENERATION THROUGH AXIAL LOADING ON THE LUMBAR SPINE: A RABBIT MODEL

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**Introduction:** Intervertebral disc degeneration (IDD) is thought to be the root cause of numerous musculoskeletal disorders of the spine. However, there is no clear understanding of its pathophysiology. Animal models of IDD play a crucial role in clarifying its pathological mechanisms and providing a means for evaluating new treatment modalities. However, no ideal animal model of IDD currently exists. The purpose of this study is to establish a novel *in vivo* rabbit model of early IDD, and explore the possible mechanisms based on this model.

**Methods:** Twenty-four New Zealand white rabbits were randomly assigned to two study groups. Each rabbit in the experimental group (n = 12) was placed into a plastic tube specially designed to maintain the animal in an upright posture. Following a 1-week adaptation period, a collar, weighing 600 g, was placed onto the neck of each experimental rabbit to begin the formal experiment. Rabbits in the experimental group were confined in their tubes for 6 hours every day, while rabbits in the control group (n = 12) were regularly fed in their cages throughout the entire experiment. X-ray and MRI examination were carried out every four weeks to monitor the dynamic changes of lumbar intervertebral discs. 14 weeks later, all animals were sacrificed. Specimens were obtained for analysis of degenerative changes with histologic methods.

**Results:** The lateral radiograph of the rabbits in the experimental group showed an obvious kyphotic curvature on the lower lumbar spine, and the disc height was much smaller than in the lateral decubitus position (Figure 1). Serial lateral radiographs of rabbits in the control and experimental groups showed a steady decrease in DHI values with time for both groups. However, no significant difference was observed between the two groups at any lumbar level or any time points. Serial MRI scans of the lumbar spinal areas of animals in the experimental and control groups showed that animal in the experimental group present a progressive decrease in the signal intensities of their lumbar discs over the 14-week period, and especially in the lower lumbar discs. In contrast, NP signal intensities in the control group decreased more slowly during the same period. Histologic examination further showed significant structural changes in the experimental group, including the fibrocartilage-like tissue ingrowth and accelerated fibrotic changes of the nucleus pulposus (Figure 2).

**Conclusion:** The upright posture combined with noninvasive external loading method used in this study induced accelerated degenerative changes in rabbit lumbar discs from the result of radiological and histological examination. On the basis of physiological mechanisms, our rabbit model partially resembles the human cumulative occupational lumbar load-induced disc degeneration, and thus could lead to new investigations on mechanisms of disc degeneration.



## BIOLOGICAL CHARACTERISTICS AND POTENTIAL OF NUCLEUS PULPOSUS DERIVED STEM CELLS IN HUMAN DEGENERATIVE INTERVERTEBRAL DISC WITH DIFFERENT PFIRRMANN GRADE

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**Introduction:** Degenerated disc disease (DDD) is the main cause of low back pain that significantly affected individual with quality of life and life expectancy. Tissue engineering and regeneration medicine of nucleus pulposus (NP) are thought to provide a promising approach for this and highlighted by the founding of nucleus pulposus derived stem cells (NPDCs). However, the biological characteristics of NPDCs in degenerated human intervertebral disc with different Pfirrmann grades may be different in certain extent that affect the regeneration ability and need further research.

**Methods:** Nucleus pulposus were obtained from 25 patients as surplus surgical material and NPMSCs were harvested by colony screening. The groups were divided according to different Pfirrmann grades. After in vitro expansion, the properties such as cell morphology, cell proliferation rate, colony-forming ability, the immunopheno-type and multi-directional differentiation were all compared within different Pfirrmann grades.

**Results:** From Pfirrmann grade I to V, the cell morphology were translating from spindle-shape to polygonal and the SEM showed the smooth and full cell shape changing to shrinking outline. Regarding the proliferation capacity and colony-forming ability, the cells in grade I to III showed significant better proliferation abilities than the rest groups. For the identification of cell surface antigen profile, all the NPDCs were positive for many stem cell markers including CD73, CD90, CD105, CD166, GD2, Tie 2 and negative for CD34, CD44, CD45, HLA-DR. However, the expression of CD105 (92.4±8.1 %, 90.3±7.5 %, 83.7±7.8 %, 66.1±10.3 %, and 62.3±9.6 %, from grade I to v), CD166 (95.4±4.8 %, 93.3±5.5 %, 85.9±8.3 %, 76.1±6.3 %, and 72.3±9.6 %, from grade I to v), Tie 2 (62.4±18.4 %, 56.3±17.7 %, 43.7±14.8 %, 26.1±15.4 %, and 12.3±8.2 %, from grade I to v) and GD2 (70.2±28.4 %, 65.2±20.7 %, 42.4±20.4 %, 25.2±19.4 %, and 10.2±6.8 %, from grade I to v) were decreasing according to different Pfirrmann grades and the last two grades showed significant difference. In addition, the ability to differentiate into osteoblasts and adipocytes were both reducing from grade I to V with obviously weakening in the grade III to V groups, while the chondrocytes differentiation were of no difference.

**Discussion:** This study demonstrated the different characteristics and potential of NPDCs with different Pfirrmann grades, indicating constant dynamic changes in the process of DDD. The outcome may imply different regeneration ability in different Pfirrmann grades of degenerated intervertebral disc (IVD). Moreover, these results may improve our understanding of IVD pathophysiology and provide us a new strategy in cell-based regenerative medicine and tissue engineering of DDD.

## MR EVALUATION OF THE CHARACTERISTICS OF THE INTERVERTEBRAL DISC IN SUBJECTS AFTER A SINGLE TRAUMATIC EVENT: CERVICAL SPINE.

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**Objective:** To investigate the magnetic resonance imaging characteristics of normal and pathologic cervical discs and adjacent vertebral bodies in victims of vertebral trauma and in a control group.

**Materials and methods:** 506 cervical spine MR examinations of patients with neck pain were compared with 86 normal controls. Investigated parameters were: Modic changes, uncovertebral joint arthrosis, disc herniation, bulging, protrusion, annular fissures, high intensity zones (HIZs), Pfirrmann classification, position of the centre of the nucleus pulposus (NP), disc height, signal intensity of the NP.



**Results:** Previously unreported findings are: all HIZs were present at the caudal part of the annulus; discs with adjacent Modic changes or uncovertebral arthrosis had reduced height; discs with a HIZ had no reduced height; herniation did not influence the disc height; common cervical trauma had no influence on the position of the centre of the NP; there was no correlation between scoliosis and the location of herniation.

We confirm previously published findings: magnetization transfer caused darkening of discs at higher levels of the spine; signal intensity of the NP decreased with ageing; degeneration was most prevalent at level C5-C6.

**Conclusion:** New findings on disc pathology were found.

*Fig. 1: Illustration of the ROI measurements. The image shows the measurements of the nucleus pulposus and annulus at all levels and the measurement of air surrounding the patient.*

## SCALE UP AND IN VIVO EVALUATION OF A DISC-LIKE ANGLE PLY STRUCTURE (DAPS) FOR TOTAL DISC REPLACEMENT IN A PRECLINICAL LARGE ANIMAL MODEL

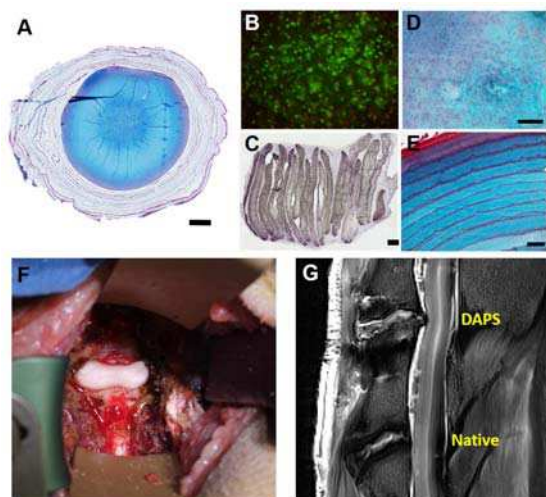
Sarah E Gullbrand<sup>1</sup>, Beth G Ashinsky<sup>1</sup>, Dong Hwa Kim<sup>1</sup>, John T Martin<sup>1</sup>, Thomas P Schaefer<sup>1</sup>, Dawn M Elliott<sup>2</sup>, Lachlan J Smith<sup>1</sup>, Robert L Mauck<sup>1</sup>, Harvey E Smith<sup>1</sup>

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**Introduction:** Replacement of the intervertebral disc with a viable, tissue engineered construct that recapitulates native disc structure and function is an attractive alternative to standard fusion or mechanical arthroplasty for the treatment of disc degeneration. Our group has previously developed disc-like angle ply structures (DAPS) at small size scales for *in vivo* evaluation in the rat caudal spine.<sup>1</sup> In order to translate the DAPS technology towards clinical use, successful fabrication and maturation of these constructs at larger size scales is necessary. The purpose of this study was to evaluate viability and matrix production of scaled-up DAPS over 5 weeks of *in vitro* culture and following *in vivo* implantation into the rat subcutaneous space or the goat cervical disc space.

**Methods:** DAPS were fabricated in two sizes – medium DAPS (n=5, 3mm high x 10 mm diameter) and large DAPS (n=5, 6 mm high x 20 mm diameter). The AF region was composed of layers of aligned poly( $\epsilon$ -caprolactone), seeded with bovine AF cells, and the nucleus pulposus (NP) region was composed of bovine NP cells seeded within an agarose or hyaluronic acid hydrogel. DAPS were cultured in chemically defined media with TGF- $\beta$ 3 for 5 weeks. DAPS of each size were assayed for NP cell viability (live/dead staining), AF cell metabolic activity (MTT assay), and glycosaminoglycan (GAG) content (DMMB assay). 3 large DAPS were implanted subcutaneously in athymic rats for 2 weeks, and NP viability, AF metabolic activity and matrix distribution (histology) assessed. 2 large DAPS were seeded with goat MSCs, precultured for 10 weeks as above, and implanted at the C2-C3 level of the goat cervical spine with anterior plate fixation. Four weeks post-implantation, T2-weighted MRI images were obtained of the cervical spine at 3T.



**Figure 1.** (A) Alcian blue (GAG) and picrosirius red (collagen) stained histological section of large DAPS after 5 weeks pre-culture. After subcutaneous implantation, cells remain viable in the central NP region (B, live/dead stain), and metabolically active in the AF (C, MTT assay, purple staining). Abundant Alcian blue and picrosirius red staining is evident in the NP (D) and AF (E) regions following subcutaneous implantation. Large DAPS implanted in the goat cervical spine (F) for 4 weeks retain high T2 signal similar to the native disc (G).

**Results:** After 5 weeks of culture, cell viability in the NP region were ~88% and ~89% for large and medium DAPS, respectively. Normalized MTT absorbance in the AF region, AF GAG content, and NP GAG content were not different between medium and large DAPS after 5 weeks culture. Histology demonstrated collagen and proteoglycan matrix distributed throughout the large DAPS (Fig. 1A), with more intense Alcian blue staining at the NP periphery. Following 2 weeks subcutaneous implantation, viability and metabolic activity were preserved in both NP and AF regions (Fig. 1B, C), and abundant collagen and proteoglycan matrix was evident throughout the DAPS (Fig. 1D, E). Goat MSC seeded DAPS were successfully implanted in the goat cervical spine (Fig. 1F), and maintained high signal intensity on T2-weighted MRI after 4 weeks of implantation (Fig. 1G).

**Discussion:** Through these studies, we have demonstrated the feasibility of scaling up DAPS for total disc replacement to clinically relevant size scales. Despite increases in height and diameter, large DAPS had similar viability and matrix production compared to the medium DAPS. Viability and matrix production in the large DAPS were maintained *in vivo* following subcutaneous implantation. Furthermore, pilot implantation of the DAPS in a goat cervical disc replacement model suggest that DAPS hydration and composition are maintained after 4 weeks *in vivo*.

- References: [1] Martin + 2015 ORS Proceedings

## INVESTIGATION OF INFLUENCE BY DIFFERENT HYDROGEL FEATURES AND GROWTH HORMONE ON THE DIRECTION OF HUMAN MESENCHYMAL STEM CELLS INTO THE CHONDROGENIC LINEAGE

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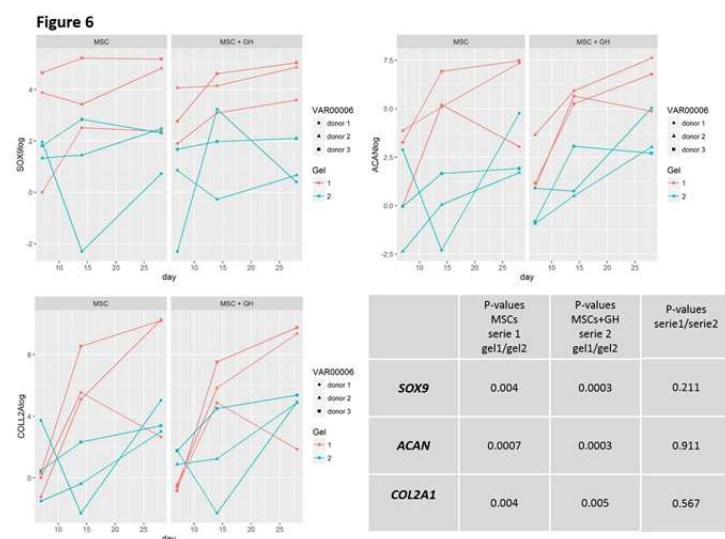
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**INTRODUCTION** Low back pain is a major public health issue in the Western world, one main cause is believed to be intervertebral disc (IVD) degeneration. To halt/diminish IVD degeneration, stem cell therapy using different biomaterials e.g. hydrogels as cell carriers has been suggested. In this study, two different hydrogels were compared and examined (*in vitro*) as potential cell carriers for stem cell therapy using human mesenchymal stem cells (hMSCs) intended for transplantation to degenerated IVDs. The aim was to investigate differentiation of hMSCs into the chondrogenic lineage in two different hydrogel microenvironments; Puramatrix® (Prm) or Hydromatrix® (Hrm) and potential effects of stimulation with growth hormone (GH).

**METHODS** hMSCs from three donors were isolated and cultured in Prm and Hrm hydrogels using a defined chondrogenic cell medium (series1) supplemented with GH (series2). The cell/hydrogel cultures were harvested at the time points day 7, 14 and 28. hMSCs/hydrogel cell cultures were investigated for cell viability by TUNEL assay. The samples were analyzed for cellular attachment/migration by B1 integrin expression by immunohistochemistry (IHC) and by transmission electron microscopy (TEM). Differentiation of the hMSCs was monitored in hMSCs/hydrogel cell cultures gene-expression analyses of **SOX9** (sex-determining region Y-box-9), **COLL2A1** (collagen2a1) and **ACAN** (aggrecan) by Real-time PCR. Histology stainings (Alcian Blue Van Gieson) for examination of accumulation of extracellular matrix (ECM) components glycosaminoglycans (GAGs) and collagen was performed.



**RESULTS** The TUNEL assay analysis demonstrated that the cells remained viable in the Hrm and Prm hydrogel cell cultures for at least 28 days (end point of study). In both types of cell/hydrogel cultures, the average cell viability was >95% at all time points. In both hydrogel types, hMSCs expressed integrin  $\beta 1$  and small cellular protrusions were observed by TEM which indicates adhesion of hMSCs. Gene expression of **SOX9**, **ACAN** and **COL2A1** was detected in cells after cell culture in chondrogenic medium in both types of hydrogels (series1). For all the investigated genes, a significant higher gene expression **SOX9** (P=0.004), **ACAN** (P=0.0007) and **COLL2A1** (P=0.004) was detected for the cells cultured in Hrm hydrogel compared to cells cultured in the Prm hydrogel (all time points included). In series 2, a significant higher gene expression **SOX9** (P= 0.0003), **ACAN** (P= 0.0003) and **COLL2A1** (P= 0.005) was detected for the cells cultured in Hrm hydrogel compared

to cells cultured in the Prm hydrogel (all time points included) in chondrogenic medium supplemented with GH. **Figure 1**. The hMSCs/hydrogel cultures stimulated with growth hormone (GH) displayed no clear effects on chondrogenesis.

In histology stainings of Hrm hydrogel cell cultures, a distinct positive histological staining for ECM (GAGs) were observed at the time points day 14 and peaked at day 28 (3/3 donors). No clear staining for ECM (GAGs) was detected in cell/Prm hydrogel cell cultures in any time points.

**DISCUSSION** In conclusion, both hydrogels, especially Hrm, was demonstrated a promising cell carrier *in vitro* when directing hMSCs into the chondrogenic lineage, but no clear effect was observed of GH on chondrogenesis in any hydrogel type. This knowledge could be useful in the context of biological approaches for regeneration of degenerated human IVDs.

## ROLE OF SEMAPHORIN 3A IN INTERVERTEBRAL DISC DEGENERATION

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**Introduction:** Intervertebral disc degeneration (IVDD) is affected by several factors including aging, inflammatory cytokines, oxidative stress, innervation, and angiogenesis. Vascular endothelial growth factor (VEGF) plays an important role in angiogenesis, and its expression increases in IVDD. An axon guidance molecule, semaphorin 3A (Sema 3A) shares the neuropilin 1 (Nrp1) receptor with VEGF and is a VEGF signaling antagonist in endothelial cells. However, the expression and function of Sema 3A in IVDD is not well understood.

**Aim:** The primary study objective was to clarify the role of Sema 3A in IVDD.

**Methods:** To construct an animal IVDD model, the intervertebral discs of the third to tenth coccygeal vertebrae of 8-week-old anesthetized Wistar rats were punctured using a 23-gauge needle. Human intervertebral discs (IVD) samples were surgically obtained following Keio University Hospital Ethical approval and receiving informed consent. Rat annulus fibrosus (AF) cells were microscopically isolated and cultured as previously reported (ref). All measurements were performed in triplicate. The significance of differences between groups was determined using Student's *t*-test ( $p < 0.05$ ).

**Results:** The expression of von Willebrand factor (vWF) protein, a marker of vascular endothelial cells was evaluated to assess angiogenesis in human IVDD samples (fig). Immunohistochemistry confirmed that vWF expression increased in AF as the IVDD grade higher. To determine the distribution of VEGF, Sema 3A, and Nrp1, we divided rat IVDs into nucleus pulposus (NP) and AF and evaluated the mRNA expression of these genes in each area. Real-time RT-PCR showed that the expression of VEGF and Nrp1 was higher in NP than in AF. Sema 3A expression was predominant in AF, but was significantly suppressed in the AF tissue of IVDD model rats compared with sham rats. To investigate the cause of the reduction of Sema 3A expression in IVDD, we treated cultured rat AF cells with interleukin (IL)-6 and tumor necrosis factor- $\alpha$  which are involved in IVDD and then assayed expression of Sema 3A mRNA with real-time RT-PCR. Treatment with both inflammatory cytokines significantly reduced Sema 3A expression. Treatment with DHMEQ, an inhibitor of NF- $\kappa$ b signaling, significantly inhibited the reduction of Sema 3A expression mediated by inflammatory cytokines.

**Discussion:** Sema 3A expression was higher in AF than in NP and was suppressed in the rat IVDD model. Sema 3A expression in cultured AF cells was downregulated by inflammatory cytokines through NF- $\kappa$ b signaling. These results indicate that Sema 3A may function as an anti-angiogenesis factor and may be involved in IVDD.



Figure . Immunohistochemistry of vWF in intervertebral disc degeneration. 75 y.o. female. Diagnosis of degenerative scoliosis. Disc sample was derived from L3/4 level.

## STIMULATION OF MITOGEN-ACTIVATED PROTEIN KINASES BY CYCLIC TENSILE STRESS IN HUMAN ANNULUS FIBROSUS CELLS INDUCES THE EXPRESSION OF PRO-INFLAMMATORY GENES

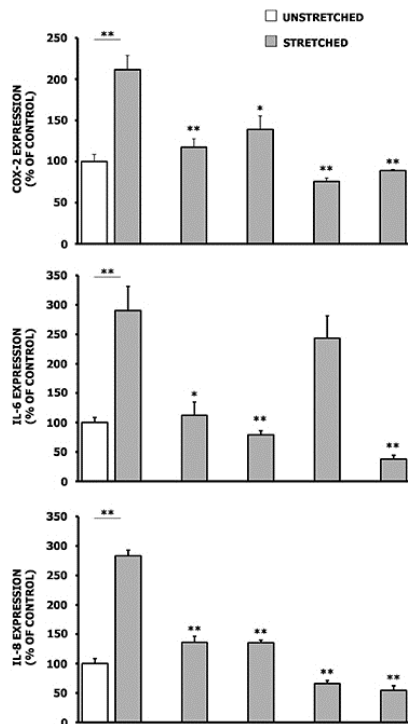
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**Introduction:** Mechanical forces due to occupational and lifestyle factors are considered to contribute to intervertebral disc (IVD) degeneration. On the other hand, normal levels of mechanical stimulation may be beneficial for IVD physiology. Especially in the area of annulus fibrosus (AF), cells are experiencing predominantly intermittent tensile forces. Hence, the effects of cyclic tensile stress (CTS) on AF cell cultures have been studied using a variety of models originating from species, such as rat, rabbit, calf or human. However, studies examining CTS-induced mechanotransduction in AF cells are rather scarce. Accordingly, objective of the present work was to study the role of mitogen-activated protein kinases (MAPKs) in human AF cells subjected to cyclic tensile stress (CTS) within physiological range.



PD98059 (ERK)	-	-	-	-	+	+
SP600125 (JNK)	-	-	-	+	-	+
SB203580 (p38)	-	-	+	-	-	+

**Methods:** Primary cultures from outer AF were developed from consenting patients and subjected to CTS using fibronectin-coated silicone dishes and a custom-built cell-stretching device allowing for the regulation of both magnitude and frequency of the strain. MAPK phosphorylation was studied by Western analysis, using antibodies against each one of the three members of the family (i.e. ERK, SAPK/JNK, and p38), as well as, corresponding specific pharmacologic inhibitors. Gene expression was assessed using quantitative RT-PCR. Cell proliferation was determined using both tritiated thymidine incorporation into DNA and flow cytometric analysis of cell cycle-phase distribution, and collagen synthesis using tritiated proline incorporation and the protease-free collagenase method.

**Results:** All three members of the MAPK family were found to be phosphorylated immediately after CTS application, with a second phosphorylation-peak appearing at later time points. In general, MAPK activation was proportional to the CTS magnitude, with the exception of ERK phosphorylation which peaked at a magnitude of 4%. Furthermore, all three MAPKs exhibited more intense phosphorylation at the highest frequency tested (1.5 Hz). CTS did not stimulate significantly DNA synthesis in AF cells. Moreover, CTS did not affect matrix metalloprotease-1, -2, and -3 gene expression and activity in the supernatant, neither collagen gene expression and overall accumulation. On the other hand, CTS stimulated the expression of the proinflammatory genes, cyclooxygenase-2 (COX-2), interleukin-6 (IL-6), and interleukin-8 (IL-8). This stimulation was more intense at the highest magnitude (8%) tested and at the median frequency (1 Hz) and time interval (12 h). Blocking of all three MAPKs attenuated the CTS-induced stimulation of COX-2 and IL-8. On the other hand, IL-6 expression was mediated only by SAPK/JNK and p38 MAPK.

matrix turnover of human AF cells, but initiates an inflammatory response. Delineating the mechanisms of IVD cell behavior under mechanical stresses will contribute to the understanding of disc pathophysiology and, possibly, to the design of novel therapeutic interventions.

**Discussion:** In conclusion, activation of MAPKs in human AF cells due to CTS was described for the first time, along with evidence that CTS within physiological range does not alter the proliferative status and extracellular



## A POSSIBLE ROLE OF THE TERMINAL COMPLEMENT COMPLEX TCC IN INTERVERTEBRAL DISC DEGENERATION

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**Introduction:** Inflammation factors and immune-mediated mechanisms are assumed to be involved in the pathomechanism of disc degeneration, but there is only limited knowledge regarding a possible role of the complement system in disc degeneration diseases (DDD). Activation of the complement system, specifically formation of the terminal complement complex TCC (C5b-9) at the cell membrane can be considered as a trigger for inflammatory responses. In the development of osteoarthritis a central role of TCC has been confirmed<sup>1</sup>. TCC formation can be activated by several factors some of which are also known contributors to disc degeneration and a previous study has demonstrated the occurrence of TCC in degenerated and herniated discs but not in normal discs<sup>2</sup>. Based on these findings we hypothesize that the involvement of TCC and complement related factors varies across different disc degeneration diseases and can be triggered by activators that play a role in the degenerative pathway.

**Material/Methods:** Histological sections of human disc tissue samples from patients with disc degeneration (DD, n=12, mean age 68, Pfirrmann 3-5), age-matched control discs (CD, n=4, mean age 61), one trauma patient (52 y) and four scoliosis patients (n=4, mean age 14) were analyzed by immunohistochemistry for TCC deposition (antibody against C5b-9), and the complement activation products C3/C3b, and C4d (classical pathway). Cells isolated from tissue samples of 3 donors were exposed to different concentrations of human standard serum with/without the addition of fibronectin fragments in a cell-based ELISA to determine if the formation of TCC can be activated on the cell membrane<sup>3</sup>. Heat-inactivated serum and C6-depleted serum served as controls. Results were evaluated by descriptive statistics.

**Results:** Preliminary results of our immunohistochemical investigation showed immune-positivity for TCC in most of the tissue biopsies from DDD patients (10 of 12 samples) with strong positive signals in cell clusters or in the vicinity of vascularization. The traumatic disc tissue was positive for TCC deposition while the age-matched controls of autopsy donors were negative or showed only very few cells with a weak TCC deposition. Most histological sections of scoliosis discs were negative or had only few positive cells (Fig. 1). The activation product of the classical pathway C3/C3b and C4d, could be detected in the environment of only few cells in degenerated disc tissue samples but not in the controls. In a cell-based immunoassay, we induced TCC deposition on IVD cells in the presence of human serum in a dose-dependent response. TCC formation was enhanced by the addition of fibronectin fragments.

**Discussion:** These data suggest that the complement system plays a role in the development and progression of disc degeneration. IVD cells are susceptible to TCC deposition in the presence of complement components and fibronectin fragments can increase TCC deposition. Ongoing studies to further elucidate the role of TCC formation in the pathogenesis of disc degeneration may contribute to the identification of new therapeutical targets.

**References:** 1. Wang et al. Nat. Med. 13(3):280-286 (2011) 2. Gronblad et al. Spine 28(2):114-118 (2003) 3. Jeon et al. J Immunol Methods 415:57-62 (2014)

## IDENTIFICATION OF INTRACELLULAR SOURCES OF REACTIVE OXYGEN SPECIES IN INTERVERTEBRAL DISCS UNDER INFLAMMATORY CONDITION

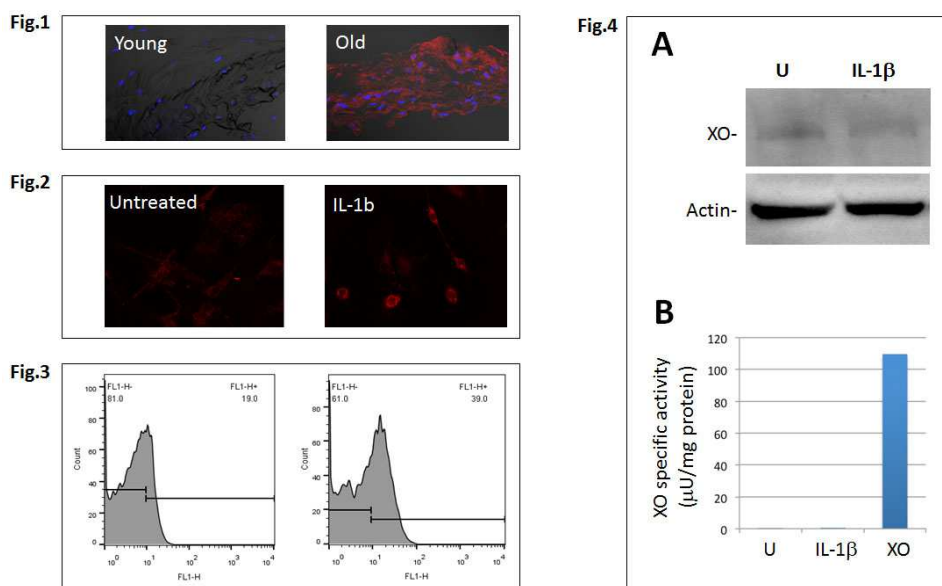
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**Introduction.** Oxidative damage is a key driver of aging. Increased oxidative damage has been well documented in aged and degenerative disc tissue, as evidenced by elevated levels of carboxymethyl-lysine and advanced glycation end products which are biomarkers of oxidized proteins and lipids<sup>1,2</sup>. Reactive oxygen species (ROS)-dependent oxidation of intracellular lipids, proteins and DNA leads to the accumulation of damaged biological molecules, which are thought to promote intervertebral disc degeneration (IDD)<sup>2,3</sup>. However the intracellular sources of ROS in discs are not known. The goal of this study is to determine the oxidant sources in disc cells in order to reveal the potential therapeutic targets for IDD treatment.

**Methods.** 5,5-Dimethyl-1-Pyrroline-N-Oxide (**DMPO**) spin trap detection of superoxide free radicals in disc sections of young (21 wks) and old (2.5 yrs) mice was performed<sup>4</sup>. Human NP cell cultures grown in hypoxia (5% O<sub>2</sub>) were treated with and without the pro-inflammatory cytokine IL-1b (1ng/ml) for 24 hrs to induce inflammatory stress. Total ROS was measured by flow cytometry by the DCF probe, and mitochondria-generated ROS was measured using MitoSox. Protein expression and enzymatic activity of xanthine oxidase, another cellular source of ROS, were measured by Western blot and XO specific activity assay.

**Results.** The **DMPO** spin trap assay detected a substantially higher level of superoxide radicals in disc tissue of old mice compared to young mice (Fig.1). IL-1b treatments of hNP cell cultures elevated the total cellular ROS (Fig. 2) as well as mitochondria ROS (Fig. 3) by two to three fold. Negligible protein expression and enzymatic activity of xanthine oxidase were detected in hNP cells, regardless of the presence or absence of IL-1b (Fig.4).

**Discussion.** Increased inflammation is closely associated with disc aging and degeneration. Inflammation is known to promote ROS production in various tissues, but this has not been demonstrated in the intervertebral disc until now. Here we showed that discs of old mice, previously reported to have increased inflammatory stress<sup>5</sup>, also contain elevated levels of ROS. We also demonstrated that inflammatory stress caused by IL-1b increased the production of total cellular ROS in human NP cells, the majority of which appeared to be mitochondria generated. Interestingly, xanthine oxidase, a major ROS producer under hypoxia and inflammation in other tissues, contributed little to hNP cell ROS production. These findings agree with our previous report of improved disc health in a mouse model of age-associated IDD treated with XJB-5-131, a mitochondria-targeted ROS scavenger<sup>6</sup>. Thus, mitochondria-generated ROS represents a potential target for therapeutic treatment of disc pathologies.



**Fig.1:** DMPO assay detecting superoxide radicals (red) in disc tissue of mice.

**Fig.2:** Detection of mitochondria-generated ROS by MitoSOX (red) in treated and untreated hNP cells.

**Fig.3:** Detection of total cellular ROS by flow cytometry with DCF probe in in treated and untreated hNP cells

**Fig.4:** Protein expression (A, Western blot) and enzymatic activity (B) of xanthine oxidase (XO) in untreated (U) and IL-1b-treated hNP cells. +Control showing enzymatic activity of purified XO (B).

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## THE EFFECT OF CAPACITIVELY COUPLED ELECTRICAL STIMULATION ON HUMAN INTERVERTEBRAL DISC CELLS FROM DISCS OF DIFFERENT DEGREES OF DEGENERATION

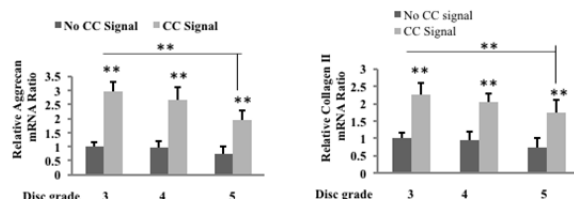
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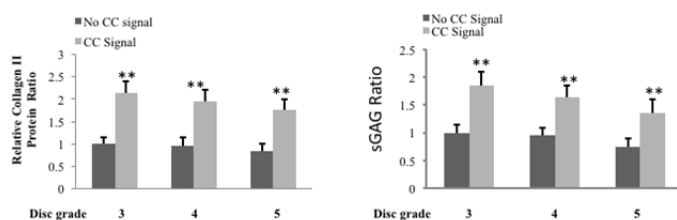
**Introduction:** Capacitively coupled (CC) electrical stimulation is a non-invasive treatment strategy with the ability to stimulate cells and produce many anabolic effects at the cellular level. While it is known to promote bone and wound healing, its effect on intervertebral disc (IVD) cells has not been well characterized. Its easy application and potential for repeated treatments over a long period of time makes it well-suited to treat chronic conditions such as IVD degeneration. In addition, the safety profile of CC around the spine is already established, as it is the only non-invasive technology that is FDA approved for promoting spinal fusion. As research potentially progresses towards a clinical strategy of using CC stimulation to treat IVD degeneration, it is important to determine how cells from varying degrees of disc degeneration respond to CC stimulation. To answer this question, CC was applied to human IVD cells *in vitro* from varying grades of disc degeneration and the resulting mRNA and protein levels of matrix macromolecules were determined.

**Methods:** Human nucleus pulposus (NP) tissue was collected from patients who underwent spinal fusion surgery. The amount of degeneration present in each disc specimen was determined by the consensus of three investigators on mid-sagittal T2 MRI images using the Pfirrmann grading system (grades III [N=3], IV [N=4], V [N=4]). After NP cells were isolated by sequential enzyme digestion with proteinase/collagenase, they were cultured in monolayer and then treated with CC stimulation for 7 days under previously determined optimal conditions (260 mV peak for 4 hrs per day, data not shown). The mRNA levels of collagen II and aggrecan were measured by real-time PCR and protein levels were determined by ELISAs. Sulfated glycosaminoglycan (sGAG) content was assayed using the DMMB method.

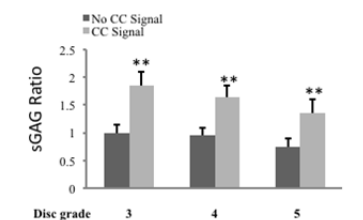
**Results:** Compared to controls, CC stimulation significantly up-regulated the production of mRNA of both aggrecan and collagen II (Figure 1) ( $P < 0.01$ ), regardless of Pfirrmann grade. Similarly, the protein levels of collagen II (Figure 2) and sGAG



**Figure 1.** The mRNA levels of aggrecan and collagen II in the cells from different Pfirrmann grades of IVD tissue (grades III, IV, and V) were measured by real-time PCR (\*\* $P < 0.01$  compared with no CC signal control).



**Figure 2.** The collagen II protein level in the cells from different Pfirrmann grades of IVD tissue (grades III, IV, and V) were measured by ELISAs.



**Figure 3.** The sulfated glycosaminoglycan (sGAG) content in the cells from different Pfirrmann grades of IVD tissue (grades III, IV, and V) was assayed using the DMMB method.

(Figure 3) were also upregulated regardless of Pfirrmann grade. This anabolic response was blunted, however, with more severe degeneration. For instance, NP cells from grade III discs had the greatest response to CC (i.e., 2.75x greater aggrecan expression), while cells from grade V discs had a smaller response (only 1.8x greater aggrecan expression,  $P < 0.05$ ). Similar blunted responses in grade V discs were seen for collagen II expression, aggrecan and collagen II protein levels, and sGAG levels.

**Conclusion:** CC stimulation significantly up-regulates the production of the matrix macromolecules aggrecan, collagen II, and sGAG in human NP cells *in vitro*, independent of Pfirrmann grade (grades III-V). However, the anabolic response of cells from higher degrees of degeneration was blunted. These data suggest that CC can be used to stimulate disc cells from all degrees of degeneration, however, Pfirrmann grade III and IV discs (not endstage degenerated

discs) may be the best target for CC treatment. Overall, these data are exciting in the progress towards using CC as a non-invasive treatment for IVD degeneration.

## SOUND THE 'ALARMIN:' DISC DEGENERATION AND TOLL-LIKE RECEPTORS IN MICE AND MEN

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**Introduction:** Intervertebral disc degeneration is a major cause of chronic low back pain. During degeneration, proteolytic enzymes degrade and fragment the extracellular matrix of the disc, and expression of proinflammatory cytokines and neurotrophins increase. These processes contribute to chronic pain, but poor understanding of the pathomechanisms limits treatment. Toll-like receptors (TLR) are activated by endogenous 'alarmins' such as extracellular matrix fragments like fibronectin, HMGB1 or S100 proteins. Recent evidence indicates that TLR2 regulates neurotrophin, cytokine and protease production in cultured human disc cells and thus likely has a role in degeneration. This study investigates whether TLR2 activation induces degeneration in an *ex vivo* human disc organ culture system and if TLR4 inhibition improves pain and disc phenotype in a well-characterized mouse model of disc degeneration and back pain (Sparc-null mice). TLR4 was chosen as a target in rodents and TLR2 in humans based on the receptor that is the more responsive to alarmins in each species.

**Methods:** Lumbar spines were collected from human organ donors following consent. Discs lacking radiographic signs of degeneration were excised, injected with Pam2CSK4, a TLR2/6 agonist; 30 kDa fibronectin (FN-f), a TLR2 activating alarmin; or vehicle and then cultured for 28 days. Glycosaminoglycan (GAG) content in nucleus pulposus (NP) tissue and release into medium was measured by DMMB. Collagen type II levels and fragmentation patterns and MMP 3 and 13 levels were assessed by western blot. Cytokine secretion was assessed by protein arrays. A well characterized mouse model of disc degeneration and low back pain (Sparc-null mice) were used for TLR4 inhibition studies. 8 month old mice were injected *i.p.* with TAK-242, a TLR4 specific antagonist, every 2-3 days for 8 weeks. Behavioral signs of back pain previously validated in this, and other mouse models of degeneration, were assessed weekly for 8 weeks. Behavioral assays included acetone evoked behavior and the grip force test. Following 8 weeks, discs were excised and cultured for 2 days. Cytokine release into the media was measured by protein arrays.

**Results:** TLR2 activation by Pam2CSK4 or FN-f decreased GAG levels in NP tissue and increased GAG levels in culture media compared to vehicle. Collagen type II fragmentation was also increased. MMP3 and 13, proteases that degrade matrix components, were both increased in NP tissue and in culture medium. TLR2 agonist injected discs also secreted more proinflammatory cytokines than vehicle injected discs. Sparc-null mice displayed increased acetone evoked behavior and decreased grip strength compared to wild type mice. Furthermore, discs excised from Sparc-null mice secreted increased levels of many proinflammatory cytokines compared to wild type mice. However, TLR4 inhibition decreased acetone evoked behavior, increased grip strength and decreased proinflammatory cytokine release compared to vehicle treated Sparc-null mice.

**Discussion:** Taken together, these results indicate TLR2 activation induces degeneration in human discs while TLR4 inhibition reduces pain and improves disc phenotype in mice. Therefore, inhibiting alarmin receptors, such as TLRs, could be a therapeutic strategy to treat degeneration and chronic low back pain.

## THE EFFECT OF THE INTERVERTEBRAL DISC ENVIRONMENT ON THE SPECIFIC PHENOTYPE OF SENESCENT NUCLEUS PULPOSUS CELLS

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**Introduction** Aged and degenerated intervertebral discs (IVDs) are characterized by the presence of an increased amount of senescent cells. The mechanisms leading to senescence have recently started to be delineated and are mainly attributed to the specific stresses prevailing in the harsh environment of the IVD. Senescent cells in general are characterized by a pro-inflammatory, catabolic phenotype – called Senescence Associated Secretory Phenotype (SASP) - and it is hypothesized that due to this phenotype they affect tissue homeostasis locally. However, the characterization of this phenotype is usually done in cells cultured under classical culture conditions being far from the conditions of the disc and especially nucleus pulposus. Accordingly, aim of this study was to investigate the effect of specific parameters of the IVD environment on the phenotype of young and senescent nucleus pulposus cells.

**Methods** Young and senescent bovine nucleus pulposus cells were grown under classical two-dimensional (2D) culture conditions, as well as, under conditions that mimic the specific environment of nucleus pulposus, i.e. three-dimensional (3D) cultures (in alginate beads), absence of serum, reduced nutrient support, increased osmolality and hypoxia. Senescent cells were characterized by BrdU incorporation and SA- $\beta$ -gal staining. RNA was collected and subjected to quantitative RT-PCR for studying gene expression, while protein lysates were subjected to western analysis for the evaluation of the expression of senescence-related proteins. Finally, the matrix metalloproteinase (MMP) activity of young and senescent cells cultured in classical and IVD-like conditions was estimated in media conditioned by these cells by using zymography and FRET-based activity assays.

**Results** Senescent IVD cells cultured under classical conditions express the typical senescence markers, e.g. lack of DNA synthesis, increased SA- $\beta$ -gal staining and expression of cell cycle inhibitors at the mRNA and protein levels. In parallel, they overexpress senescence-related catabolic and inflammatory genes (e.g. p21<sup>WAF1</sup>, p16<sup>ink4a</sup>, MMP-3, ICAM-1, IL-1, IL-6), while they secrete a significantly increased catabolic (i.e. MMP) activity. Interestingly, at least for the parameters tested, the expression of these genes remained practically unchanged under IVD conditions (i.e. absence of serum, reduced nutrient support, increased osmolality and hypoxia). Finally, the same results were obtained whether the cells were cultured in 2D or 3D environment (in classic or IVD conditions).

**Discussion** The above mentioned results indicate that under IVD conditions senescent nucleus pulposus cells retain the classical senescent phenotype, as already characterized under conventional culture conditions. These data will enable the use of appropriate cell systems for the study of the mechanisms leading to cellular senescence, of IVD physiology and of future anti-ageing interventions.

## PROTEOMIC PROFILE OF HERNIATED INTERVERTEBRAL LUMBAR DISC

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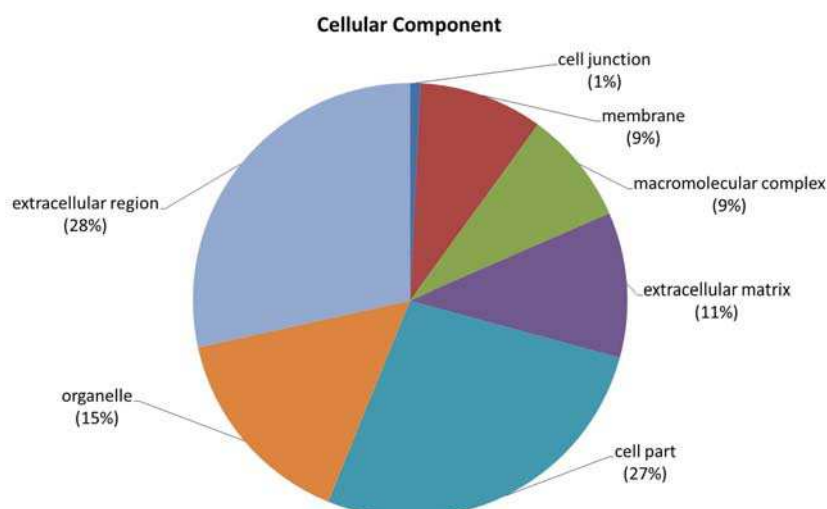
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**Introduction** The sequence of events occurring *in-vivo* in the intervertebral disc leading to lumbar disc herniation (LDH) is not clearly understood. Research to establish the cascade of events resulting in LDH, as reported in earlier literature have used the tools of radiology, histopathology, in-vitro mechanical loading models and genomic analysis. Proteomics offers an opportunity to understand the entire proteins and its complements present in the system at any given point of time and may hold the key in unraveling this controversy. We aimed to better understand the changes occurring in LDH by analyzing the proteome wide alterations of the disc tissues.

**Methods** Fifteen cases with LDH undergoing micro lumbar discectomy for sciatica had discectomy samples processed for proteomic profiling. Total proteins were extracted in two stages. Using radioimmunoprecipitation assay buffer (RIPA) buffer the soluble proteins were isolated; the resulting pellet was subjected to boiling with 2% Sodium dodecyl sulphate (SDS) to isolate the insoluble (membrane and hydrophobic) proteins. Protein samples for each fraction (400µg) were pooled. Further both the fractions were cleaned using methanol: chloroform. Around 100µg of total proteins were subjected to pre-fractionation on SDS-PAGE (Polyacrylamide gel electrophoresis) and proteins were analysed using LC-MS/MS (Liquid Chromatography- tandem mass spectrometry) shotgun proteomics. The raw files were subjected to protein identification using Proteome discoverer version 1.4.1.14. Post identification, gene ontology analysis for biological process, molecular function and cellular component of disc tissue was identified based on PANTHER database tools. Functional protein association network in the disc tissue were analysed using STRING database.

**Results** We have 12 males and 3 females with 8 having L4-5 disc herniation and 7 having L5-S1 herniation. Total numbers of unique peptides/unique proteins combining both the fractions were 2859 peptides /945 proteins. Classification based on biological process (figure) revealed that these proteins are mainly involved in cellular process (26%), metabolic process (21%), cellular component organization/biogenesis (11%), multicellular organismal process and localization (7%), biological regulation, developmental process, response to stress (6%), localization (4%) and reproduction (1%). In molecular function (figure), major categories relied on catalytic activity (40%), binding (37%), structural molecular activity (11%), transporter activity (4%), antioxidant activity and signal transducer activity (2%). In cellular component (figure), the top four subcategories are extracellular region (28%), cell part (27%), organelle (15%) and extracellular matrix (11%). Out of 945 proteins, 691 proteins were mapped in STRING protein association network. The biological process of the identified proteins of the herniated discs showed significant number of proteins as a response to herniation such as: angiogenesis (39); apoptosis (74); programmed cell death (61); inflammation (33); defense response (86); defense response specific to bacterium (16); immune process (116); wound healing (81) and response to stress (192).

**Conclusion** This is the first report of proteins and its complements in nucleus pulposus of LDH. Proteins from LDH show a specific pattern towards defense response specific to bacterium, wound healing, angiogenesis, apoptosis, inflammation and immune processing. This provides evidence that defense mechanisms and inflammatory response proteins are concurrently expressed in LDH. Further, absolute quantification of these proteins would aid in understanding LDH in a comprehensive manner.



## COMPARATIVE PROTEIN PROFILING OF DEGENERATIVE INTERVERTEBRAL DISC AND DISC HERNIATIONS USING PROTEOMICS

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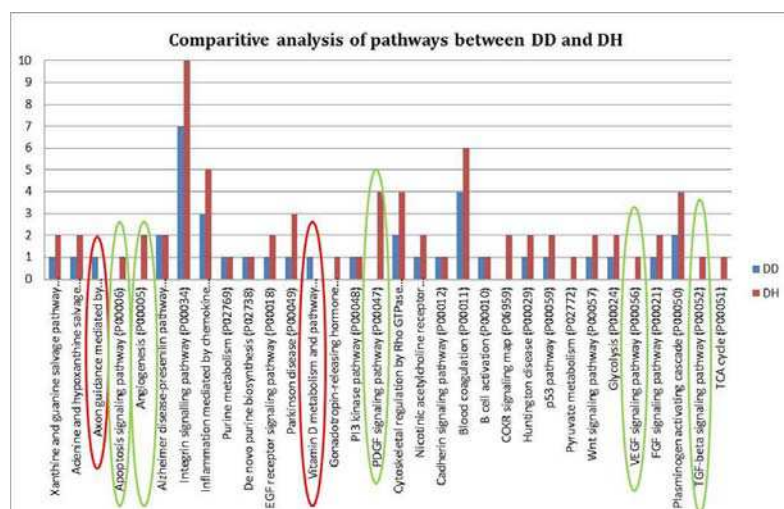
**Introduction** Disc degeneration (DD) and disc herniation (DH) are the two most common causes of low back pain. Proteomics will assist in understanding the differential expressions of low abundant proteins (expressed at a magnitude of  $10^{-15}$ , which might serve as a potent biomarker for understanding disease progression at various stages. We aimed to assess and compare the proteomic profile of intervertebral disc tissue expressed in the clinical scenario of disc degeneration and disc herniation.

**Methods** We performed a comparative proteomic profiling of intervertebral disc tissue between 15 cases of disc herniation (DH) undergoing microlumbar discectomy and 5 cases of severe disc degeneration (DD) treated with lumbar fusion. Total proteins were extracted from all these samples using two buffers; radioimmunoprecipitation assay buffer (RIPA) and 2% Sodium dodecyl sulphate (SDS). The resultant soluble and insoluble proteins were cleaned using methanol:chloroform. Around 100µg of total proteins were pre-fractionated on SDS-PAGE (Polyacrylamide gel electrophoresis) and proteins were analysed LC-MS/MS (Liquid Chromatography- tandem mass spectrometry) shotgun proteomics. Protein identification was performed using Proteome discoverer(PD) version 1.4.1.14 and Gene Ontology (GO) analysis for biological process, molecular function and cellular component of disc tissue was identified based on PD. Functional protein association network in the disc tissue were analysed using STRING database.

**Results** Total number of proteins identified in DH group were 945 and in DD group were 514. Pathways unique in DH are Vascular endothelial growth factor (VEGF) pathway, Transforming growth factor beta (TGF-β) signaling pathway, Platelet derived growth factor (PDGF) pathway, Epidermal growth factor (EGF) pathway, P-53 pathway, Wnt Signaling pathway, angiogenesis and apoptotic pathways. Presence of VEGF, TGF- β, PDGF pathway proteins such as Rho-GTPase activating 1 (VEGF), Inhibin beta A chain (TGF- β), PDGF factor subunit B, PDGF receptor like protein suggests angiogenesis. Similarly apoptotic pathway proteins Myosin 13 (Wnt signalling) and Heat shock protein family A5 supports IVD cells undergoing apoptosis during disc herniation. Interestingly analysis of the unique proteins of herniated discs using STRING protein functional association network shows around 106 proteins expressed in response to stress.

Pathways unique to proteins to DD group are- axon mediated guidance pathway and vitamin D metabolic pathway. Protein semaphorin 3A (axon mediated guidance pathway) was observed in DD group which is a potent inhibitor of axon outgrowth and pathological innervations. Vitamin D binding protein levels were elevated in DD group. Analysis of the unique protein's functional association using STRING revealed, around 12 proteins specific to oxidative stress, 12 proteins of receptor mediated endocytosis and 25 proteins involved in vesicle mediated transport in DD group.

**Conclusion** This is the first comparison of proteomic profile in the disc herniations and disc degeneration. The disc herniation group showed a more abundance of proteins compared to disc degeneration group. This abundance was due to pro angiogenic, pro apoptotic and stress response proteins when compared to degeneration group. In contrast disc degeneration group had more evidence of receptor mediated endocytosis and vesicle mediated transport proteins.



## FOLLISTATIN-LIKE PROTEIN 1 HAS AN ANTI-INFLAMMATORY EFFECT ON THE NOTOCHORDAL NUCLEUS PULPOSUS CELL LINE, U-CH1-N

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**Introduction:** The nucleus pulposus (NP) of the intervertebral disc (IVD) is derived from the notochord, a rod-like structure of mesodermal origin. The decline in notochordal cell number in the NP is thought to be causally related to IVD degeneration. By gene expression profiling, we found that Follistatin-like protein 1 (FSTL1) was highly expressed in notochordal cell line U-CH1-N. FSTL1 was reported to be responsible for diverse biological processes including cell proliferation, differentiation and inflammation. However, the role of FSTL1 in NP is largely unknown. The aim of present study was to clarify the regulation of FSTL1 expression and its function in NP.

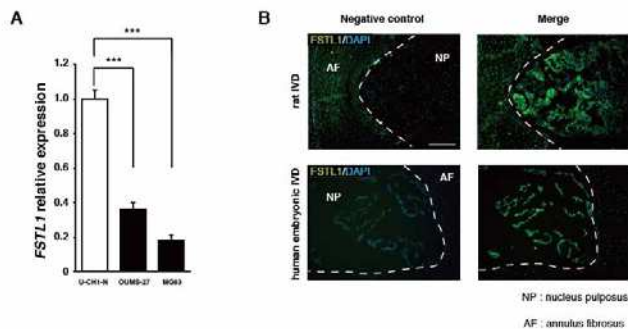
**Methods:** Gene expression profiling of U-CH1-N was performed by microarray analysis. FSTL1 expression was analyzed by real-time RT-PCR, western blotting, and immunohistochemical staining. To evaluate the activity of NF- $\kappa$ B signaling, U-CH1-N was transfected with a human NF- $\kappa$ B luciferase reporter. ShRNA mediated knockdown of hypoxia-inducible factor (HIF)-1 $\alpha$  and FSTL1 was performed by lentiviral system. All measurements were performed in triplicates. Data are presented as mean  $\pm$  standard deviation (SD). Differences between groups were analyzed using the Student *t* tests.

Gene expressing profiling for U-CH1-N

Gene	Gene Symbol	Delta Signal
Hydroxymethylase 10	HMSH10	4356.19
Hydroxymethylase oxidase subunit II	COX2	4110.92
Hydroxymethylase 4, R-isoform	HMSH4	4057.61
Tubulin, alpha 1a	TUBA1A	4053.31
Hydroxymethylase oxidase subunit II	COX2	4037.60
Keratin 19	KRT19	4033.65
...	...	...
IL27A	IL27A	3047.06
...	...	...
Follistatin-like 1	FSTL1	2954.18
connective tissue growth factor	CTGF	2922.7

Table. Microarray analysis was performed in nucleus pulposus (NP) cell line, U-CH1-N.

Figure. FSTL1 is specifically expressed in U-CH1-N, rat and human embryonic nucleus pulposus.



A. mRNA expression level of FSTL1 was analyzed in U-CH1-N, a chondrosarcoma cell line, OUMS-27 and an osteosarcoma cell line, MG63 by real-time PCR. Data are presented as means  $\pm$  standard deviation (SD) (\*\**p* < 0.001).  
B. Immunohistochemical analysis to detect FSTL1-positive NP cells was performed in rat and human embryonic intervertebral disc (IVD). Bar = 100 $\mu$ m.

cells, we measured the luciferase reporter activity of NF- $\kappa$ B in FSTL1 and/or TNF- $\alpha$ -treated cells. FSTL1 treatment significantly neutralized TNF- $\alpha$ -mediated induction of luciferase activity in U-CH1-N. Moreover, Western blotting confirmed that FSTL1 remarkably diminished TNF- $\alpha$ -mediated phosphorylation of NF- $\kappa$ B/p65.

**Discussion:** We first demonstrated that FSTL1 expression levels in NP are high, and the expression is regulated by HIF-1 $\alpha$ , an essential transcriptional factor for NP cells. Moreover, our results suggest that FSTL1 downregulates inflammatory cytokine-mediated catabolic effects via the NF- $\kappa$ B pathway. These results indicate that FSTL1 functions as an anti-inflammatory agent in an autocrine/paracrine manner. Although further study is needed, FSTL1 has the potential of being a therapeutic option for IVD degeneration.

**Results:** Microarray analysis showed that FSTL1 expression levels were prominently high in U-CH1-N (Table). Real-time RT-PCR analysis and immunohistochemistry confirmed that FSTL1 expression levels were specifically increased in rat and human embryonic NP (Fig). To determine the mechanism by which FSTL1 expression is regulated in notochordal NP cells, shRNA specific for an essential transcription factor in hypoxic NP, HIF-1 $\alpha$ , was transfected using a lentiviral system into U-CH1-N. HIF-1 $\alpha$  silencing cells showed downregulation of FSTL1 expression compared with control cells, indicating that FSTL1 expression was regulated by HIF-1 $\alpha$  in notochordal NP cells. Next, to investigate the function of FSTL1 in notochordal NP cells, we assessed the phenotype of FSTL1 silencing U-CH1-N. We found that anabolic cartilage-related genes type II collagen and aggrecan expression levels were significantly downregulated in the silencing cells, whereas catabolic cartilage markers, such as IL-6, IL-8, MMP3, and Syndecan4, expression levels were significantly upregulated. To further analyze the effect of FSTL1 on the inflammatory response in NP

## BIOLOGICAL CHARACTERISTICS AND POTENTIAL OF NUCLEUS PULPOSUS DERIVED STEM CELLS IN HUMAN DEGENERATIVE INTERVERTEBRAL DISC WITH DIFFERENT PFIRRMANN GRADE

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**Introduction:** Degenerated disc disease (DDD) is the main cause of low back pain that significantly affected individual with quality of life and life expectancy. Tissue engineering and regeneration medicine of nucleus pulposus (NP) are thought to provide a promising approach for this and highlighted by the founding of nucleus pulposus derived stem cells (NPDCs). However, the biological characteristics of NPDCs in degenerated human intervertebral disc with different Pfirrmann grade may be different in certain extend that affect the regeneration ability and need further research.

**Methods:** Nucleus pulposus were obtained from 25 patients as surplus surgical material and NPMSCs were harvested by colony screening. The groups were divided according to different Pfirrmann grades. After in vitro expansion, the properties such as cell morphology, cell proliferation rate, colony-forming ability, the immunopheno-type and multi-directional differentiation were all compared within different Pfirrmann grades.

**Results:** From Pfirrmann grade I to V, the cell morphology were translating from spindle-shape to polygonal and the SEM showed the smooth and full cell shape changing to shrinking outline. Regarding the proliferation capacity and colony-forming ability, the cells in grade I to III showed significant better proliferation abilities than the rest groups. For the identification of cell surface antigen profile, all the NPDCs were positive for many stem cell markers including CD73, CD90, CD105, CD166, GD2, Tie 2 and negative for CD34, CD44, CD45, HLA-DR. However, the expression of CD105 (92.4±8.1 %, 90.3±7.5 %, 83.7±7.8 %, 66.1±10.3 %, and 62.3±9.6 %, from grade I to v), CD166 (95.4±4.8 %, 93.3±5.5 %, 85.9±8.3 %, 76.1±6.3 %, and 72.3±9.6 %, from grade I to v), Tie 2<sup>+</sup> (62.4±18.4 %, 56.3±17.7 %, 43.7±14.8 %, 26.1±15.4 %, and 12.3±8.2 %, from grade I to v) and GD2<sup>+</sup> (70.2±28.4 %, 65.2±20.7 %, 42.4±20.4 %, 25.2±19.4 %, and 10.2±6.8 %, from grade I to v) were decreasing according to degenerated Pfirrmann grades and the last two grades showed significant difference. In addition, the ability to differentiate into osteoblasts and adipocytes were both decreasing from grade I to V with obviously weakening in the grade III to V groups, while the chondrocytes differentiation were of no difference.

**Discussion:** This study demonstrated the different characteristics and potential of NPDCs with different Pfirrmann grades, indicating constant dynamic changes in the process of DDD. The outcome may imply different regeneration ability between different Pfirrmann grade of degenerated intervertebral disc (IVD). Moreover, these results may improve our understanding of IVD pathophysiology and provide us a new strategy in cell-based regenerative medicine and tissue engineering of DDD.

## STIMULATION OF PRIMARY HUMAN OSTEOBLASTS AND HUMAN STROMAL CELLS WITH THE BMP ANTAGONISTS GREMLIN AND NOGGIN

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**Introduction:** The standard treatment for intervertebral disc (IVD) degeneration is discectomy followed by spinal fusion. During spinal fusion the removed IVD is replaced by bone substitute or an autograft and the two adjacent vertebral bodies are fixed with a cage. Clinical observations showed, that partial removal of the IVD during discectomy can lead to a failure of bone formation during the spinal fusion of the affected section. One possible explanation for this phenomenon could be a secretion of BMP antagonists by IVD cells. The BMP pathway plays a crucial role in bone turnover by inducing osteogenesis. BMP antagonists like Gremlin (GREM) and Noggin (NOG) inhibit the osteogenesis by binding to bone morphogenic protein-4 (NOG and GREM) or bone morphogenic protein-2 (GREM) [1]. We hypothesized that human primary osteoblasts (OB) or primary human mesenchymal stem cells (MSC) stimulated with NOG and GREM show an inhibition of the osteogenic phenotype.

**Methods:** OB were isolated from patients undergoing total knee replacement and MSC from spinal surgery patients. Cells were cultured in monolayer up to passage two to minimize dedifferentiation effects. All protocols involving human tissue were ethically approved. OB were seeded at a density of 10'000 cells/cm<sup>2</sup> and MSC at a density of 5'200 cells/cm<sup>2</sup>. OB/MSC were stimulated with 10/100 ng/mL NOG and GREM respectively and were applied with osteogenic medium. The control groups were stimulated with osteogenic medium (positive control) and with control medium,  $\alpha$ -MEM + 10% FCS (negative control). The respective medium for each experimental group was refreshed every second or third day. After 21 days of culturing in hypoxic conditions (2% CO<sub>2</sub>), matrix mineralization of OB and MSC monolayers were measured by Alizarin red (ALZR) staining. ALZR was quantified by absorbance and normalized to cell activity (Resazurin assay).

**Results:** After 21 days, a significant increase of ALZR staining of mineralized matrix was observed in the OB culture in osteogenic medium ( $0.341 \pm 0.040$ , mean  $\pm$  SEM) compared to OB grown in control medium ( $0.056 \pm 0.009$ ) (M-W test:  $P = 0.0286$ ). OB stimulated with 100 ng/ml of NOG and GREM showed a significant higher mineralization than the negative control (NOG  $0.820 \pm 0.336$  (Friedman test:  $P = 0.0124$ ) and GREM  $0.659 \pm 0.180$ , Friedman test:  $P = 0.0393$ ). The same trend was observed in stimulated MSC (Fig. 1).

**Discussion:** In this study we investigated the exogenous effect of BMP antagonists like NOG and GREM on human OB and MSC. After the monitoring and quantification of calcium deposit could we not confirm the hypothesis, that the exogenous stimulation of OB and MSC will lead to an inhibition of the osteogenic phenotype and so to a reduction of matrix mineralization. Conversely, the calcium deposition in both, OB and MSC monolayer, were stimulated with the addition of the BMP antagonists. These findings, question the role of GREM1 and NOG for bone inhibition pathway.

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1. Chan, Tekari, Benneker, Heini, Gantenbein. "Osteogenic Differentiation of Bone Marrow Stromal Cells Is Hindered by the Presence of Intervertebral Disc Cells." *Arthritis Res Ther* 18, no. 1 (2015)



## THREE-DIMENSIONAL CHARACTERIZATION OF THE MORPHOLOGY CHANGES IN THE INTERVERTEBRAL DISC AND ENDPLATE AND THEIR CROSS TALK DURING AGING: A PROPAGATION PHASE CONTRAST SYNCHROTRON CT STUDY

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**INTRODUCTION:** The interaction between intervertebral disc and endplate after aging has not been fully investigated. We Aims to characterize the 3D morphology changes of the endplate and intervertebral disc (IVD) and their cross talking after aging using propagation phase contrast synchrotron CT.

**METHODS:** Animal experiments were performed according to a protocol approved by the Animal Care Committee of Central South University. Lumbar vertebral level 4 and level 5 intervertebral discs with adjacent vertebral endplates harvested from 15-day-, 4-month-, and 24-month-old mice were initially evaluated by propagation phase contrast synchrotron microtomography (PPCST) scanning for 3D morphometric analysis. Samples then underwent sectioning for histological examination.

**RESULTS SECTIONS:** Qualitative and quantitative assessments of age-related trends indicated that in younger 15-day-old mice, the endplate was cartilage and no canals were detected, while during aging, canal formation in the endplate and mean diameter, volume fraction and connectivity of the canal as well as the endplate porosity and thickness reached a peak at 4 months and significantly decreased at 24 months. The intervertebral disc (IVD) volume consistently exhibited the same trend of variation (Figure 1, 2, 3).

**DISCUSSION:** In this study, PPCST provided essential and comprehensive details regarding the morphology changes of the 3D canal network in the endplate and IVD as well as their cross talk after aging. These data suggest that the endplate change would have occurred earlier if associated with a narrowing of the canal diffuse to the IVD with the onset of IVD degeneration. The PPCT allowed us to directly characterize the 3D morphology of the canal in the endplate and IVD simultaneously.

**SIGNIFICANCE:** This method is expected to provide a new platform for attaining deeper insight and interpretation of the pathogenesis of DDD.

**ACKNOWLEDGEMENTS:** This work was performed at the SSRF BL13W1, Shanghai, China, and supported by the National Natural Science Foundation of China (Nos 81301522, 81371956). We thank Prof. Tiqiao Xiao and Jiwen Zhang for kind assistance in PPCT measurements at the BL13W1 station.

## ULTRASTRUCTURAL ANALYSIS OF ANNULUS FIBROSUS ELASTIC FIBERS USING A RAPID MATRIX DIGESTION TECHNIQUE

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**INTRODUCTION:** Using different light microscopy methods, the organization of elastic fibers in the annulus fibrosus (AF) has been described previously. However, little is known about their ultrastructural organization. Therefore the aim of this study was to develop a rapid matrix digestion technique for ultrastructural analysis of the disc elastic fibers. Through the ultra-structural analysis, the relationship between structure and function, as well as the role of elastic fibers on the AF mechanical properties can be studied.

**METHODS:** Four samples from adjacent sections (thickness = 30  $\mu\text{m}$ ) were cut from the anterior AF at an angle of 30° to the transverse plane using a cryostat microtome from four ovine discs. The first sample was not digested (control). The second sample was stained with Orcein to visualize elastic fibers. The final two samples were digested in 0.5 M NaOH solution and sonicated for 15 min at 37 °C (digested). One of these two samples was then soaked in water at 70 °C for 5 min to remove collagen fibers, leaving the elastic network (digested + heat treatment). The two treated samples were prepared for SEM imaging. ImageJ software identified the distribution of fiber orientation (relative to the tangent to the circumferential direction). A univariate ANOVA having fiber orientation as a dependent variable with a fixed factor of sample preparation with a post-hoc Bonferroni correction was conducted.

**RESULTS:** At the light microscopy level, control and digested samples (Figures 1a-b) didn't reveal any structural organization of elastic fibers, as they are surrounded by other matrix components. When compared with the orcein treated sample (Figure 1c), the masking effect of matrix was decreased in digested samples (Figure 1d). Elastic fibers were not visible in undigested (control) samples (Figure 2a). In digested samples (Figure 2b), both collagen (appearing as strands and larger in size) and elastic fibers (smaller diameter) can be observed as digestion without heat treatment only removed matrix and micro-fibrils. In heat treated samples it was possible to observe elastic fibers (Figure 2c); however, remnants of non-digested matrix and other components still obscured the underlying elastic fibers. A loose network of elastic fibers was observed in heat treated samples, which were comprised of almost parallel large fibers (0.5-1.5  $\mu\text{m}$  diameter) and very fine interconnecting fibers of less than 0.2  $\mu\text{m}$  diameter (Figure 2d). Three different symmetrically organized angle of orientations (Figure 2d) were detected with a common peak orientation of approximately 45° between all preparations. The overall effect of sample preparation on fiber orientation was significant ( $p=0.031$ ), with post-hoc comparisons revealing that the control orientation (mean $\pm$ SD: 48.75 $\pm$ 2.5°) was significantly larger than the digested orientation (43.0 $\pm$ 2.1°) ( $p=0.033$ ), with no significant differences between the control and digested + heat treatment orientations (45.0 $\pm$ 2.9°) ( $p=0.203$ ), nor between the digested and digested + heat treatment orientations ( $p=0.891$ ).

**DISCUSSION:** The novel method allowed for effective visualization of the elastic network ultrastructure. The method may alter the overall fiber structural organization by  $\approx$ 12%, while the negligible alteration in fiber orientation, subsequent to heat treatment, was consistent among samples

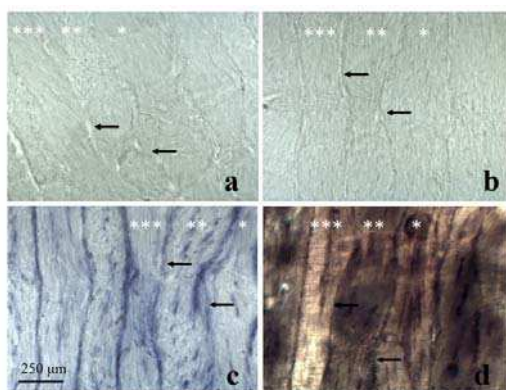


Figure 1. Light microscopy images at the same magnification of (a) control and (b) the adjacent digested and (c) orcein treated samples. Figure 1d indicates the adjacent sample histologically stained with orcein after digestion. White stars represent corresponding lamellae in all samples. Arrows indicate the regions between lamellae.

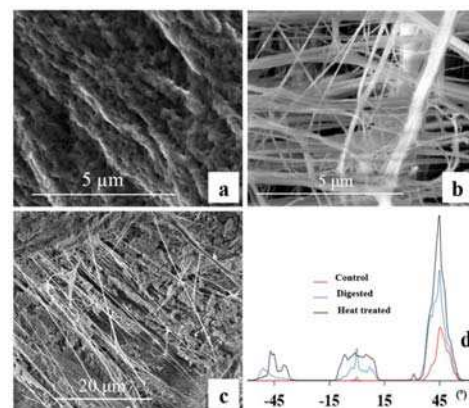


Figure 2. SEM images of (a) control, (b) digested and (c) digested + heat treated samples. Figure 2d shows the comparison of AF fiber orientation for the samples.

## DIFFERENT TYPES OF SENEESCENCE LEAD TO A SIMILAR TRANSCRIPTIONAL REGULATION OF CATABOLIC AND INFLAMMATORY GENES IN HUMAN INTERVERTEBRAL DISC CELLS

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### Introduction

The presence of senescent intervertebral disc (IVD) cells has been linked to disc degeneration. In general, cellular senescence can be the result of consecutive replications (replicative senescence). Alternatively, it can be induced by exposure of the cells to exogenous genotoxic stresses or overexpression of cell cycle inhibitors, a process called stress induced premature senescence (SIPS). Senescent cells in several tissues have been reported to possess a pro-inflammatory and catabolic phenotype, known as senescence associated secretory phenotype (SASP). However, it has been suggested that different types of senescent cells have a different transcriptional profile; more specifically, it has been shown in human fibroblasts that SIPS mediated by p16<sup>INK4</sup> overexpression does not lead to a typical inflammatory phenotype. Accordingly, aim of the current study was to compare the transcriptional profile among young, senescent after successive replications, senescent after exposure to  $\gamma$ -irradiation and senescent after overexpression of p16<sup>INK4</sup> human nucleus pulposus and annulus fibrosus IVD cells.

### Methods

Replicative senescence (RS) was achieved by repeated subculturing of human nucleus pulposus and annulus fibrosus IVD cells. Irradiation-senescence (IS) was triggered by an exposure of IVD cells to ionizing radiation followed by subculturing. Senescence due to p16<sup>INK4</sup> overexpression (p16 O/E) was induced using the lenti-viral expression vector pLenti7/Bsd carrying Ilastididine resistance gene, which was constructed modifying pLenti7.3/V5 Dest vector from Invitrogen. p16<sup>INK4</sup> gene was cloned into the vector and virus production was carried out in HEK293T cells using Vira Power Lenti Viral Expression System (Invitrogen). IVD cells were infected with lenti-viruses carrying the empty vector or the p16<sup>INK4</sup> vector. Infected cells were selected with 3  $\mu$ g/ml blasticidine for a total time period of 15 days. Senescent cells were characterized by BrdU incorporation and SA- $\beta$  gal staining. Total RNA was collected for gene expression analysis with quantitative RT-PCR.

### Results

Senescent IVD cells were characterized by cell cycle arrest, decreased BrdU incorporation and increased SA- $\beta$  gal staining. In addition, even though up-regulation of the p16<sup>INK4</sup> transcript was always the highest in p16 O/E cells, increased p16<sup>INK4</sup> mRNA levels were also observed in RS and IS cells. All senescent cells demonstrated a catabolic phenotype, characterized by increased MMP-1, MMP-2, MMP-3 and MMP-9 mRNA levels. Furthermore, senescent IVD cells exhibited an inflammatory phenotype, as shown by IL1 $\beta$ , IL6, IL8 and IFN $\gamma$  up-regulation, independent of the means used to trigger senescence. Finally, similar responses were observed in nucleus pulposus and annulus fibrosus IVD cells.

### Discussion

In this study we showed that different types of senescence lead to similar alterations in the gene expression of human nucleus pulposus and annulus fibrosus IVD cells. The catabolic and inflammatory phenotype of senescent IVD cells could be associated with the deterioration of the aged and degenerated disc. Our findings suggest that general anti-ageing therapeutic strategies could be used to attenuate the SASP phenotype in senescent IVD cells irrespective of the stimulus in order to delay or impede IVD degeneration.

## CONTROLLED RELEASE OF CELECOXIB FROM POLYESTERAMIDE MICROPARTICLES IN A CANINE PRE-CLINICAL INTERVERTEBRAL DISC DEGENERATION MODEL

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### Introduction

Low back pain affects 80% of the people worldwide at least once in their lives. Low back pain is often related to degeneration of the intervertebral disc (IVD). The process of IVD degeneration and its clinical representation in dogs resembles the human situation and therefore, dogs are a suitable large animal model to study IVD disease. Pro-inflammatory mediators such as the COX-2 mediated prostaglandin E2 play an important role in the sensitization to pain. Oral COX-2 inhibitors are effective in reducing low back pain, although they are associated with side effects. Moreover, it is not known how much of the orally administered drug reaches the avascular IVD. Therefore, local delivery of drugs directly into the IVD could be a suitable treatment strategy for back and neck pain. We have previously demonstrated safety of intradiscally injected Poly-Ester-Amide Microparticles (PEAMs) in a canine model with long term follow up of 6 months. The aim of the present study was to find the optimal loading dose of locally administered celecoxib in a controlled release system based on PEAMs, in a canine model with induced IVD degeneration as a first step towards clinical translation.

### Methods

After ethical approval, IVD degeneration was induced in lumbar IVDs of beagle dogs by puncture with an 18G needle and partial nucleotomy by aspiration. IVDs that were not punctured served as controls. Four weeks thereafter, dogs received intradiscal injections with PEAMs, loaded with 0.23 mg/mL or 7 mg/mL celecoxib or unloaded microparticles (sham), with n=6 discs per treatment. At 16 week follow-up period, MRI was performed. Post mortem, after CT scan of the spinal column, IVDs were harvested for macroscopic and histopathological evaluation and biochemical analyses (DNA-, collagen-, and glycosaminoglycan content).

### Preliminary results

At 16 weeks after intradiscal injection with 40µL unloaded PEAMs (sham), low (0.23 mg/mL) or high (7 mg/mL) dose celecoxib, no adverse effects were visible on imaging modalities (MRI, CT) or macroscopic evaluation. The macroscopic and MRI scores were significantly higher in the IVDs where degeneration was induced compared to control IVDs. The IVDs treated with the PEAMs containing low and high dose CXB did not statistically differ from either non-induced and sham groups. Total- and PGE2/DNA levels were significantly increased in both the NP and AF of the sham IVDs, compared to non-induced IVDs. PGE2 levels decreased after treatment with both dosages of celecoxib. Sustained release of celecoxib, regardless of the dose, resulted in a significantly increased glycosaminoglycan content of the nucleus pulposus. Intradiscal injection of PEAMs had no effect on glycosaminoglycan-, total collagen- or DNA content of the annulus fibrosus.

### Discussion & conclusions

Celecoxib incorporated in PEAMs was safely administered intradiscally in experimental dogs, exerted anti-inflammatory and regenerative. Ongoing histological and quantitative MRI analyses will shed light on changes at the biochemical and histological level. Follow up studies in a large animal model with naturally occurring clinical IVD disease as a preclinical model for translation to humans are warranted to determine the efficacy of celecoxib loaded PEAMs in inhibiting low back pain.

## THE ROLE OF TGF—CCL3/4 IN REVERSING IVDD AND RELIEVING PAIN

Zhaomin Zheng, Jian Zhang, Jianru Wang

### Background:

Nonspecific low back pain ,which is a worldwide health problem and perplexing spine surgeon,has already attracted all society's attention.There are growing evidence show that intervertebral disc degeneration(IVDD) plays an important role in contributing to nonspecific low back pain.

### Object:

The aim of this study was to analyze the role of TGF-ERK-CCL3/4 in reversing IVDD and relieving pain.

### Method:

In vitro,TGF-beta-inhibited CCL 3/4 expression were analyzed by qPCR, ELISA and cell immunofluorescence. Involvement of MAPK and NF-κB signaling pathways were studied by siRNA .In vivo,Rat L4/5 disc degeneration model was established by annular puncture using a 0.4mm needle posteriorly. And magnetic resonance imaging (MRI) ,histological analyses and pain behavioral tests were performed after puncture or TGF-beta intradiscal injection.

### Result:

In the vitro,we demonstrated that TGF-β inhibited CCL3 and CCL4 expression,especially CCL4,through MAPK and NF-κB signaling pathway in the NP cells.Furthermore,in the vivo,through intradiscal inject TGF-β multiple times,we found that TGF-β could delay the process of the disc degeneration.Moreover,compared to control group,the pain behavior of the rat in experimental group were significantly decreased.

### Discussion:

Based on our findings,we propose that TGF-β regulate the activity of MAPK and NF-κB signaling pathway in the NP cells,which lead to decrease the expression of CCL3 and CCL4.Further more,we suggest that inhibiting the expression of CCL3 and CCL4 in the NP cells may play an important role in TGF-β anti-inflammatory ,alleviate inflammatory pain and neuropathic pain in rat IVDD model.This study might provide a possible therapeutic target for controlling the inflammatory response and pain associated with IVDD.

## ENHANCED MYOFIBROBLAST ACTIVITY IN HUMAN AND RAT DISC DEGENERATION

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### Introduction:

Disc degeneration is characterized by reduced proteoglycan content in the nucleus pulposus (NP). In addition, NP of the degenerative discs exhibits enhanced collagen I and III expression. Interestingly, previous study in animal models of induced disc degeneration indicates progressive fibrotic changes in the NP. To date, the components of profibrotic events in disc degeneration remains elusive. We questioned if disc degeneration is associated with an elevated activity of myofibroblasts, the known effector cells in tissue fibrosis.

### Methods:

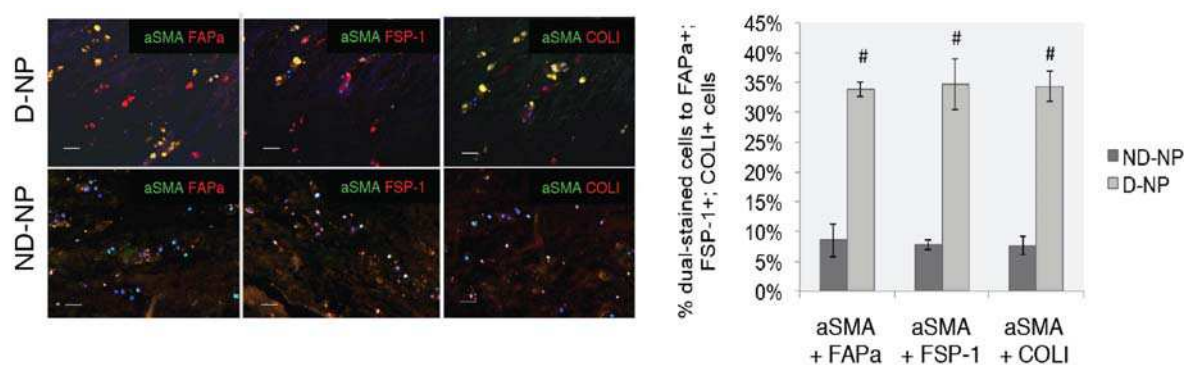
Grade III/IV (Schneiderman scale) degenerative human NP tissues (D-NP) and non-degenerative control discs (ND-NP) derived from adolescent scoliosis subjects were obtained (n=3). By immunostaining, we assessed the expression of fibroblast markers FAPa (fibroblast activation protein, alpha), FSP-1 (fibroblast-specific protein 1), and COL1 (collagen I), as well as the myofibroblast marker aSMA (alpha smooth muscle actin). Double staining was also performed and positive cells were quantified. Similar marker expression analysis was conducted in corresponding cell culture (n=3) using flow cytometry and quantitative PCR. We also established a progressive rat tail disc degeneration model by intradiscal bleomycin injection and analyzed the marker expression in vivo.

### Results:

By immunostaining, we found that D-NP exhibits over 2-fold more of cells positive for FAPa, FSP-1, and COL1 compared to ND-NP. Remarkably, we found a 5-fold increase in cells positive for aSMA in D-NP, which co-express with FAPa, FSP-1, and COL1. Consistent with the finding, flow cytometry indicated a majority of cells (>81% for all markers) in the D-NP cell culture express the myofibroblastic phenotype when compared to ND-NP control (aSMA 2.4%; aSMA/FAPa/FSP-1/COL1 24-34%). Gene expression study validated a significantly higher expression of aSMA, FAPa, FSP-1, COL1A1 and COL3A1 in D-NP cell culture. Myofibroblast-like cells were observed in the rat NP after 2 weeks of bleomycin injection, with a peak at 8 weeks (~70% positive NP cells).

### Discussion:

While disc degeneration is related to increased fibrous matrices, the identity of cells that synthesize these matrices is still obscure. Our in vitro and in vivo results support an increase of fibroblastic cells in the NP in disc degeneration. Part of these fibroblasts carry an activated, myofibroblast-like phenotype. The enhanced fibroblast- and myofibroblast-like activity might explain the observed fibrous transformation of the NP in disc degeneration. The source of these fibroblastic cells and their contribution to NP fibrosis and fibrous matrix deposition warrant further investigations.



## SMALL MOLECULE ANTAGONIST OF C-C CHEMOKINE RECEPTOR 1 CAN REDUCE DISC INFLAMMATION IN THE RABBIT MODEL

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### Introduction

Targeting chemokines or chemokine receptors is a promising treatment strategy for diseases with chronic inflammation such as rheumatoid arthritis and discogenic pain. Identifying specific molecules and determining their effectiveness in animal models are the first steps in developing these treatments. Macrophage markers have been detected in the intervertebral disc tissues of patients with disc degenerative disease and discogenic pain and in different animal models. Macrophage recruitment into the disc may play a role in initiation of inflammation and if unresolved may lead to chronic inflammation and subsequent back pain. The aims of this study are to 1) identify chemokine receptor inhibitors that can block rabbit immune cell migration induced by disc cells in vitro and 2) determine if intradiscal treatment with these inhibitors can block macrophage migration, reduce inflammation and disc degeneration in vivo.

### Methods

**In vitro.** Rabbit primary splenocytes were isolated and assayed for migration using 3 µm Corning Transwell inserts and conditioned media of interleukin (IL)-1 treated rabbit annulus fibrosus cells. Inhibition of macrophage migration was evaluated using different concentrations of small molecule antagonists of C-C chemokine receptor (CCR)1 and CCR2 (ChemoCentryx, USA).

**In vivo.** New Zealand White rabbits (n = 40) underwent disc injury and treatment with saline, CCR1 or CCR2 inhibitors. Serum samples and X-ray and MR images were taken for analysis of IL-8 serum levels, disc height and MRI grade. Intervertebral discs were isolated for RNA analysis of inflammatory and disc phenotypic markers and for immunohistochemical analysis of macrophage markers. The outcome measures were compared between the three treatment groups.

### Results

**In vitro.** Migration of rabbit splenocytes was inhibited by an average of 10-50% in presence of CCR1 inhibitor (5-100 µM) while CCR2 inhibitor (10-100 µM) was not effective in preventing migration.

**In vivo.** In the MRI analysis, discs treated with CCR1 inhibitor had significantly better MRI grades than those treated with CCR2 inhibitor. In the gene expression analysis, discs treated with CCR1 inhibitor expressed less inflammatory markers than discs treated with saline or CCR2 inhibitor. Also, a higher ratio of collagen type 2 to collagen type 1 (marker of favorable disc matrix production) were expressed in the CCR1 inhibitor treated discs compared to those treated with saline. While inflammatory cytokine IL-8 serum levels of the CCR2 inhibitor treated group rose after 6 weeks compared to 3 weeks, serum IL-8 decreased significantly in the CCR1 inhibitor treated group. There were no significant differences between all three treatment groups in regards to disc height indexes or macrophage marker detection.

### Discussion

These studies demonstrate that small molecule antagonist against CCR1 and not CCR2 is effective in blocking rabbit splenocyte migration in vitro. While neither inhibitor blocked general macrophage migration in vivo, CCR1 treatment resulted in reduced disc inflammation and decreased degeneration. Clinical studies have found that CCR1 inhibitor was safe, tolerable and clinically active in reducing inflammation in rheumatoid arthritis patients. These studies suggest that CCR1 inhibitor may be a promising biological treatment for back pain.

### Acknowledgements

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## HIGH-RESOLUTION MRI ENABLES NON-INVASIVE SIZE DETERMINATION OF HERNIA-LIKE NODULES FORMED AFTER EXPERIMENTAL DISC PUNCTURE IN THE RAT

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**Introduction:** Human disc hernias not only consist of herniated disc material, such as nucleus pulposus (NP) and annulus fibrosus (AF), but also of granulation tissue. Granulation tissue has also been shown to develop on the surface of the disc after experimental disc puncture in the rat due to presence of NP in the spinal canal. This animal model may be used to study the granulation component of human hernias morphologically, which constitutes a new experimental approach to disc herniation. The purpose of this study was to evaluate a high-resolution MRI method for non-invasive assessment of hernia-like nodule size, which would enable longitudinal *in-vivo* assessments, and use this method to assess the natural progression of the size of the hernia-like nodule.



Figure 1. Sagittal MRI showing the hernia-like nodule formed at the level of disc puncture (arrow). The 3 mm scale over the L5 spinous process is included for size reference

**Methods:** Eight female Sprague-Dawley rats underwent unilateral facetectomy and disc puncture at L5/L6. Imaging experiments were performed on week 1, 2, 4 and 8 post-op, using sagittal, T2-weighted, 3D RARE acquisitions with isotropic voxels of 150  $\mu\text{m}$  in a 7T small animal MRI system. The size of the hernia-like nodule was assessed by measuring the area of the disc dorsal to its natural margins on each sagittal section obtained. The volume of the hernia-like nodule was calculated for each animal by multiplying the total number of hernia-like nodule voxels by the voxel volume. Nodule size was also approximated by visual inspection, using an ordinal scale from 0 to 4. The intervertebral discs on L6/S1 were assessed as control.

**Results:** Hernia-like nodules were discerned at the level of puncture in the MRIs of all but one animal. The mean hernia-like nodule volumes (expressed in  $\text{mm}^3 \pm 1\text{SD}$ ) were  $0.39 \pm 0.19$ ,  $0.53 \pm 0.18$ ,  $0.52 \pm 0.13$  and  $0.55 \pm 0.22$  on week 1, 2, 4 and 8, respectively. No nodules were detected on the adjacent control discs.

**Discussion:** This study demonstrates that MRI can be used to measure the size of hernia-like nodules induced by experimental disc puncture in rats, and that the mean size of such nodules is consistent over time. Since the hernia-like nodule likely represents the granulation tissue found in human hernias, we believe this model and method can be used to evaluate potential new medical treatments affecting the granulation tissue of disc hernias. The relatively large uncertainty in our data is likely in part due to difficulties to separate the lateral aspects of the hernia-like nodules from surrounding post-operative scar tissue. Changing the surgical approach, preferably to a less invasive, facet-sparing disc puncture technique, may reduce uncertainty and further improve the method. However, the accuracy of the method presented here should be sufficient to detect larger differences in mean hernia-like volume size between groups.

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## EFFECT OF DISC DIMENSIONS ON DIFFUSION OF SOLUTES IN HEALTHY HUMAN INTERVERTEBRAL DISCS

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### Introduction

Diffusion of solutes is one of the important sources of intervertebral disc nutrition. Many factors were found to influence the diffusion properties of intervertebral disc. The effect of disc dimensions on the diffusion characteristics has not been fully understood due to lack of reliable techniques to study the diffusion of intervertebral disc in-vivo. The present study evaluates the effect of disc dimensions in particular, height, width and length of on diffusion characteristics in-vivo in human healthy lumbar discs by post-contrast MR imaging.

### Methods:

25 lumbar discs of five healthy volunteers were included in the study. Serial post-contrast (Gadodiamide 0.3mmol/kg) MR images were taken at 10 min, 2 hrs, 4 hrs, 6 hrs, 12 hrs and 24 hrs. Sagittal and Axial images at cranial, middle and caudal zones of the each disc were obtained. Signal intensities of various regions of intervertebral disc were calculated including central and peripheral nucleus pulposus (superior, inferior, anterior, posterior, right and left). The enhancement percentage at each time period (EP) and time to attain peak enhancement ( $t_{max}$ ) were calculated. The effect of sagittal height, axial length and width on diffusion characteristics was analysed.

### Results

The peak signal intensity was seen at 6 hours at all the regions studied in the intervertebral disc. The average height of lumbar intervertebral discs in the study population was 9.6 mm (range 6.7-12 mm). The mean antero-posterior length was  $34.9 \pm 2.4$  mm and the width was  $48.2 \pm 3.4$ . The mean enhancement percentage of central nucleus pulposus was  $37.1 \pm 15.2$ . Regarding the effect of disc dimensions, the axial width and length of the disc were not found to influence the diffusion characteristics of the intervertebral disc. Even though with increasing height, there was a trend towards reduction in enhancement percentage of central nucleus pulposus, there was no significant influence of sagittal disc height on diffusion in the intervertebral discs shorter than 10 mm in height. In the discs taller than 10 mm, with increasing height there was a significant reduction in the peak enhancement percentage.

### Discussion

The present study documents the influence of disc dimensions on diffusion characteristics of human lumbar inter vertebral discs. Length, width and sagittal height less than 10 mm doesn't seem to influence diffusion characteristics whereas height more than 10 mm was found to negatively influence the disc diffusion.

**EFFECT OF EXOGENOUS NITRIC OXIDE ON PROTEOGLYCAN METABOLISM OF DISC CELLS IN VITRO****Shigeru Kobayashi**<sup>1</sup>, **Takahiro Asai**<sup>2</sup>, **Adam Meir**<sup>3</sup>, **Jill Urban**<sup>3</sup>

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**INTRODUCTION:** The inflammatory response that occurs around hernia tissue in the epidural space is believed to play a major role in the spontaneous regression of lumbar disc hernias.<sup>1</sup> Numerous macrophages invade within the hernia tissue, along with newly formed blood vessels. This suggests that inflammatory cytokines and nitric oxide produced by macrophages are involved in the onset of inflammation around the hernia, and that stimulation by these chemical mediators causes the production and release in macrophages of proteases, such as MMP, which break down and digest the extracellular matrix of intervertebral disc. Sodium nitroprusside (SNP) acts as a drug by releasing nitric oxide. In the present study, we examined how SNP influence the rate of proteoglycan accumulation in a three-dimensional disc-cell culture system.

**METHODS:** Cells were isolated from the nucleus pulposus of 18-24 month bovine disc by enzyme digestion. They were initially cultured for 14 days in alginate beads in DMEM containing 6% FBS (50 beads/50 ml) at  $4 \cdot 10^6$  cells/ml under 21% oxygen to accumulate matrix. The medium was not changed. They were then cultured for 6 days (10 beads/ 2ml-DMEM containing 6% FBS) under 21% oxygen and with or without SNP (0.1 mM). The medium was changed every third day. The cell viability profile was determined by manual counting using trypan blue staining. Lactate production were measured enzymatically as markers of energy metabolism.<sup>2</sup> Glycosaminoglycan (GAG) accumulation (as a measure of proteoglycan) were measured using a DMB assay.<sup>3</sup> Rates of sulphated GAG synthesis were measured using a standard <sup>35</sup>S-sulfate incorporation method.<sup>4</sup> MMP activity (MMP-2/ MMP-7) was measured using coumarin fluorescent assay.<sup>5</sup>

**RESULTS:** The viability profile was decrease with SNP. At cell densities found in vivo in the disc nucleus viz.  $4 \cdot 10^6$  cells/ml and at 21% oxygen the concentration of GAG in the bead reached  $0.91 \pm 0.20$  mg/ml in 14 days i.e. around 1% of the GAG concentration found in situ. Total GAG/million cells was  $0.027 \pm 0.009$  mg after 14 days. The results showed that SNP had no significant effect on GAG accumulation and production in comparison with control. Total GAG/million cells rates increased in the presence of SNP. Lactate production increased in the presence of SNP. Sulphate incorporation rates decreased in the presence of SNP. Treatment with SNP showed a significant increase in the rate of MMP activity with APMA (paminophenyl mercuric acetate). SNP is effective in causing an inhibition in the rate of GAG production in alginate beads.

**CONCLUSION:** Exogenous SNP will activate MMP activity and will digest the extracellular matrix of intervertebral disc. This study suggests that the influence of NO and MMP production increased MMPs will degrade the herniated tissue.

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## TO STUDY THE EFFICACY OF TREATMENT ALGORITHM IN THE MANAGEMENT OF POSTOPERATIVE DISCITIS

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**INTRODUCTION:** Postoperative discitis is a rare but often misdiagnosed cause of failed back syndrome. There is paucity of literature regarding management guidelines of postoperative discitis. We propose a treatment algorithm for the management of postoperative discitis.

**MATERIALS AND METHODS:** The study was carried out in a single centre in cases operated by a single surgeon in the period from 2009 to 2015. 26 consecutive cases of postoperative discitis following lumbar discectomy were included in the study. Conservative management with antibiotics, analgesics and bed rest was started in all the study cases. The patients were observed for a period of 4 weeks and analysed using Visual Analogue Scale and modified Oswestry Disability Index.

**RESULTS:** Of the 26 cases studied, 11 were females and 15 were males. 5 out of the 26 cases failed the conservative trial and were subjected to posterior spinal instrumentation and posterolateral fusion.

**DISCUSSION:** Early diagnosis and appropriate management is the key to effective treatment of postoperative discitis. Conservative management leads to excellent results in majority of cases using this treatment algorithm. Surgical intervention with posterior stabilization and posterolateral fusion is helpful when conservative treatment fails and eventually shows good results.

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## HALF AN HOUR'S EFFECT OF THE JACKKNIFE STRETCH ON THE FLEXIBILITY OF THE LEG AND TRUNK: A COMPARATIVE STUDY

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**Introduction:** There have been reported that tight hamstrings increased the risk of the onset of low back pain and that the static stretches enhanced hamstring flexibility, but this effect lasted only 3 minutes after cessation of the stretching. The purpose of this study was to compare the half an hour's effect on the flexibility of the leg and trunk between the jackknife stretch and the conventional static stretch.

**Methods:** Approval of this hospital's ethics committee and informed consent to inclusion in this study from 35 healthy adults were obtained. They were allocated to either the jackknife stretch group (n=17) or the static stretch group (n=18). The subjects in the jackknife stretch group were fully extended the knees from the squat down position with their ankles holding. The subjects in the static stretch group were sat on a chair with their hip joint at moderate flexion and their knee joint at extension, and were leaned forward their pelvis. These were alternated with left leg and right leg: Fig. (upper). They were repeated these stretches for 10 seconds and 10 times over. Finger-floor distance (FFD) and right and left straight-leg raising angles (SLAs) were measured as the indexes of the flexibility of the trunk and leg. We also calculated the differences in FFD and SLAs between before and at half an hour after cessation of the stretches. The results were statistically compared between before and at half an hour after cessation of the stretches, and between the jackknife stretch and static stretch groups. A P value < 0.05 was considered statistically significant. Values were expressed as mean±sd.

**Results:** FFDs were significantly increased at half an hour after cessation of the jackknife stretch (from 1.1±9.6cm to 5.4±9.0cm) and static stretch (from 1.6±8.2cm to 2.8±8.0cm). Right SLAs were significantly increased at half an hour after cessation of the jackknife stretch (from 70.0±8.3° to 76.2±9.4°) and static stretch (from 70.3±9.9° to 72.2±9.6°). Left SLAs were significantly increased at half an hour after cessation of the jackknife stretch (from 66.8±8.5° to 75.6±9.5°) and static stretch (from 69.4±8.7° to 71.1±8.5°). The increases in FFD, right SLA, and left SLA in the jackknife stretch group (4.4±2.2cm, 6.2±5.5°, and 8.8±4.9°, respectively) were significantly larger than those in the static stretch group (1.2±1.2cm, 1.9±2.5°, and 1.7±3.0°, respectively): Fig. (lower).

**Discussion:** The results indicated that the half an hour's effects of the jackknife stretch were significantly greater than those of the static stretch. There have been reported that the increased flexibility of the hamstrings after jackknife stretch was caused by reciprocal inhibition of the contraction of the quadriceps femoris as an antagonist muscle. Therefore, we think that the jackknife stretch is a useful active-static stretch technique that leads to efficiently increase the flexibility of the hamstrings for patients with low back pain which was caused by the tight hamstrings.

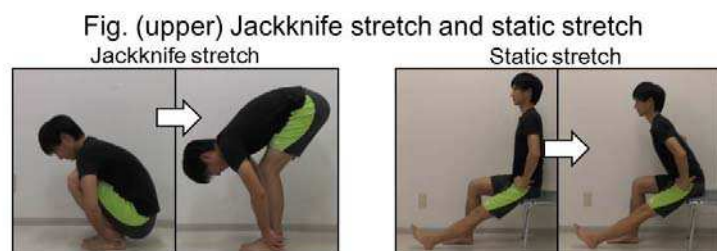


Fig. (lower) Increases in FFD, RSLA, and LSLA after jackknife stretch and static stretch

	Jackknife stretch group	Static stretch group	P value
FFD(cm)	4.4±2.2	1.2±1.2	P = 0.000*
RSLA(degree)	6.2±5.5	1.9±2.5	P = 0.000*
LSLA(degree)	8.8±4.9	1.7±3.0	P = 0.000*

\*P<0.05

## POSTURAL CHANGE EFFECTS ON T1 PELVIC ANGLE AND OTHER SPINO-PELVIC ALIGNMENT IN ADULT SPINAL DEFORMITY ARE LESS THAN THOSE IN NONDEFORMITY: CRITERION-RELATED VALIDATION STUDY

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**Introduction:** T1 Pelvic Angle (TPA) is introduced as a radiographic parameter of sagittal global alignment, accounting for both spinal inclination and pelvic tilt (PT). TPA is believed to be less affected by postural change, and its main purpose is to help consider the ideal spino-pelvic alignment in correction surgery for adult spinal deformity (ASD) during both, perioperative periods and operation. Thus, the influence of postural change on TPA is important. However, it has not been well established and validated yet.

**Aim:** To investigate changes on TPA and other spino-pelvic alignment during postural changes, and compare those in ASD patients to those in nondeformity (ND) patients.

**Material and Methods:** Consecutive 31 patients who were admitted for spinal surgery were enrolled in this study, and divided into 2 groups according to their spinal alignment: 16 into ASD group, and 15 into ND group. No patient had undergone previous long spinal fusion. The patients' demographics were collected, and TPA, sagittal vertical axis (SVA), and pelvic incidence (PI) in both standing and decubitus positions were measured using lateral whole spine X-ray films. Effects of postural change on those parameters were examined in the whole cohort and two patients groups. Each parameter was measured three times, and the mean values were used for evaluation. Two-way ANOVA was used to analyse the mean difference, and Inter-class correlation coefficient was used to assess the agreements in the measurement values between standing and decubitus positions. Intra- and inter-rater reliabilities were also assessed.

**Results:** There were 13 men and 18 women, with a mean age of 67.8 years. ASD group were significantly older than ND group, however there was no significant difference in sex between the groups. The mean TPA, SVA, and PI in standing and decubitus positions are summarized in Table, and there was no significance in mean difference values between the postures on the three parameters. Also, three parameters except SVA had good to excellent agreements in the whole cohort. However, the ND group have significant larger mean difference values on TPA than the ASD group did ( $p = 0.024$ ). The agreement analysis in standing and decubitus position measurements is also summarised in Table, and shows that the ASD group showed good agreement on TPA (0.895), whereas the ND group failed to show any significant agreement. Good to excellent agreements in both groups were observed on PI, whereas, poor agreements were observed on SVA.

**Conclusion:** In ASD patients, TPA was less affected by postural change than in ND patients, and it could be a good indicator for global alignment, regardless of the setting for X-ray. By contrast, TPA is easily affected in ND patients, thus it should be used with careful consideration.

Parameters	Patients groups	Mean values			Agreement	
		Standing	Decubitus	p value	Inter-class correlation coefficient	p value
TPA (degrees)	Whole patients	22.2	24.4	0.42	0.831	<0.001
	ASD group	32.2	30.9		0.895	<0.001
	ND group	11.5	17.4		(0.379)	0.07
PI (degrees)	Whole patients	49.0	49.3	0.91	0.946	<0.001
	ASD group	54.3	54.3		0.944	<0.001
	ND group	43.3	44.0		0.882	<0.001
SVA (mm)	Whole patients	54.0	53.5	>0.99	(0.280)	0.06
	ASD group	73.4	59.3		(0.276)	0.14
	ND group	33.3	47.3		(-0.208)	0.78

## RELATIONSHIP BETWEEN FEAR OF MOVEMENT AND HEALTH RELATED QUALITY OF LIFE IN PATIENTS WITH CHRONIC PAIN

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### Introduction

Chronic musculoskeletal pain relates to impaired health related quality of life (HRQoL), pain and disability. Patients with chronic pain report lower scores on several factors related to HRQoL compared to controls. Variables related to fear avoidance model (FAM) have demonstrated association to HRQoL. However, there is lack of studies regarding relationship between HRQoL and fear of movement. Aim of the cross-sectional study was evaluate association between (HRQoL) and fear of movement among patients with chronic musculoskeletal pain.

### Methods

Study sample is drawn from database of Orton Rehabilitation Centre. Patients with chronic musculoskeletal pain referred by the Social Insurance Institute of Finland (SII) to the in-patient pain management program between the years 2005 and 2008. The main goal of the program was to regain the functional ability of the patients. All measurements were part of the rehabilitation programme. SII funded the rehabilitation services and provided rehabilitation allowance during the rehabilitation. The patients did not get any extra compensation.

Questionnaires were completed at admission of rehabilitation. Self-report of disability was assessed using the Finnish versions of the Oswestry Disability Index (ODI), The average pain intensity during the past week on a 0–100mm was assessed by visual analogue scale (VAS). Fear of movement was assessed using the Finnish version of Tampa scale for kinesiophobia (TSK-FIN). Health related quality of life was assessed using RAND36 questionnaire.

### Results

Sample consists 637 (54% were women) chronic pain patients (pain over 3 months), mean (SD) age was 47.7 (7.7) yrs. Mean (SD) pain intensity was 68.9 (21.6). Men had higher ( $p < 0.001$ ) scores [mean (SD) 40.8 (8.0)] in the TSK-FIN compared to women [mean (SD) 36.2 (8.4)]. Cronbach's alpha for TSK-FIN was 0.82 (95% CI: 0.80 to 0.84). Mean (SD) Oswestry index was 34.5 (14.2). Only 2.7 % of the patients did not have any sick leave and 3.3% were retired.

Age and sex adjusted correlations between TSK-FIN and all RAND36 scales were significant ( $p < 0.001$ ) after Sidak multiple adjustment. Role physical –scale had lowest correlation [-0.32 (95% CI -0.39 to -0.26)] and General health –scale had highest correlation [-0.47 (95% CI -0.53 to -0.40)]. Correlation between the TSK-FIN and physical component score (PCS) was [-0.36 (95% CI -0.30 to -0.43)] and with mental component score (MCS) [-0.39 (95% CI -0.32 to -0.45)], respectively. Age and sex adjusted correlation between TSK-FIN and OSW was 0.49 (0.43 to 0.55) and correlation between TSK-FIN and VAS was 0.26 (0.18 to 0.34). Using best subsets variable selection with Akaike's information criterion the TSK-FIN items 1, 3 and 4 explained 16% of variance of the PCS. Respectively, items 3, 5, 6 and 15 explained 19% of variance of the MCS.

### Discussion

Among this sample of chronic musculoskeletal pain patients fear of movement showed significant inverse association to all scales of HRQoL measured by RAND36. Further studies assessing relationship between fear of movement and HRQoL and the clinical significance of observation are warranted.

## NEW GLOBAL CLASSIFICATION OF RADIOLOGICAL IMAGING FOR LESIONS OF THE LUMBAR SPINE . DEVELOPMENT AND FEASIBILITY

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### Introduction

Phenotypisation of the lumbar spine and its lesions was the topic of last 4 meetings of the ISSLS Focus Group on disc degeneration. No consensus exists for definitions of different degenerative diseases nor for classification of these diseases. The existing scoring systems are usually limited to a single structure e.g. disc, facets, spinal canal etc.

### Purpose

The aim of this study is to present a simple method to describe the normal and global radiological changes of the lumbar spine and by that to get a tool for classification.

### Method

Our tool is derived from the TNM classification system used for tumors. It includes 10 main categories and for each one up to 4 levels of modifiers. The findings are encoded in a standardized manner. As an example some categories and modifiers are summarized in table 1

### Results

In a first trial 200 MR examinations of consecutive patients of different age and gender referred to MRI for lumbar spine examination were encoded by 3 radiologists (kappa : 0,74). The mean time for encoding one MR-examination was 3 minutes after description of the case. Examples of correlations were done with respect to age and gender. There was strong correlation of disc degeneration with age (r : 0,8) not with gender. There was no difference in the distribution of protrusion and extrusion in the categories of age and gender (p : <0,5). The number of phenotypes depends on the number of characteristics introduced into the system. Algorithms were used to find clusters of phenotypes mainly with regard to age and gender.

### Conclusion

The presented proposal for phenotypisation of changes of the lumbar spine seems to be a valuable tool to describe these changes and allow to form groups of phenotypes. This method is applicable for all imaging modalities (MR, CT, X-ray, Discography, Myelography). It can be the base to compare groups and subgroups and to allow correlations within the groups and subgroups. the system can easily be extended with additional characteristics. It allows better comparison of different studies which contain imaging modalities of the lumbar spine

Table 1

Main categories	1st order modifiers	2nd order modifiers	3rd order modifiers	4th order modifiers
Age <b>A</b>	decade <b>(1-9)</b>			
Gender <b>G</b>	Female <b>F</b> Male <b>M</b>			
Dural sac impression <b>I</b>	Disc herniation <b>H</b>	Sort of disc herniation bulging <b>B</b> protrusion <b>P</b> extrusion <b>E</b> sequester <b>S</b>	Level of herniation L1-L2 <b>I</b> L2-L3 <b>II</b> L3-L4 <b>III</b> L4-L5 <b>IV</b> L5-S1 <b>V</b>	Side of herniation right sided <b>R</b> central <b>C</b> left sided <b>L</b>
	Osteochondrosis <b>O</b>		Level of osteochondrosis L1-L2 <b>I</b> L2-L3 <b>II</b> L3-L4 <b>III</b> L4-L5 <b>IV</b> L5-S1 <b>V</b>	

Bold figures mean the code for categories and modifiers.

In the same way other main categories like Disc Height, End plate Changes, Neuroforaminal Stenosis, Deformities are to be coded.

Example for coding: male patient (**G,M**) in 3rd decennium (**A,3**) spinal narrowing (**I**)by herniation (**H**)with extrusion(**E**) in Segment

L 5/S1 (**V**) in central position (**C**) = **A,3;G,M;I,H,E,V,C**

## PREDICTIVE RISK FACTORS FOR STENOSIS IN THE THORACIC AND LUMBAR SPINES OF PATIENTS WITH CERVICAL MYELOPATHY

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**INTRODUCTION:** Patients with cervical myelopathy can have concurrent thoracic or lumbar stenosis. However, cervical myelopathy may obscure thoracic or lumbar symptoms such that no workup for those areas is performed. To our knowledge, there is no study that has identified radiographic features in cervical MRIs of patients with symptomatic cervical myelopathy that can predict the concurrent presence of thoracic or lumbar stenosis. Our purpose is to identify radiologic features of cervical MRI in the patients with cervical spondylotic myelopathy that predict concurrent thoracic or lumbar stenosis.

**METHODS:** Whole spine T2 sagittal MRI images of all patients, who underwent surgery for cervical spondylotic myelopathy between February 2004 and December 2013, whose MRIs were available for review, were evaluated retrospectively. We measured the anterior-posterior diameters of the vertebral body, bony spinal canal and spinal cord, and anterior or posterior epidural stenosis at the level of the disc for the cervical, thoracic and lumbar levels. Epidural stenosis was defined as obliteration of more than 50% of the anterior or posterior subarachnoid space. We compared the radiologic parameters on the cervical MRIs of the subgroups with and without thoracic stenosis and those with and without lumbar stenosis.

**RESULTS :** There were 71 patients, 26 females, 45 males, ages 29-86 (mean  $59.2 \pm 12.6$  years). Thirty of the 71 with cervical spondylotic myelopathy (42.3%) had concurrent radiographic thoracic stenosis and thirty-seven (52.1%) had concurrent lumbar stenosis. Anterior epidural stenosis at C2-C3 was associated with a high prevalence of thoracic stenosis (16/30, sensitivity 53.3%, specificity 95.1%). Anterior epidural stenosis at C7-T1 was associated with a high prevalence of lumbar stenosis (9/37, sensitivity 24.3%, specificity 94.1%).

**DISCUSSION:** In the patients with C2-C3 anterior epidural stenosis it might be better to take the MRI on thoracic spine to rule out the thoracic myelopathy. In the patient with C7-T1 anterior epidural stenosis it might be better to take the MRI on lumbar spine to rule out the lumbar stenosis.



## SAGITTAL ALIGNMENT BASED ON END VERTEBRAE ACCORDING TO DIFFERENT AGE GROUPS

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**INTRODUCTION:** The scoliotic coronal alignment has been evaluated by the end vertebrae. However, there was no report that elucidates lordotic and kyphotic sagittal alignment based on end vertebrae. The purpose is to determine lordotic and kyphotic sagittal alignment based on end vertebrae and changes according to different age groups.

**METHODS:** Whole spine lateral radiographs of one hundred forty seven patients within a single health-care system from 2003 to 2012 were analyzed. They consist of 73 male and 74 female patients, and mean age was 44.0 years old (range 20-74). They were 49 patients in twenties, 50 in forties and 48 in sixties. We identified 1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup>, 4<sup>th</sup> and 5<sup>th</sup> end vertebra from bottom. We drew lower horizontal margin of lateral radiograph and McGregor's line. Next, we measured the Cobb's angles of the first kyphotic angle between lower horizontal margin and 1<sup>st</sup> end vertebra, first lordotic angle between 1<sup>st</sup> and 3<sup>rd</sup> end vertebra, second kyphotic angle between 3<sup>rd</sup> and 5<sup>th</sup> end vertebra, and second lordotic curve between 5<sup>th</sup> end vertebra and McGregor's line and the distance from 1<sup>st</sup>, 3<sup>rd</sup> and 5<sup>th</sup> end vertebra to C2 plumb line. We arbitrarily assigned a positive value when the end vertebra was located anterior to the C2 plumb line.

**RESULTS :** The 1<sup>st</sup> end vertebra was S1 in 147 patients (100%). The 3<sup>rd</sup> end vertebra was L1 in 35 patients (23.8%), L2 in 64 patients (43.5%) and L3 in 25 patients (17.0%). The 5<sup>th</sup> end vertebra was C7 in 22 patients (15.0%), T1 in 62 patients (42.2%) and T2 in 29 patients (19.7%). The mean Cobb's angles of first kyphotic curve was 34.39°, first lordotic curve was 37.04°, second kyphotic curve was 45.92° and second lordotic curve was 27.19°. The mean distance from 1<sup>st</sup> end vertebra was -2.28 mm, 3<sup>rd</sup> end vertebra distance was -16.49 mm, and 5<sup>th</sup> end vertebra distance was -13.85 mm. There were no differences of distribution of 3<sup>rd</sup> end vertebra between age groups, but 5<sup>th</sup> end vertebra was C7 commonly in older age group ( $p=0.014$ ). There was tendency to decrease angle of the first kyphotic and first lordotic curve in older age group ( $p=0.002$ ,  $p=0.005$ ), but no differences of second kyphotic and second lordotic curve between age groups. C2 plumb line migrated anterior in older age group. The distance from 1<sup>st</sup> and 3<sup>rd</sup> end vertebra differed among age groups, but that from 5<sup>th</sup> end vertebra distance didn't differ.

**DISCUSSION:** There were tendency of decreased pattern of the first kyphotic and first lordotic curve in older age group and 5<sup>th</sup> end vertebra migrated from T1 to C7.

**CERVICAL SPONDYLOLISTHESIS COMBINED WITH LUMBAR SPONDYLOLISTHESIS**

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**INTRODUCTION:** Concurrent cervical and lumbar spondylosis has been reported on. Given that severe spondylosis can result in degenerative spondylolisthesis, one might expect that concurrent spondylolisthesis of the cervical and lumbar spine might also be prevalent. On the other hand, the incidence of spondylolistheses in the lumbar and cervical spines might differ due to anatomical differences between the two areas. We are unaware of a study concerning concurrent cervical and lumbar spondylolisthesis.

**METHODS:** We evaluated the standing cervical & lumbar lateral radiographs of all patients over 50 years old who had neck or back pain, radiating arm or leg pain, from February 2006 to August 2012. Patients with non-degenerative disease (trauma, infection, tumor, deformity, inflammation) or with history of previous spine surgery in the lumbar and cervical spine were excluded. Lumbar spondylolisthesis was defined as more than one Meyerding grade on standing lateral radiographs and cervical spondylolisthesis was defined as greater than 2 mm of displacement on standing lateral radiographs.

**RESULTS :** There were 2,529 patients; 1,410 females and 1,119 males. There were 1,172 in their 50's, 675 in their 60's, 512 in their 70's, 155 in their 80's, and 15 in their 90's. Lumbar spondylolisthesis was found in 148 patients (5.9%) and cervical spondylolisthesis was found in 202 patients (8.0%). Twenty-one patients had both cervical and lumbar spondylolistheses (0.8%). Lumbar spondylolisthesis is a risk factor for co-existing cervical spondylolithesis (odd ratio of 1.933). Cervical spondylolisthesis is a risk factor for co-existing lumbar spondylolithesis (odd ratio of 1.933). Lumbar spondylolisthesis was more common in females than males, with an odds ratio of 2.297. In contrast, cervical spondylolisthesis had no gender differences. Lumbar spondylolisthesis had no difference according to age groups. In contrast, cervical spondylolisthesis was more common in older patients.

**DISCUSSION :** There was higher incidence of cervical spondylolithesis in patients with lumbar spondylolisthesis. Cervical but not lumbar spondylolisthesis appears to increase in prevalence with age.

## TWO-YEAR FOLLOW-UP OF PHYSICAL THERAPY VERSUS SURGICAL THERAPY FOR PATIENTS WITH LUMBAR SPINAL STENOSIS

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**Introduction:** A previous systematic review comparing surgical versus nonsurgical treatment for lumbar spinal stenosis (LSS) reported that surgery led to better results for pain, disability, and quality of life but not for walking ability. However, the nonsurgical treatments applied were not systematic or methodical and involved different modalities, including bracing, physical therapy, and epidural steroid injection. The purpose of this study was to compare the 2-year follow-up outcomes of physical therapy and surgery for patients with LSS.

**Methods:** This study was a retrospective review of prospectively collected clinical data. Patients presenting with bilateral symptoms of neurogenic claudication caused by central LSS (confirmed by magnetic resonance imaging or computerized axial tomography scan) were enrolled from April 2011 to October 2012. Patients with concomitant conditions that could compromise outcome assessment, such as previous spinal surgery, degenerative scoliosis, or spondylolisthesis, were excluded. The patients chose whether to undergo surgery. Patients who decided against surgery were treated with manual therapy, stretching and strengthening exercises, and body-weight-supported treadmill walking once a week for 6 weeks. All patients were asked to undertake a home exercise program. Clinical outcomes were measured using the Zurich Claudication Questionnaire (ZCQ); a visual analog scale (VAS) of low back pain, leg pain, and leg numbness; the Medical Outcomes Study 36-item Short-Form General Health Survey (SF-36); and the Roland–Morris Disability Questionnaire (RMDQ). Patients who chose surgery underwent lumbar decompression surgery without spine fusion. Two-year follow-up outcomes in patients treated surgically (Surgery group) were compared prospectively with those for patients who underwent physical therapy (PT group). Differences with  $P < 0.05$  were considered to be significant.

**Results:** Twenty-eight patients (18 men and 10 women, average age 70.8 years) were allocated to the Surgery group and 38 patients to the PT group. Of the 38 patients in the PT group, eight underwent surgery after physical therapy. Complete data were available for 21 patients (9 men and 12 women, average age 71.5 years) at the 2-year follow-up. Age and gender did not differ between groups, but BMI differed significantly (21.7 and 23.6 kg/m<sup>2</sup> in the PT and Surgery groups, respectively;  $P < 0.05$ ). At baseline, the VAS for low back pain, physical function on the ZCQ subscale, physical functioning, role physical, and general health on the SF-36 subscales, and RMDQ scores were worse in the Surgery group than in the PT group ( $P < 0.05$ ). However, at 2-year follow-up, these patient-reported outcomes had improved for both groups, and there were no significant differences between groups for VAS, ZCQ, SF-36, or RDQ ( $P > 0.05$ ).

**Discussion:** In this study, the patients with neurogenic claudication induced by central LSS who chose surgery had more severe preoperative symptoms. Patients in the PT group had improved symptoms after intensive physical therapy for 6 weeks, and at 2-year follow-up, the patient-reported outcomes in the PT group did not significantly differ from those in the Surgery group. These results suggest that methodical and intensive physical therapy is effective for LSS patients with mild bilateral neurogenic claudication.

## GENDER DIFFERENCE OF DYNAMIC POSTURAL STEADINESS DURING ONE LEG STANDING IN OLDER ADULTS WITH RECURRENT LOW BACK PAIN

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**Introduction:** Although postural deficits in subjects with recurrent low back pain were reported, gender difference in dynamic postural steadiness from the ground reaction force is unknown. This study was conducted to compare the dynamic postural steadiness index based on medio-lateral, anterior-posterior, and vertical directions as well as one leg standing duration in older adults with recurrent low back pain.

**Methods:** Fifty-eight individuals participated in the study, including 30 females and 28 males with recurrent low back pain. Each subject stood upright on his/her non-dominant leg with and without visual input. The outcome measures included one leg standing duration and the dynamic postural steadiness index, which is the combined mean square deviations assessing fluctuations around a zero point of the frontal, sagittal, and vertical axes of the force plate.

**Results:** Male adults demonstrated significantly longer standing durations than the female adults in the eyes-open condition ( $t = -2.19$ ,  $p = 0.03$ ). The dynamic postural steadiness index demonstrated an excellent relationship with the vertical steadiness index for the males, especially during the eyes-closed condition ( $r = 0.99$ ,  $p = 0.001$ ). The dynamic postural steadiness index demonstrated significant interactions with visual input ( $F = 4.21$ ,  $p = 0.04$ ) as well as visual input and gender ( $F = 4.70$ ,  $p = 0.03$ ).

**Discussion:** The male group demonstrated significantly higher dynamic postural steadiness with vertical steadiness during one leg standing. Improved postural correction in sagittal standing alignment might enhance the chain reaction of postural steadiness in subjects with recurrent LBP. Clinicians need to implement vertical steadiness rehabilitation strategies to enhance dynamic postural stability in older female adults with recurrent low back pain.

**Keywords:** Gender; dynamic postural stability; recurrent low back pain; one leg standing; vertical steadiness.

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## CHARACTERISTICS OF PATIENTS WITH LUMBAR FACET SYNDROME SHOWING EFFICACY OF LUMBAR FLEXION EXERCISE

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**Introduction:** Lumbar flexion exercise (flexion exercise) has reportedly shown efficacy for some patients with lumbar facet joint syndrome (LFS). The pathological processes underlying LFS resemble those for degenerative disc changes. Flexion exercises thus may not be suitable for some patients with LFS. We used imaging modalities including MRI to examine the characteristics of patients for whom flexion exercise shows efficacy against LFS.

**Material & Methods:** Subjects comprised 126 outpatients who had been diagnosed with LFS based on clinical evaluations at the first consultation, and who then performed flexion exercises. Features on radiography and MRI were examined. Therapeutic effects were evaluated using the Japanese Orthopaedic Association (JOA) score for subjective symptoms. Patients were grouped according to JOA subjective symptom scores at initial evaluation and follow-up, with improved scores indicating effectiveness of flexion exercise and unchanged or worsened scores indicating ineffectiveness. For clinical imaging, standing sagittal and functional X-rays were performed at the first consultation. Functional X-ray results comprised maximum lumbar flexion and maximum lumbar extension on side-lying. The following parameters were measured: 1) vertebral body angles (VBA) of the lumbar spine; 2) lordotic lumbar angle (LLA); 3) L5-S1 angle; 4) sacral slope (SS); and 5) posterior shift (PS). Lumbar ranges of motion (ROMs) were also measured, as lumbar extension ROM (E-ROM) and lumbar flexion ROM (F-ROM). Total ROM (T-ROM) was defined as the range from maximum flexion to maximum extension. MRI of the lumbar spine was performed using sagittal T2-weighted imaging, and presence of herniation masses and grade of disc degeneration were evaluated. Disc degeneration was categorized using the Pfirrmann grading system. Stepwise multiplex logistic-regression analysis was used for statistical analysis. Dependent variables were effectiveness or ineffectiveness of flexion exercise, and independent variables were sex, age, LLA, PS, SS, VBA, E-ROM, F-ROM, T-ROM, presence of herniations and grade of disk degeneration.

**Results:** Among the 126 patients with LFS, 108 patients (85.7%) showed effectiveness of flexion exercise, and 18 patients (14.3%) did not. Factors associated with effectiveness of flexion exercise according to multiplex logistic-regression analysis were postural factors of SS, standing VBA of L1/2, L3/4 and L5/S1 and LLA, range of motion factors of L4/5 ROM, F-ROM, and the MRI factor of grade of disc degeneration. The model chi-square p-value were less than 0.01, and the Hosmer-Lemeshow test adapted in higher than 0.05. The percentage of correct classifications was 92.8%.

**Conclusion:** Characteristics of patients for whom flexion exercise was effective against LFS were: 1) mild disk degeneration; 2) relatively small lumbar lordosis and sacrum slope; and 3) The patient had kept flexion ROM of total lumbar and lower lumbar vertebrae. Flexion ROM of VBA reportedly decreases as ROM factor in LFS. L4/5 ROM and F-ROM tended to be larger in patients for whom flexion exercise was effective. We therefore suggest that flexion exercise would tend to be ineffective in patients with LFS who were unable to improve lumbar ROM, because patients did not show changes in lumbar alignment after lumbar flexion exercise.

## PROSPECTIVE STUDY OF CHARACTERISTICS OF LOW BACK PAIN IN ADOLESCENT PATIENTS WITH EARLY-STAGE SPONDYLOLYSIS EVALUATED BY QUESTIONNAIRE

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**Introduction:** Early-stage spondylolysis (ESS) is a common cause of acute low back pain (LBP) in adolescent patients. Magnetic resonance imaging (MRI) is useful for diagnosing ESS. However, because of high costs, MRI cannot be utilized in all adolescent patients with LBP. We previously reported possible specific characteristics of ESS: (i) having severe pain in motion, but less pain while standing and sitting; (ii) fingertip-sized LBP in pain extent; and (iii) unilateral or bilateral LBP in pain location. Based on these characteristics, in this study, we designed a patient-based questionnaire to detect patients with ESS, and prospectively examined the usefulness of the questionnaire. The purpose of this study was to evaluate the correlation between each question in our questionnaire and the presence of ESS in adolescent patients with LBP.

**Methods:** Adolescent patients (n=69, >18 yrs-old) with acute LBP (>1 month) were included. All patients were evaluated by the following questionnaire: exercise frequency per week (0-1, 2-4, 5-7 times), training time per day (<1.5 hours, 1.5 to <3 hours, >3 hours), the necessity for stopping sports activity (never, sometimes, frequently), pain-provoking situations (in sitting, or standing, or in motion), pain quality (sharp/dull), pain provocation in hyperextension or hyperflexion, pain location (center/unilateral or bilateral) and pain extent (ping-pong ball-sized area/palm-sized area). All patients were evaluated by plain radiography and MRI; patients who showed obvious pathological findings other than ESS (e.g., disc herniation, infection, etc.) were excluded. To evaluate the usefulness of our originally developed questionnaire, any correlation of each question and gender, with the presence of ESS was determined.

**Results:** Of 69 patients, 24 had ESS (ESS group: mean age: 13.9 yrs-old; 21 males/3 females) and 45 had no pathological findings that explained the LBP origin (NS-LBP group: mean age: 14.6 yrs-old; 28 males/17 females). Correlation analyses showed weak associations between the presence of ESS and (i) higher exercise frequency per week ( $r=0.306$ ,  $p=0.03876$ ), (ii) longer training time per day ( $r=0.326$ ,  $p=0.0271$ ), and (iii) pain-provoking situations (motion > sitting or standing:  $r=0.329$ ,  $p=0.0254$ ), and showed a moderate association between ESS and gender (male:  $r=0.422$ ,  $p=0.0227$ ).

**Discussion:** This questionnaire, designed for and evaluated in the present study, constitutes a new diagnostic instrument that may be helpful to detect ESS. Within the parameters of this questionnaire, exercise frequency, training time, pain-provoking situations and gender could be important items to detect ESS. Furthermore, it is possible to obtain this information with only the use of this questionnaire. However, pain location and pain extent, which we had previously reported as specific characteristic ESS, did not correlate with the presence of ESS in this study. From these observations, we believe that this questionnaire provides useful information to determine the probability of the presence of ESS when evaluating adolescent patients with LBP.

## SAFETY AND EFFICACY OF AGGRESSIVE EXERCISE THERAPY FOR PATIENTS WITH EARLY-STAGE SPONDYLOLYSIS

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**Introduction:** In patients with early-stage spondylolysis thought to be a stress fracture of the pars interarticularis, bony union can be obtained by use of a rigid corset and refraining from sports activity. However, refraining from sports activity for a long period of time may lead to decreased physical fitness. The aim of this study was to investigate the safety and efficacy of aggressive exercise therapy for patients with early-stage spondylolysis.

**Materials and Methods** Patients (n=33, <19 years-old; 29 males/4 females) diagnosed with unilateral early-stage spondylolysis by MRI and CT, were divided into a light intensity exercise group (L group: n=18; mean age: 14.6 years-old; 16 males/2 females; thermotherapy and stretching) and an aggressive exercise group (A group: n=15; mean age: 13.9 years-old; 13 males/2 females; muscle strengthening exercises and aerobic training). Diagnosis of early-stage spondylolysis was made when the lumbar spine pedicle showed bone marrow edema on MRI, even though a fracture line was faint or not observed on CT. Patients who showed bilateral spondylolysis, progressive or terminal stage spondylolysis on CT, and patients who did not refrain from sports activity were excluded. All patients were treated with a rigid corset and received light intensity (L group) or aggressive (A group) exercise therapy for 2-3 months. After treatment, assessment of bony union was performed using MRI and CT. The mean time interval between the initial and second CT examinations, and drop-out rates from the treatments were examined.

**Results** The results of the second CT examination showed that bony union was either obviously improved or achieved in all patients in both groups. The mean time interval between the initial and second CT examination was  $71.8 \pm 14.9$  days in the L group and  $74.1 \pm 11.1$  days in the A group, showing no statistically significant difference. The drop-out rate was higher (n=5, 27.8%) in the L group, compared with the A group (n=1, 6.7%), although no significant difference was observed.

**Conclusion** Our study indicated that aggressive exercise therapy was safe and effective in patients with unilateral early-stage spondylolysis because all patients in the A group, as well as the L group, showed bony union after treatment. Moreover, the lower drop-out rate in the A group suggests that aggressive exercise therapy may have contributed to maintaining patients' motivation for long-term treatment.

## SECULAR CHANGES OF LUMBAR CANAL DIMENSIONS IN WESTERN SWITZERLAND: AN MRI STUDY

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### INTRODUCTION:

Improvement of living conditions has resulted in increased stature in younger generations. Contrary to what was expected a previous CT based study showed that there was a generational trend towards narrowing of the lumbar and cervical bony spinal canals measured at pedicle level particularly in polytrauma patients (1). We aimed to verify whether this also held true using MRI as well as study the morphology of the dural sac in particular the CSF/ rootlet ratio.

### METHODS:

We included 175 patients with abdominal (n=131) or whole-body (n=44) MRI, divided in two groups of “younger” (born during the 1970s, n=86) and “older” (born during the 1940s, n=89) patients, matched for gender (p=0.588). Two independent observers measured the cross-sectional area (CSA) pedicle level from L1 to L5 on axial-oblique fluid-sensitive MRI sequences, and assessed the morphology of the neural content of the dural sac at both pedicle and disc levels using the A-D morphological grading (2).

### RESULTS:

Inter- and intra-observer reproducibility for measurements were excellent ( $p \geq 0.829$ ), while agreement for morphological grading was moderate to excellent (weighted kappa=0.54-1.00). Males had numerically larger bony spinal canals at all pedicle levels, albeit reaching statistical significance only at L4 (p=0.007) and L5 (p=0.013). Mean CSAs were significantly larger in the “younger” group at all pedicle levels (p $\leq$ 0.032). There was, however, no significant difference in morphological grades at pedicle nor at disc levels (p $\geq$ 0.10).

### CONCLUSION:

This study showed that contrary to previous publications, the bony canal has grown larger in western Switzerland in younger subjects. This increase is not mirrored by a significant difference in the neural content. The clinical implication of this finding is that despite better living conditions degenerative changes may still lead to symptomatic stenosis at disc level given the absence of significant secular change in the morphology of the dural sac and its contents.

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2. Qualitative grading of severity of lumbar spinal stenosis based on the morphology of the dural sac on magnetic resonance images. Schizas C, Theumann N, Burn A, Tansey R, Wardlaw D, Smith FW, Kulik G. *Spine (Phila Pa 1976)*. 2010 Oct 1;35(21):1919-24. doi: 1



## MAGNETIC RESONANCE IMAGING OF ANTERIOR THORACOLUMBAR VERTEBRAL ENDPLATE LESIONS IN YOUNG GYMNASTS

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**Introduction:** We previously reported that the prevalence of anterior thoracolumbar vertebral endplate lesions were significantly higher in young gymnasts than non-gymnasts who played other sports (40<sup>th</sup> ISSLS Annual Meeting). However, the association between anterior thoracolumbar vertebral endplate lesions and back pain remains controversial. Additionally, few studies have focused on the signal intensity changes in vertebral endplate lesions on magnetic resonance imaging (MRI). The present study was designed to evaluate the signal intensity changes and clinical significance of vertebral endplate lesions on MRI.

**Methods:** The number of gymnasts who visited our hospital between 2010 and 2015 with a complaint of back pain was 227. In 71 (31%) subjects, anterior thoracolumbar vertebral endplate lesions were observed on X-ray. Thirty-two subjects (15 men and 17 women; mean age, 16.1 years) underwent MRI after X-ray. Among these 32 gymnasts, anterior vertebral endplate lesions, including T10 to S1, were found in 47 vertebrae (three T11, seven T12, eight L1, five L2, two L3, five L4, eight L5, and nine S1 vertebrae). Endplate lesions were evaluated using sagittal T1-weighted image (T1WI), T2-weighted image (T2WI), and short T inversion recovery (STIR).

**Results:** Signal intensity changes in the vertebral endplate lesions were found in 32 of 47 vertebrae. Ten vertebrae had low-signal intensity on T1WI and high-signal intensity on T2WI; 9 of these vertebrae showed high-signal intensity on STIR. On both T1WI and T2WI, 12 vertebrae had high-signal intensity, whereas 3 vertebrae showed low-signal intensity. Four vertebrae showed intermediate-signal intensity on T1WI and high-signal intensity on T2WI. Three showed low-signal intensity on T1WI and intermediate-signal intensity on T2WI. The remaining 15 vertebrae showed no-signal intensity changes on both T1WI and T2WI.

**Discussion:** MRI of anterior thoracolumbar vertebral endplate lesions revealed several signal intensity changes. The main finding of this study was that 10 vertebrae showed low-signal intensity on T1WI and high-signal intensity on T2WI. Furthermore, 9 of these 10 vertebrae showed high-signal intensity on STIR. These signal intensity changes may represent bone marrow edema of the vertebrae from gymnastics injuries and are likely to be involved in the manifestation of back pain. Vertebral endplate lesions result in intervertebral instability, which intensifies mechanical stress to the vertebral endplate. Such mechanism may play a role in the pathogenesis of bone marrow edema of the vertebrae adjacent to the damaged endplates. To confirm the relevance of these findings to back pain, the MRI signal changes over time need to be assessed. Qualitative and quantitative evaluation of back pain resulting from anterior endplate lesions needs to be established.



**Fig.** Anterior lumbar vertebral endplate lesion. Sagittal MR imaging obtained in a 13y.o male gymnast showed low signal intensity on T1WI and high signal intensity on both T2WI and STIR (*white allows*).

## LUMBAR DEGENERATIVE KYPHOSIS WITH CONSERVATIVE TREATMENT : DO CLINICAL SYMPTOMS AND RADIOLOGICAL PARAMETERS PROGRESS?

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**Introduction:** The correlation between the clinical and radiologic parameters of general adult spinal deformity(ASD) is widely known. However, in lumbar degenerative kyphosis(LDK), dynamic sagittal imbalance shows during ambulation so its pathogenesis and natural history is different and not widely recognized compared to other ASD resulting many controversial for treatment. The purpose of this study is to evaluate whether the clinical symptoms and radiological parameters progress with conservative treated lumbar degenerative kyphosis patients.

**Methods:** From June 2006 to January 2014, 31 patients, who were diagnosed with a LDK and underwent conservative treatment, were studied. Mean age of the patients was 72.5 years old and the mean follow-up period was 59.2 months. Clinical and radiologic evaluation was conducted on the initial and last follow-up. Clinical evaluations were done using the visual analogue scale(VAS) and the Oswestry disability index(ODI), radiologic evaluations were performed using spinal and pelvic parameters for a follow-up period of at least 24 months.

**Results:** Patients who were diagnosed with LDK and underwent conservative treatment showed no significant differences in the clinical outcomes between the first and final follow-up. Of the radiologic evaluation, some radiological parameters significantly increased. There were no significant correlation between the clinical and radiologic parameters of the initial and final follow-up.

**Discussion:** During the follow-up period of patients diagnosed with LDK, radiologic parameters have progressed. However, its progress and the clinical symptoms expressed by the patients had no significant differences. Decisions for surgical treatment of LDK should not be made by the radiologic parameters showing the deformity degree, but by carefully determining the patients' disability level.

## PREVALENCE AND RELATED CLINICAL FACTORS OF THORACIC OSSIFICATION OF THE LIGAMENTUM FLAVUM - A CT-BASED CROSS-SECTIONAL STUDY-

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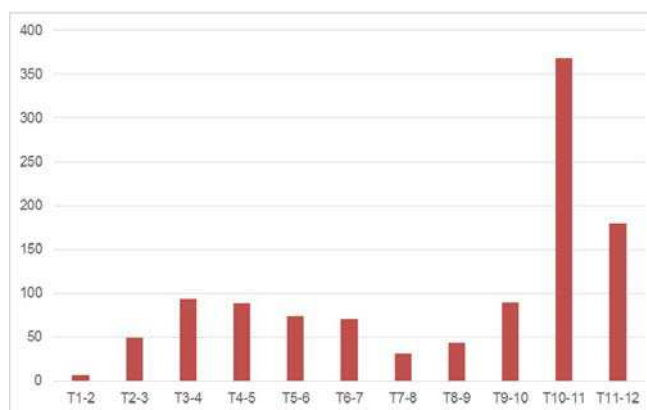
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**Introduction:** Thoracic ossification of the ligamentum flavum (TOLF) is an uncommon pathology but it may grow and cause serious neurologic manifestations. Little has been demonstrated yet about the epidemiology and etiology of TOLF. The purpose of this study was to estimate the prevalence and clinical characteristics of TOLF.

**Methods:** Of all patients who had undergone chest computed tomography (CT) for the evaluation of pulmonary disease or for medical examination for one year at our institute, 4999 patients were included. Prevalence and distribution of TOLF, thoracic kyphosis (TK, Figure 1) and concurrent ossification of posterior longitudinal ligament (OPLL) were analyzed on CT scans. Through reviews of their medical records, clinical characteristics including age, gender, body mass index (BMI), and diabetes were investigated. Logistic regression analysis was performed to determine the risk factors of TOLF.

**Results:** A total of 4999 patients (2929 males and 2070 females) were included. TOLF was found in 1090 patients (21.8%, 674 males and 416 females). A single TOLF lesion was noted in 592 patients and multiple lesions were noted in 498 patients. The most commonly involved level was T10-T11. Distribution of TOLF showed two peaks, and the highest peak was at the lower thoracic spine (T10-12) and the second highest peak was at T3-T5 (Figure 2). TK was  $31.5^{\circ} \pm 9.5$  in the TOLF group and  $29.7^{\circ} \pm 8.9$  in the non-TOLF group ( $P < 0.001$ ). Logistic regression analysis showed that gender and TK were significantly associated with TOLF.

**Discussion:** Although there are several putative hypotheses for the development of TOLF, little is yet known about the etiology and pathophysiology of TOLF. Until now, proposed theories were about the mechanical, degenerative, metabolic, and genetic factors. Mechanical stress has been proposed as a key factor in the development of TOLF. The location most frequently affected by TOLF was known to be the lower thoracic segments (T10-12), and our study showed that individuals with TOLF had higher TK than others significantly although it was measured with subjects in the supine position. The upper and lower thoracic spine are transitional areas in terms of spinal curvature, and especially the thoracolumbar junction is the area of high stress concentration, with the posterior column under high tensile force. Degenerative factors also seemed to have a role in the development of TOLF. Our result showed that TOLF was presented more frequently as age grows, suggesting that degeneration of the LF might have a role in the development of TOLF. To the best of our knowledge, this epidemiologic study about TOLF is the largest scale to date. Gender and TK were thought to have some correlation with TOLF. Further studies are needed to find out mechanical, metabolic, or genetic etiologies.



## RECENT TRENDS IN GENDER- AND AGE-SPECIFIC RATES OF VERTEBRAL FRACTURES: A COMPUTED TOMOGRAPHY-BASED STUDY

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**Introduction:** Vertebral fractures increase the risk of sustaining new fractures regardless of aging or decreasing bone mineral density. Previous studies have shown that 25% of Japanese women in the first half of their 70s and 40% of people over 80 have some vertebral fracture, of which more than half are asymptomatic. Over the past decade, the treatment of osteoporosis has become popular. Therefore, the recent rate of prevalent vertebral fractures is unknown since it was reported over ten years ago. The purpose of this study was to investigate recent trends in the gender- and age-specific rates of prevalent vertebral fractures using computed tomography (CT).

**Methods:** Enrolled subjects were 566 patients who visited our hospital during the period from July 2015 to January 2016, and underwent CT examination of the lumbar spine or abdomen for reasons other than lower back disorders or trauma. Patients visiting orthopedic outpatient clinics were excluded. We investigated prevalent vertebral fractures from CT images of the sagittal thoracolumbar (Th10 to L5) spine.

**Results:** No fractures were observed in patients less than 30 years of age. We studied the 496 patients who were older than 40 years (men n=285; women n=211). The mean age was 69.5±13.6 (40–95) years. The rate of vertebral fracture was 29.9% (n=63) in women and 12.3% (n=35) in men. The fracture rate in women was significantly higher than in men (p<0.05). The fracture rate by age group was 3.9% (n=2/51) in subjects in their 40s, 4.4% (n=3/68) in subjects in their 50s, 8.6% (n=10/115) in subjects in their 60s, 21.3% (n=26/122) in subjects in their 70s, and 40.7% (n=57/140) in subjects who were 80 years of age or older. Of all 157 fractures in the enrolled patients, 110 fractures (men n=33; women n=77) were of the thoracolumbar spine and 47 fractures (men n=10; women n=37) were of the middle and lower lumbar spine. The incidence of fracture in women over 60s who had middle and lower lumbar spine fracture was significantly higher than in men (p<0.0001).

**Discussion:** Even though we should be careful in comparing these results to findings from the normal population, since this study's subjects were patients, the rate of prevalent vertebral fractures was nearly equal to that reported previously. Therefore, awareness about osteoporosis treatment in our community is needed. Furthermore, we speculate that the middle and lower lumbar vertebral fractures were the result of osteoporosis since the fracture rate in aging women, many of whom have osteoporosis, was higher than that in men.

## EVALUATION OF PROGNOSTIC FACTORS AND A MODIFICATION TO THE MODIFIED TOKUHASHI SCORE IN PATIENTS WITH SPINAL METASTASES FROM BREAST CANCER

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**Introduction:** Breast cancer is the second leading cause of cancer-related death globally in females, and is a common cause of spinal metastases. The advent of targeted molecular based therapies has led to improvements in quality of life and increased survival in these patients. This is especially so in patients with breast cancer, Estrogen receptor (ER), progesterone receptor (PgR), and human epidermal growth factor receptor 2 (Her-2) are important receptors in the treatment of patient with breast cancer. Current prognostic systems do not take these receptor subtypes into account and it has been suggested that they be modified to take them into account.

**Methods:** This study is a retrospective cohort study of 185 histologically confirmed breast cancer patients treated for spinal metastases at our institution between May 2001 and April 2012 which aims to evaluate the prognostic value of receptor subtypes in Lung cancer patients with spinal metastases and the accuracy of a modification of the modified Tokuhashi score based on these receptor subtypes.

The primary outcome measure was survival from the time of diagnosis. Potential prognostic factors were investigated using Cox regression univariate and multivariate analyses. Patients were scored according to the modified Tokuhashi score labelled Tokuhashi A and modification labelled Tokuhashi B where patients who were Hormone receptor negative (ER and PgR negative) and triple negative (ER, PgR and Her-2 negative) had their histological score reduced from 5 to 3. Scoring predicted survival was compared with actual survival Predictive values of each scoring system for 6- and 12-month survival were measured via receiver operating characteristic (ROC) curves.

**Results:** Univariate analysis revealed that ER receptor status, PgR, Her-2 receptor status and previous hormone therapy were significant predictors of survival, and multivariate analysis revealed that the ER receptor status ( $p=0.004$ ) and Her-2 receptor status ( $p=0.01$ ) were significant predictors of survival. Cox regression analysis revealed that the Tokuhashi B score was significantly associated with patient survival ( $p=0.011$ ). There was a significant association between the Tokuhashi B subgroup 9-11 and survival ( $p=0.005$ ), although there was no significant association with survival in subgroup 12-15. Tokuhashi A had an AUROC (area under receiver operating curve) of 0.57 while Tokuhashi B had an AUROC of 0.62 at 6 months while at 12 months the Tokuhashi A had an AUROC of 0.62 while the Tokuhashi B had an AUROC of 0.70 at 12 months and this was statistically significant ( $p=0.046$ ).

**Discussion:** ER and Her-2 negative status are predictive of poor survival. The Tokuhashi B score was predictive of survival, however its AUROC at 6 months was only 0.62 and poor, and its AUROC at 12 months was 0.70 which was fair. The effect of histological subtype and the effect of newer targeted molecular therapy should be taken into account when managing patients with spinal metastases from breast cancer and surgical management should not be based on the results of prognostic scoring systems.

## FUNCTIONAL ASSESSMENT OF LUMBAR NERVE ROOTS USING DIRECT CORONAL SINGLE-SHOT TURBO SPIN-ECHO DIFFUSION TENSOR IMAGING - APPLICATION TO PATIENTS WITH BILATERAL SPINAL CANAL STENOSIS SHOWING UNILATERAL NEUROLOGICAL SYMPTOM

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**PURPOSE:** Diffusion Tensor Imaging (DTI) based on single-shot Echo Planner Imaging sequence (EPI-DTI) is established method to evaluate lumbar nerve roots compression, because several studies have shown that DTI and tractography of human lumbar nerves can visualize and quantitatively evaluate lumbar nerves by fractional anisotropy (FA). However, EPI-DTI has several problems such as long acquisition time and high geometric distortion. To solve these problems, we attempt to apply DTI based on single-shot Turbo Spin Echo sequence (TSE-DTI). In previous study, we reported that TSE-DTI has a lower geometric distortion and it might more accurately evaluate compressed lumbar nerve roots compared to conventional EPI-DTI. Clinically, there are some patients with spinal canal stenosis who have unilateral neurological symptom despite the existence of bilateral nerve compression on the conventional MRI images. The purpose of this study was to investigate the availability of TSE-DTI for patients with bilateral spinal canal stenosis who have unilateral neurological symptom.

**METHODS:** All subjects were examined with 1.5T whole-body clinical system (Ingenia, Philips Healthcare). Five patients with spinal canal stenosis, who have unilateral neurological symptom despite the existence of bilateral nerve compression on the conventional MRI images (median age, 69.8 years; range, 65–76 years), were examined by use of direct coronal TSE-DTI. FA values were continuously measured 18 points both proximally and distally to the bilateral lumbar foraminal zone at and adjacent to the levels responsible for symptoms. We evaluated the relationship between average FA values and symptomatic side, and changes of the FA values in measurement point.

**RESULTS AND DISCUSSION:** At the level responsible for symptom, the average FA values of symptomatic side were significantly lower than those of asymptomatic side ( $p < 0.05$ ). Also, the FA values of symptomatic side were lower than those of asymptomatic side on multipoint measurement. Intraneural edema and demyelination caused by compression injury, was encouraged decreasing the FA values because of decreased diffusion anisotropy of the nerves. Therefore, FA values of TSE-DTI might be helpful in the differential diagnosis for patients of bilateral spinal canal stenosis who have unilateral neurological symptom. The average FA values of asymptomatic level showed no significant differences between right and left side. The FA values of distal points tended to higher than those of proximal points. Functional assessment of lumbar nerve roots with the FA values was required multipoint measurement, because FA values dynamically changed according to measurement points.

**CONCLUSION:** FA values of TSE-DTI might be helpful in identification of responsible lumbar nerves roots for patients with bilateral spinal canal stenosis who have unilateral neurological symptom.

## DETECTING STRESS AT THE SACRUM WITH BONE SINGLE-PHOTON EMISSION COMPUTED TOMOGRAPHY/COMPUTED TOMOGRAPHY AFTER INSTRUMENTED LUMBAR FUSION

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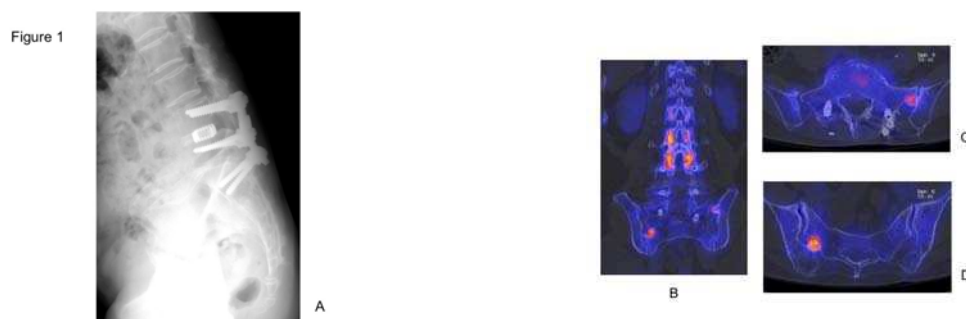
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**Introduction:** The clinical role of bone single-photon emission computed tomography/computed tomography (SPECT/CT for evaluating strain to the sacrum including sacroiliac joint (SIJ) arthritis and sacrum insufficiency fracture (SIF) after instrumented lumbar fusion with features of clinical adjacent segment pathology (CASP) has not been established. The purpose of this study was to determine the clinical role of bone SPECT/CT to detect stress at the sacrum in patients with CASP after instrumented lumbar/lumbosacral fusion.

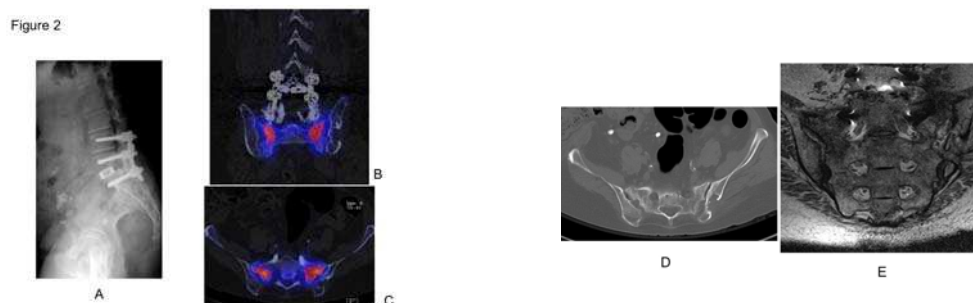
**Methods:** Sixty-six patients, who were diagnosed with CASP after satisfactory lumbar or lumbosacral fusion, were examined by bone SPECT/CT. SIJ arthritis and SIF were defined as anatomic abnormalities along with increased activity lesions. Lesions of the sacrum and SIJ were classified into the following categories: (1) normal, absence of any foci or the presence of a focus on one image dataset, (2) SIJ arthritis, defined as increased focal bone metabolic activity along the SIJ, (3) SIF, defined as a bilateral or unilateral sacral fracture line with increased bone metabolic activity.

**Result:** Mean patient age was 67.4 years, and the symptom-free period was 7.6 years after surgery. Mean bone mineral density (BMD) was  $-3.1$ . Sixteen of the 66 (24.2%) patients showed hot uptake in the sacrum; 11 had SIJ arthritis (16.7%) and 5 had SIF (7.5%). Patients showing increased activity in the sacrum ( $n = 16$ ) tended to be older than those in the normal activity group ( $n = 50$ ) ( $p = 0.117$ ). No difference was observed between the two groups regarding fused levels (2.2 vs. 2.3,  $p = 0.458$ ), BMD ( $-3.2$  vs.  $-3.2$ ,  $p = 0.563$ ) or symptom-free period (7.6 years vs. 6.8 years,  $p = 0.880$ ).

**Conclusion:** Symptoms in patients with CASP may be related to distal SIJ arthritis or SIF. We assessed pain generators of patients with CASP using plain radiographs, bone SPECT/CT, and MRI. However, our data suggest that plain radiographs and MRI missed the correct diagnosis in patients with undisplaced SIF even though plain radiographs indicate CASP, and MRI can detect edema and inflammatory changes. MRI image quality is affected by the instrument; thus, it was difficult to detect pathological foci. Similarly there is a limit to identify whether the degeneration changes are normal aging or a pain generator on CT scan. Bone SPECT/CT provides information about anatomical abnormalities by CT with functional outcome detected by SPECT. Thus, bone SPECT/CT could be a useful screening method to rule out SIJ arthritis or SIF after instrumented lumbar fusion.



**Figure 1:** **A:** Plain radiograph showing anterior listhesis of adjacent segments after L4-5-S1 instrumented fusion. **B:** Axial bone SPECT/CT scan demonstrates increased activity of the SIJ and the adjacent segments and, implying sacroiliitis and adjacent segment pathology, respectively. **C and D:** Coronal bone SPECT/CT scan demonstrates increased activity at SIJ.



**Figure 2:** **A:** Plain radiograph showing collapse of the adjacent segments after L4-5-S1 instrumented fusion. Coronal (**B**) and axial (**C**) bone SPECT/CT scans showing bilateral sacrum insufficiency fracture. CT (**D**) and MRI (**E**) showing sacral fracture.

## THE INFLUENCE OF HISTOLOGIC SUBTYPE IN PREDICTING SURVIVAL OF LUNG CANCER PATIENTS WITH SPINAL METASTASES

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### Summary of Background Data:

Recent advancements in systemic treatment of lung cancer have significantly improved the survival of patients with certain histopathologic and molecular subtypes. Existing prognostic scores do not account for this and patients with lung cancer spinal metastases are grouped together as poor prognostic candidates, and consequently, some may inappropriately be denied palliative spine surgery.

### Objective:

The objective of the study was to study whether the expected survival in patients with lung cancer spinal metastases is affected by histopathologic and molecular subtypes in the context of modern systemic therapy.

### Materials and Methods:

We retrospectively reviewed all patients with histologically confirmed lung cancer treated for spinal metastases at our institution between 2001 and 2012. Patients' demographics, histopathologic details, treatment modalities, and survival data were collected. The primary outcome was survival from time of spinal metastases diagnosis. The Cox regression analysis was used to evaluate the influence of tumor histology, molecular profile and treatment modality on survival. The Kaplan-Meier survival analysis was conducted to compare lung cancer subtypes, as well as various treatment regimens.

### Results:

Out of 180 patients, 51 underwent surgery for spinal metastases. Female sex ( $P=0.019$ ), absence of palsy ( $P=0.023$ ), good Karnofsky performance scores ( $P<0.001$ ), and non-small cell lung cancer (NSCLC) ( $P=0.002$ ) were favorable prognostic factors. Patients who received systemic therapy, including tyrosine kinase inhibitors, platinum doublet chemotherapy, or both showed increased survival ( $P<0.01$ ). The median survival time was 2.40 months [95% confidence interval (CI), 2.13–2.68] in the small cell lung cancer cohort, with no patients surviving past a year; 5.10 months (95% CI, 3.78–6.41) in the NSCLC cohort, with 25.9% 1-year survival; and 13.3 months (95% CI, 2.26–24.40) in adenocarcinoma patients who received both tyrosine kinase inhibitors and platinum doublet therapy, with 50.0% 1-year survival.

### Discussion & Conclusions:

NSCLC, systemic therapy, female sex, absence of palsy and good Karnofsky performance scores are all independent favorable prognostic factors for patients with lung cancer spinal metastases. These should be routinely considered during prognostication.

**Key Words:** spine metastases, lung cancer, tyrosine kinase inhibitors, epidermal growth receptor factor, survival, prognosis, non-small cell lung cancer



## RELATION BETWEEN RESIDUAL LOW BACK PAIN AND LOCAL/GLOBAL SPINAL ALIGNMENT IN OSTEOPOROTIC VERTEBRAL COMPRESSION FRACTURE

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### Introduction

Patients with osteoporotic vertebral compression fracture (OVCF) remain to have low back pain even after a solid union is achieved. This study aimed to determine the risk factors affecting disability related to residual low back pain (LBP) including global spinal alignment and local kyphosis caused by OVCF.

### Methods

Forty-nine consecutive patients who were treated non-operatively for a single-level thoracolumbar fresh OVCF were enrolled in this study. The same treatment protocol except pharmaceuticals was applied; random assignment of weekly 35mg alendronate (BP) or daily 20 micrograms of teriparatide (TPD). Disability related to LBP was measured using Oswestry Disability Index (ODI). Disability related to residual LBP was defined as over 40% of ODI at six months after injury. Radiographic assessment was performed using an upright whole spine radiograph at six months after injury. Union status was assessed by three independent observers at six months after the treatment using flexion-extension radiography and CT. Multivariate logistic regression analysis was performed to determine the risk for disability regarding age (<75 or ≥75 years), gender, pre-existing vertebral fracture, union status, vertebral kyphosis (<25 or ≥25 degrees), PT (<20 or ≥20 degrees), PI-LL (<20 or ≥20 degrees), and anterior deviation of SVA (<5 or ≥5cm).

### Results

Fourteen patients had disability related to residual low back pain (Disability group), and thirty-five did not have disability (Non-disability group). The union rate was 50% in disability group and 82% in non-disability group (P=0.031). Vertebral kyphosis was 26.3 degrees versus 19.4 degrees (P=0.012). Differences were not significant in PT (26.5 degree vs 21.5 degree, P=0.094), PI-LL (27.1 degree vs 19.2 degree, P=0.084), and anterior deviation of SVA (7.3 cm vs 4.8 cm, P=0.134). Logistic regression analysis showed that vertebral kyphosis over 25 degree significantly affected for disability from residual LBP (odds ratio; 8.07 (95%CI: 1.49-59.7), P=0.015). However, other spinopelvic parameters did not show significant risk for disability related to residual LBP.

### Discussion

Recent low back pain researches are gaining interest in global spinal mal-alignment. In osteoporotic vertebral compression fracture, the current study showed that localized pain due to vertebral kyphosis and non-union is more related to disability rather than global spinal mal-alignment.

## FACTORS INFLUENCING ADHERENCE TO NON-SURGICAL TREATMENT FOR INDIVIDUALS WITH LUMBAR SPINAL STENOSIS: A QUALITATIVE STUDY

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**INTRODUCTION:** Lumbar spinal stenosis (LSS) is a highly prevalent disease in older adults that causes significant limitations in walking and other daily activities. There is a lack of research into optimal nonsurgical treatment approaches for LSS. The purpose of this qualitative study is to assess the opinions of participants in a randomized clinical trial (RCT) of non-surgical LSS treatments about the study interventions and their general experiences living with LSS. The three treatment arms in the RCT were: usual medical care, community-based group exercise, and clinic-based manual therapy and individualized exercise.

**METHODS:** Fifty participants (28 female, mean age 73 ± 7.7 years) from the RCT attended one of six focus groups. Each focus group consisted of participants from one arm of the study (two focus groups per arm). Discussion topics included: perceived effectiveness of the assigned treatment, suggestions for improvement, barriers and facilitators to completing treatment, and opinions of research outcome measures. All discussions transcribed verbatim and imported into ATLAS.ti qualitative data analysis software. Transcriptions were coded separately by two researchers, and themes were identified.

**RESULTS:** Several themes were evident across all treatment groups. First, patients prefer individualized treatment that is tailored to their specific impairments and functional limitations. They also want to learn self-management strategies to rely less upon formal health care providers. Participants consistently stated that exercise improved their pain levels and physical function. However, they noted that these effects are temporary, so commitment to exercising long-term is important. Common barriers to completing the assigned LSS treatment included transportation barriers and other comorbid health conditions. All three treatment groups cited perceived treatment benefit as a strong facilitator to continuing treatment. In addition, the ability of the health care provider to relate to the patient and listen to the patient's concerns was a common facilitator. Within the community-based group exercise treatment arm, most individuals continued group exercise after study completion and social support was often mentioned as a facilitator to continuing treatment. Usual medical care was most often associated with minimal to no effect of treatment.

**DISCUSSION:** Individuals with LSS face barriers to consistently accessing non-surgical treatment, but most are willing to commit to a long-term treatment strategy that includes exercise. Social support from others with LSS and from health care providers with good communication skills facilitate compliance with treatment recommendations. Health care providers treating patients with LSS should individualize care to each patient, spend time listening to their concerns and teach them self-management strategies. Promoting experiences with social support such as group exercise classes and support groups may promote long-term adherence to an active lifestyle.

## A VALIDATION STUDY OF 3D MRI SEQUENCES FOR THE QUALITATIVE AND QUANTITATIVE ASSESSMENT OF LUMBAR SPINAL STENOSIS

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### OBJECTIVE:

MRI plays a pivotal role in the diagnosis and surgical decision-making of lumbar spinal stenosis (LSS). Recent technological advances have permitted the advent of high-resolution 3D isotropic MRI sequences. We hypothesized that the use of these new 3D sequences would have an impact on the qualitative and quantitative assessment of LSS, as compared with traditional 2D axial sequences.

### MATERIALS AND METHODS:

We prospectively included 20 patients with at least one stenotic lumbar spine level. Lumbar spine MRIs were performed on a 3-T system and included the following three T2-weighted sequences: 2D axial turbo spin-echo (TSE), 3D sagittal SPACE with full field of view (FOV), and 3D sagittal SPACE with reduced FOV. 3D isotropic sequences were reformatted in axial oblique planes and compared to the 2D axial sequence considered as the reference standard. Two independent observers measured the cross-sectional area (CSA) of the bony spinal canal from L1 to L5, and the cerebrospinal fluid (CSF)/rootlets ratio at all pedicle and disc levels, using a semiautomated quantitative method. They also assessed the morphology of the neural content of the thecal sac at all pedicle and disc levels using the A-D grading system (1).

### RESULTS:

There were no significant differences in CSAs between 3D and 2D sequences at all disc levels ( $p=0.293$ ). CSF/rootlets ratios were significantly smaller in 3D full FOV than 2D sequences ( $p=0.028$ ), while they were comparable between 3D reduced FOV and 2D sequences ( $p=0.056$ ). The overall agreement between 3D and 2D sequences was almost perfect ( $\kappa=0.851$ ). However, the total number of grades C and D was significantly higher with the 3D reduced FOV sequence ( $p=0.001$ ). There were significant negative linear correlations between qualitative grades and CSF/rootlets ratios at all disc levels ( $p=0.021$ ).

### CONCLUSION:

New high-resolution 3D isotropic MRI sequences with reduced FOV are comparable to 2D axial sequences for the quantitative measurements of CSAs and rootlets/CSF ratios, even though higher numbers of severely stenotic levels was found using the 3D technique. Better slice orientation and thinner slices with the 3D sequences may account for this finding. It is therefore possible that 3D MRI sequences mirror better the neural content in LSS cases. Further research and comparison with CT myelography is warranted in order to confirm the above findings.

1. Qualitative grading of severity of lumbar spinal stenosis based on the morphology of the dural sac on magnetic resonance images. Schizas C1, Theumann N, Burn A, Tansey R, Wardlaw D, Smith FW, Kulik G. Spine (Phila Pa 1976). 2010 Oct 1;35(21):1919-24

## EXTRA FORAMINAL SELECTIVE NERVE ROOT BLOCK - A NOVEL TECHNIQUE FOR MANAGEMENT OF LUMBAR RADICULOPATHY.

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### INTRODUCTION

Selective nerve root blocks (SNRB) play an important role in diagnosis and management of lumbar radiculopathy. The transforaminal approach is popularly used for performing SNRB. But this approach involves frequent change of image intensifier from antero-posterior to lateral views and also provocation of pain by pricking the nerve root with spinal needle, which has risk of nerve root injury. Also in cases of severe foraminal stenosis, therapeutic transforaminal SNRB is difficult. We describe a technically simple and safer extra-foraminal approach for selective lumbar nerve root injection and evaluate its clinical efficacy.

### METHODS

112 individuals with lumbar nerve root radiculopathy of spinal origin formed the study group. Visual analogue scale (VAS) scores were obtained before injection, 30 minutes, 3 weeks and 3 months after the injection. Similarly, Oswestry Disability Index (ODI) at pre-injection and after 3 months were obtained and compared. *Technique:* In prone position, under image intensifier, the notch between pars and base of transverse process on the effected side was targeted by 23G spinal needle. The needle is slowly advanced until a bony contact was encountered at the notch and then needle is tilted into the soft tissue by sliding on the pars laterally to reach the extra-foraminal area of the nerve root. 1ml of contrast material made from salts of diatrizoic acid was injected until a radiculogram/ peri-neuro-sheathogram of the root was obtained. Subsequently 1ml bupivacaine 0.5% along with 80mg methylprednisolone acetate is injected on to the nerve root.

### RESULTS:

**There were no side effects specific to the injection procedure. None of the patient needed to be converted to the traditional transforaminal approach.** Pre block VAS score was  $7.6 \pm 1.4$ , which was reduced to  $2 \pm 1$  immediately after the injection, and the VAS at final follow-up was  $3.6 \pm 1$ . Similarly, ODI score was found to significantly reduce from  $68 \pm 17$  to  $37 \pm 12$  at 3 months. The entire procedure was carried out in the AP imaging without changing the position image intensifier.

### DISCUSSION

The described extraforaminal approach for nerve root injection was found to be safe, reliable and clinically effective. As this technique utilises familiar bony landmark in the AP projection, it can be easily adopted in day-to-day practice.

## TRANS-LATERAL RECESS VERSUS PARAMEDIAN INTERLAMINAR EPIDURAL INJECTION FOR LUMBAR DEGENERATIVE DISC DISEASE

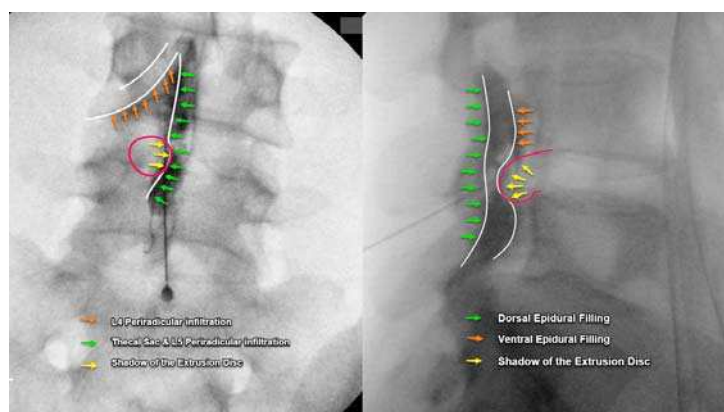
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**Introduction:** Epidural injections are one of most common conservative treatments for lumbar degenerative disc disease. The transforaminal (TF) epidural injection have been proposed as not only a target-specific modality, but also significantly advantageous with long-term effectiveness because fulfilling the aim of reaching the primary site of pathology (ventral and lateral epidural space). However, the transforaminal epidurals has been associated with catastrophic complications. Hence, there is a need for other approach with fewer complications for drug delivery in the ventrolateral epidural space. The trans-lateral recess (TRL) approach of epidural injection was regarding a direct approach to the lateral recess and ventral epidural space. We compared the therapeutic efficacy of the TRL approach and paramedian (PM) interlaminar approach. We postulated that the TRL approach may produce a better clinical outcome because of more target specific and better ventrolateral epidural spread of the drug compared with the PM approach.

**Methods:** Seventy-eight patients were randomized to receive fluoroscopically guided epidural injection either through the TRL (n = 40) or PM (n = 38) approach. Patients were evaluated for effective pain relief ( $\geq 50\%$  pain relief from baseline) by visual analogue scale (VAS) for axial back and leg radicular pain, and functional improvement by the Oswestry Disability Index (ODI) at 2 weeks, 4 weeks, 8 weeks, 3 months, and 6 months post-injection. The groups were compared with regard to repeated injection or surgery within 6 months after the initial procedure. Other clinical results measures were overall VAS and ODI, number of injections, and presence of ventral spread and periradicular infiltration.



**Results:** At the 3months follow up, a significantly higher relative success of effective pain relief was noted in the TRL group (relative risk, 3.75; 95% CI, 1.40-8.70). Significant reduction in VAS and improvement in ODI were observed at all time points post-injection compared the baseline ( $P < 0.001$ ) in the TRL group. On average, patients in the TRL group received 1.14 and patients in the PM group received 2.30 procedures during 6 month. Ventral epidural spread and periradicular infiltration was significantly higher in the TRL group. The fluoroscopic time was comparable in both groups. And, no major complications were encountered in either group.

**Discussion:** The ventrolateral epidural filling technique of the TRL epidural injection can be performed more safety and relatively familiar during lumbar interlaminar epidural steroid injection. The clinical results with TRL technique were significantly more effective for axial back and leg radicular pain relief, as well as, improvement in disability than the PM approach for 6 months in the management of lumbar degenerative disc disease.

## PREVALENCE AND CHARACTERISTICS OF SACROILIAC JOINT PAIN IN HIGH SCHOOL BASEBALL PLAYERS

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**Introduction:** Sacroiliac joint (SIJ) pain is a potential source of low back pain in athletes. However, the prevalence and characteristics of this condition have not been well studied. We hypothesized that baseball players, especially pitchers are more likely to be affected by SIJ pain compared with other athletes because of the combination of axial loading and abrupt rotation of the SIJ in the throwing motion. The purpose of this study was to investigate the prevalence and clinical characteristics of SIJ pain among high school baseball players.

**Materials and Methods:** Participants comprised 891 high school baseball players (215 pitchers, 676 fielders; mean age, 16.1 years; range, 15-17 years) who had participated in annual medical evaluations (a self-completed questionnaire and physical examination). Our study criteria defined "SIJ pain" as fulfilling the following two conditions: 1) tenderness of the SIJ; and 2) low back and/or buttock pain during the provocative Gaenslen or Patrick test. The prevalence of SIJ pain and its associations to physical function measurements (finger-floor-distance (FFD), single-leg-raising (SLR) angle, heel-buttock-distance (HBD), Thomas test, and hip joint range of motion (ROM)) were investigated. Presence of low back pain was also investigated using the questionnaire. Wilcoxon and chi-square tests were used for statistical analyses.

**Results** The prevalence of low back pain was 35.7% in all subjects. Tenderness of the SIJ and positive results for the Gaenslen and Patrick tests were confirmed in 142 (16.0%), 19 (2.2%) and 42 (4.7%) subjects, respectively. Accordingly, 22 subjects (2.5%) met the criteria for SIJ pain. Prevalence of SIJ pain was significantly higher in pitchers than in other fielders (4.9% vs 2.1%,  $p=0.044$ ). With regard to the side on which SIJ pain occurred, 30% of subjects showed bilateral symptoms, with a more common occurrence in the throwing arm side (55%) than in the non-throwing arm side (15%). The prevalence of SIJ pain as a source of low back pain has been estimated at 8.9%. The prevalence of a positive Thomas test and limitation of hip internal or external rotation ( $<30^\circ$  degrees each) on the throwing arm side were also significantly higher in subjects with SIJ pain than in those without ( $p=0.0205$ ,  $p=0.0037$ ,  $p=0.0172$ , respectively).

**Conclusion:** According to our criteria, the prevalence of SIJ pain among high school baseball players was 2.5%. The prevalence of SIJ pain as a source of low back pain has been estimated at 8.9%. SIJ pain was more frequent among pitchers and on the throwing arm side. Limitation of extension and rotation of the hip joint might have an influence on the development of ipsilateral SIJ pain.

## PSYCHOLOGICAL STRESS RESPONSE IN RELATION TO MUSCULOSKELETAL PAIN IN HIGH SCHOOL BASEBALL PLAYERS

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**Introduction:** Several musculoskeletal injuries could induce not only pain but also loss of performance in high school baseball players, and it could be one of the causes of psychological stress response. However, the association between these musculoskeletal disorders and psychological stress response remains unknown. The purpose of this study was to assess the relationship between psychological stress response and musculoskeletal pains (shoulder, elbow, wrist and low back) in high school baseball players.

**Materials and Methods:** Participants comprised 1172 high school baseball players (270 pitchers and 902 fielders; mean age, 16.1 years; range, 15-17 years) who had participated in annual medical evaluations (a self-completed questionnaire and a physical examination). Experience of shoulder, elbow, wrist and low back pain during the season were investigated. Severities of pain were grading from one to three (1: playing without disability 2: playing with a little disability due to pain, 3: playing with a strong disability due to pain). The stress response was measured using the Stress Response Scale-18 (SRS-18). The SRS-18 rates the extent of the stress response on a four-point Likert scale, where 0 represents "no stress at all" and 3 represents "high stress." The prevalence of shoulder, elbow, wrist and low back pain at grade 3 of severity of pain and its association to psychological stress response at grade 3 were investigated. Chi-square tests were used for statistical analyses.

**Results:** There was no significant association between shoulder (23.4%), elbow (22.8%), wrist (12.4%) and low back pain (26.2%) and psychological stress responses in the fielders. On the other hand, in the pitcher, the players with elbow (26.7%) or low back pain (22.0%) had experienced significantly higher psychological stress responses compared with those without ( $p=0.0363$ ,  $p=0.0379$ , respectively). The pitcher with elbow pain had experienced significantly higher response at the "irritability-anger" subscales of SRS-18 and the pitcher with low back pain has significantly higher response at the "depression-anxiety" subscales of SRS-18 ( $p=0.0162$ ,  $p=0.0022$ , respectively).

**Conclusion:** Elbow and low back pain could cause stronger psychological stress responses compared with other musculoskeletal pains in high school baseball pitchers and psychological support might be needed for them.

## CHARACTERIZING THE COURSE OF LOW BACK PAIN AFTER OSTEOPOROTIC VERTEBRAL FRACTURE: A HIERARCHICAL CLUSTER ANALYSIS OF THE PROSPECTIVE COHORT STUDY

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**Introduction:** Understanding the natural course of low back pain is important for clinicians to decide the most appropriate treatment strategy. We used latent class analysis to identify the classes of time course of low back pain after osteoporotic vertebral fractures (OVFs) and risk factors associated with persistent pain.

**Methods:** This multicenter cohort study was carried out from 2012–2015. A total of 218 consecutive patients with  $\leq 2$  weeks-old OVFs were enrolled in 11 institutions. Assessment of visual analog scale (VAS) for low back pain (LBP), plain x-rays were performed at the time of enrollment and at 1-, 3-, and 6-month follow-ups. The angular motion of the fractured vertebral body was measured between the supine and the weight-bearing positions. The VAS for months 1-6 after OVF was then used to characterize groups of subjects, using hierarchical cluster analysis.

**Results:** Hierarchical cluster analysis was performed by using pain intensity scores for 128 patients. Analysis yielded four clusters representing different pathways of back pain. Cluster 1 (“average”;  $n=65$ , 50.8%) patients had stable, mild pain. Cluster 2 (“excellent”;  $n=27$ , 21.1%) patients started with low level pain, progressing quickly to no pain. For patient in Cluster 3 (“fluctuating”;  $n=14$ , 10.9%), moderate low back pain improved at early phase but exacerbated after 3 months. Cluster 4 (“persistent severe”;  $n=22$ , 17.2%) patients had persistent high pain. At the point of distinctive patterns for each cluster, patients in cluster 4 showed significant higher number of previous VFs and degree of angular instability for months 1-6 after the baseline ( $p < 0.001$ ). Patients in cluster 4 tend to lack of regular exercise, high body mass index and high baseline pain intensity. On the other hand, patients in cluster 2 showed significant lower baseline VAS and lower angular instability for months 1-6 after the baseline ( $p < 0.001$ ).

**Discussion:** We identified 4 distinct groups of OVF patients with different pathways in the course of low back pain intensity and significant differences regarding a range of other important variables. Understanding the course of low back pain after OVF may help in the management and contribute to future trials of treatment.



## EFFECT OF EXERCISE USING AN INNOVATIVE DEVICE FOR THE ABDOMINAL TRUNK MUSCLES IN PATIENTS WITH CHRONIC LOW BACK PAIN

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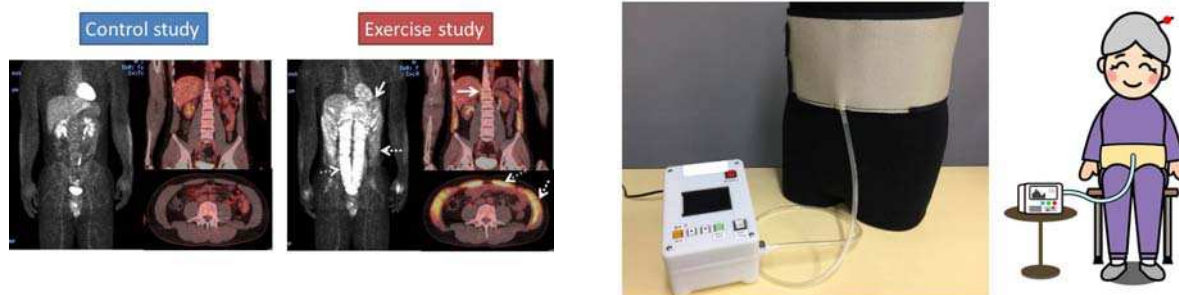
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**Introduction:** Chronic nonspecific low back pain (LBP) and associated disability impose a health and economic burden on society. Trunk muscle exercises are often recommended as the first choice of treatment. However, performing the exercises is often difficult for chronic LBP patients, especially older adults, because of muscle weakness or an increase in LBP during the exercises. We developed an innovative exercise device for abdominal trunk muscles with a built-in measurement system for muscle strength. This device enables patients to perform abdominal trunk muscle exercises in a sitting or standing position without requiring movement of the painful lower back. It has a built-in measurement system for abdominal trunk muscle strength. We investigated whether positron emission tomography (PET) can evaluate the activity of abdominal trunk muscles during exercise using our device, in addition to the effects of the exercise.

**Methods:** The device has a design similar to that of a sphygmomanometer, with an inflatable cuff and a mechanical manometer to measure pressure. The cuff is placed around the subject's abdomen, and then pressure is gradually applied on the abdominal wall. For measurement, a subject exerts abdominal muscle contraction as much as possible, and then the mechanical manometer calculates a pressure value that subtracts the baseline pressure from the peak pressure as a value of muscle strength. For the exercise, a subject contracts the muscle against the abdominal wall intermittently or continually. Six healthy male volunteers underwent two PET series consisting of examinations without exercise (control study) and with exercise (exercise study). In the control study, subjects remained in a sitting position for 20 minutes, and <sup>18</sup>F-fluorodeoxyglucose (FDG) was intravenously injected. Before the exercise study, subjects exercised using the device for 20 minutes per set, 2 sets per week for 5 weeks. On the measurement day, subjects exercised for 20 minutes, followed by injection of FDG, then exercised again for 20 minutes. PET-computed tomography images were obtained 60 minutes after FDG injection in each study. We compared differences between control and exercise skeletal muscle metabolic activity using a standardized uptake value. We also compared abdominal trunk muscle strength measured by the device before and after the pre-test exercise.

**Results:** In the exercise study, FDG uptake in the diaphragm, rectus abdominis, external and internal oblique, transverse abdominal, and levator ani muscles, all of which stabilize the lumbar spine, was significantly greater than uptake in the control study. The mean value of abdominal trunk muscle strength after the pre-test exercise was  $26.5 \pm 5.3$  kPa, which was significantly higher than the value before the exercise,  $19.5 \pm 3.9$  kPa.

**Conclusion:** The results indicate that exercise using our innovative device can strengthen the abdominal trunk muscles that stabilize the lumbar spine.



## METABOLIC SYNDROME AFFECTS ACCUMULATION OF LUMBAR EPIDURAL FAT

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**Introduction:** Amounts of lumbar epidural fat (LEF) vary, and excess LEF sometimes lead to spinal cord or nerve root compression, however, factors associated with increase in LEF is unclear. The aim of this study was to clarify the factors which affect accumulation of LEF.

**Methods:** 278 participants who underwent a medical checkup for musculoskeletal evaluation between July 2012 and March 2016 were retrospectively reviewed. The participants included 143 men and 135 women with a mean age of 63.9 years. The cross-sectional areas of epidural fat (EF) and the spinal canal (SC) at each level were measured in axial views of lumbar MRI, and the proportion of EF (EF/SC) was calculated. The correlations of average EF/SC from L1/2 to L4/5 with age, body mass index (BMI), abdominal circumference, body fat percentage, visceral fat, serum adiponectin, triglycerides (TG), high- and low-density lipoprotein (HDL and LDL, respectively), and insulin resistance (HOMA-IR) were estimated. Participants were stratified by the presence or absence of metabolic syndrome, and between-group differences in average EF/SC were compared. Metabolic syndrome was defined as central obesity, i.e., abdominal circumference  $\geq 90$  cm in men and  $\geq 85$  cm in women, coupled with any two of the following: 1) TG  $\geq 150$  mg/dl and/or HDL  $< 40$  mg/dl, 2) systolic BP  $\geq 130$  mmHg and/or diastolic BP  $\geq 85$  mmHg, and 3) fasting plasma glucose  $\geq 110$ mg/dl.

**Results:** EF/SC was higher in men than in women at every level and highest at L3/4. Average EF/SC was significantly correlated with BMI ( $r = 0.36$ ,  $p < 0.0001$ ), abdominal circumference ( $r = 0.32$ ,  $p < 0.0001$ ), and visceral fat ( $r = 0.31$ ,  $p < 0.0001$ ), but not age ( $r = 0.10$ ), body fat percentage ( $r = 0.12$ ), HOMA-IR ( $r = 0.18$ ), serum adiponectin ( $r = -0.16$ ), HDL ( $r = -0.18$ ), LDL ( $r = 0.03$ ), or TG ( $r = 0.19$ ). Average EF/SC was significantly higher ( $p < 0.0001$ ) in patients with metabolic syndrome ( $n = 47$ , 16.9%) than in those without metabolic syndrome ( $n = 231$ , 73.1%).

**Discussion:** Previous reports found that lumbar epidural lipomatosis, characterized by an abnormal accumulation of LEF, is more common in men than in women and related to obesity. In these study participants, LEF accumulation was also greater in men than in women and correlated with BMI. Furthermore, we found that metabolic syndrome was associated with the amount of LEF. Although excess fat associated with metabolic syndrome is known to induce migration of immune cells and promote systemic inflammation, the clinical and pathological significance of LEF remains unclear. Our results indicate that LEF may have effects similar to those of visceral fat. Although further study is needed, these results provide important insight into the characteristics of LEF.

## WHO CONTRIBUTED THE MOST TO THE SPINE SURGERY LITERATURE ? : PUBLICATION RATES OF THE ABSTRACTS PRESENTED AT THE ANNUAL MEETINGS OF THE NORTH AMERICAN SPINE SOCIETY BETWEEN 2009 AND 2012

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Introduction Publication rate of the abstracts presented at the international spine meetings is the recent point of interest. Previous studies have reported the publication rates of the abstracts presented at different international spine meetings. However, most of those studies did not compare the contribution of different specialties to the literature. In this study, we retrospectively analyzed previous annual meetings of the North American Spine Society (NASS) to understand who contributed the most to the field of spine surgery.

Table 1. Departments publishing oral presentations

Specialty	2009	2010	2011	2012	Total
Neurosurgery	24-24%	25-22%	21-16%	25-23%	95-21%
Orthopaedics	65-65%	74-65%	83-65%	67-60%	289-64%
PMR=PT	3-3%	7-6%	0-0%	3-3%	13-3%
Basic science	5-5%	5-4%	9-7%	9-8%	28-6%
Other	3-3%	3-3%	15-12%	7-6%	28-6%
Total	100	114	128	111	453

Table 2. Departments publishing posters

Specialty	2009	2010	2011	2012	Toplam
Neurosurgery	6-11%	5-13%	11-18%	15-23%	37-17%
Orthopaedics	35-64%	32-82%	39-64%	40-63%	146-67%
PMR=PT	3-5%	1-2,5%	0-0%	0-0%	4-2%
Basic science	5-9%	1-2,5%	7-11%	7-11%	20-9%
Other	6-11%	0-0%	4-7%	2-3%	12-5%
Total	55	39	61	64	219

Table 3. Departments publishing oral presentations and posters

Specialty	2009	2010	2011	2012	Total
Neurosurgery	30-19%	30-20%	32-17%	40-23%	132-20%
Orthopaedics	100-65%	106-69%	122-65%	107-61%	435-65%
PMR=PT	6-4%	8-5%	0-0%	3-2%	17-2%
Basic science	10-6%	6-4%	16-8%	16-9%	48-7%
Other	9-6%	3-2%	19-10%	9-5%	40-6%
Total	155	153	189	175	672

Table 4. Continents publishing their abstracts

Continents	2009		2010		2011		2012		Toplam	
	OP	Poster	OP	Poster	OP	Poster	OP	Poster	OP	Poster
Asia	12	2	18	6	22	12	7	17	59	37
Europe	6	2	11	4	8	6	6	8	31	20
North America	80	51	85	25	95	41	97	39	357	156
South America	1	0	0	2	2	1	0	0	3	3
Oceania	1	0	0	1	1	1	1	0	3	2
Africa	0	0	0	1	0	0	0	0	0	1
Total	100	55	114	39	128	61	111	64	453	219

Methods We retrieved 1416 abstracts (oral presentations and posters) from the corresponding published conference proceedings of NASS between 2009 and 2012. The abstract titles and contributing author names were searched using Pubmed/MEDLINE and Google Scholar engines. For each published abstract, we compared the content of the presented abstract in the proceedings with that of the published abstract in journals. For published abstracts, field of specialty and continent of the contributing authors were analyzed.

Results Publication rate of the abstracts presented at the annual meetings of NASS between 2009-2012 was 47%. Publication rate of oral presentation was significantly higher than that of posters (52% vs. 40%, p<0.0001). Among published abstracts (n: 672) 76% were from North America, 14% were from Asia, 8% were from Europe, and 2% were from other continents. The most contributing specialty to the spine surgery literature was Orthopedic Surgery, followed by Neurosurgery (67% vs. 17%) (Tables 1-4).

Discussion The publication rate of the abstracts presented at the annual meetings of NASS between 2009-2012 is higher comparable to the other international scientific meetings in the field of spine surgery. Orthopedic surgery has accomplished the publication process the most. Our further studies are in process to understand the underlying factors of this situation.

## EVALUATION OF LUMBAR PARASPINAL MUSCLE ATROPHY IN PATIENTS WITH SARCOPENIA

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**Introduction:** Sarcopenia is characterized by the loss of skeletal muscle mass and function with a risk of adverse outcomes, such as physical disability and poor quality of life. It has been reported that the quantity and quality of the lumbar paraspinal muscle could influence sagittal balance of the spine or postoperative proximal junctional kyphosis (PJK). However, the relationship between sarcopenia and lumbar paraspinal muscle atrophy remains unclear.

**Aim:** The aim of this study was to clarify factors associated with lumbar paraspinal muscle size and evaluate lumbar paraspinal muscle atrophy in patients with sarcopenia.

**Methods:** We retrospectively reviewed 278 participants (143 men and 135 women) who underwent a medical checkup for musculoskeletal evaluation between July 2012 and March 2016. The mean age of the participants was 63.9 years. The cross-sectional area of the bilateral paraspinal muscles at the navel level (PM) was measured in the axial view of CT images. Correlations of PM with age, body mass index (BMI), bone mineral density (BMD), grasping power (GP), lean body mass of the extremities measured using dual energy X-ray (LBM), and skeletal mass index (SMI) were estimated in men and women. Participants were stratified according to the presence or absence of sarcopenia, and the between-group differences in PM were compared. Sarcopenia was defined according to the Japanese diagnostic criteria (SMI < 6.87 kg/m<sup>2</sup> in men and SMI < 5.46 kg/m<sup>2</sup> in women). A p value <0.05 was considered to indicate statistical significance.

**Results:** PM was significantly higher in men (37.3 cm<sup>2</sup>) than in women (23.1 cm<sup>2</sup>). In men, PM was significantly correlated with age ( $r = -0.55$ ), GP ( $r = 0.51$ ), LBM ( $r = 0.63$ ), and SMI ( $r = 0.52$ ), but not with BMI ( $r = 0.19$ ) or BMD ( $r = 0.18$ ). In women, it was significantly correlated with age ( $r = -0.63$ ), BMD ( $r = 0.46$ ), GP ( $r = 0.39$ ), and LBM ( $r = 0.41$ ), but not with BMI ( $r = 0.17$ ) or SMI ( $r = 0.16$ ). Furthermore, in men, PM was remarkably lower among patients with sarcopenia (29.9 cm<sup>2</sup>,  $n = 20$ , 13.7%) than among those without sarcopenia (38.5 cm<sup>2</sup>,  $n = 123$ , 86.3%;  $p = 0.0002$ ). In women, PM tended to be lower among patients with sarcopenia (19.8 cm<sup>2</sup>,  $n = 16$ , 11.9%) than among those without sarcopenia (23.6 cm<sup>2</sup>,  $n = 119$ , 88.1%;  $p = 0.058$ ).

**Discussion:** In both men and women, the lumbar paraspinal muscle size was associated with age, GP, and LBM. Moreover, our results indicate that male patients with sarcopenia have the low lumbar paraspinal muscle size. Park, et al. reported a high prevalence of sarcopenia in patients with degenerative lumbar spinal stenosis and highlighted its negative effect on clinical outcomes (1). Moreover, Jun et al. found that thoracolumbar muscularity was lower in patients with PJK than in those without PJK before surgery (2). Therefore, these observations indicate that the presence of sarcopenia should be estimated for treating patients with degenerative spinal disorders.

1. Park, et al. Bone Joint J. 2016 98-B:1093-8.
2. Jun, et al. Neurosurgery. 2016 [Epub ahead of print]

## PRE-TREATMENT GOAL CLARITY: VALIDITY AND ASSOCIATION WITH REHABILITATION OUTCOMES FOR PEOPLE DISABLED BY CHRONIC LOW BACK PAIN

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**INTRODUCTION:** Prior studies of patients disabled by chronic low back pain (CLBP) graduating from multidisciplinary rehabilitation programs have shown that patients' long-term satisfaction depends significantly on the degree to which their personal functional recovery goals have been achieved. Our experience with CLBP patients in rehabilitation suggests that the clearer the patients' goals, the more likely they are to achieve their goals and be satisfied with their outcomes.

**METHODS:** The clarity of narrative pre-treatment work(W), recreation(REC) and daily activity(DA) goals of 100 consecutive CLBP patients completing a functional restoration program and one-year survey follow-up was rated on a 5-point scale by four blinded clinicians (MD, PT, OT and MSW), and inter-rater reliability was assessed by Gwet's AC2 and % agreement. Correlations were tested between goal clarity scores and 1-year goal achievement (GA), pain (P), function (SF36-PF) and satisfaction with outcome (SATIS). Correlations were then tested between 1-year goal achievement and P, SF36-PF and SATIS.

**RESULTS:** Correlations and % agreement between the four goal clarity raters were strong for REC (0.768, 91.3) and DA (0.702, 89.5) goals, and were somewhat less so for W (0.536, 85.7). Among the three raters with the most experience in clinical goal assessment, correlations and agreements were stronger: REC (0.821, 93.3), DA (0.784, 92.3) and W (0.653, 88.4). Correlations were weak between goal clarity scores and 1-year goal achievement (W -0.015, REC 0.085, DA -0.066), pain (W 0.018, REC 0.038, DA -0.211), function (W -0.084, REC 0.004, DA -0.156) and satisfaction (W -0.127, REC 0.074, DA 0.019). Goal clarity was not closely associated with initial patient personal and health demographics including gender, age and baseline health state. Strong correlations between goal achievement and 1-year outcomes were consistent with prior studies:

1-year Outcomes	Correlations with Goal Achievement		
	Work Goal	Recreation Goal	Daily Activity Goal
Pain	0.400 (p<0.0001)	0.482 (p<0.0001)	0.509 (p<0.0001)
SF36-PF Scale	0.607 (p<0.0001)	0.752 (p<0.0001)	0.761 (p<0.0001)
Satisfaction with Outcome	0.492 (p<0.0001)	0.768 (p<0.0001)	0.726 (p<0.0001)

**DISCUSSION:** Strong inter-rater reliability supports goal clarity as a reliable pre-treatment assessment tool, and goal achievement again proved strongly associated with patient satisfaction. However, goal clarity did not predict outcomes well. In this study, patients with CLBP and clinical raters had been coached in basic elements of goal setting. Therefore, we recommend that future studies test this goal-setting method in more common clinical situations of uncoached spine and other orthopaedic patients facing treatment decisions with greater disparity in the clarity of their goals.

## CORE MUSCLE WEAKNESS IS THE KEY RISK FACTOR OF FUNCTIONAL DISABILITY IN PATIENTS WITH DEGENERATIVE LUMBAR DISEASE

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**Introduction** Loss of muscle mass and muscle weakness with aging have been documented in many studies. These changes can affect physical function, balance and falls in seniors. Because of annoying chronic back pain, leg pain and claudication, patients with degenerative lumbar spinal disease (DLSD), mostly elderly, also have lower physical functional status. Consequently, it might cause vicious circle of muscle weakness. However, it is not clear that muscle weakness in which part of the body is most associated with functional disability in DLSD. Therefore, in this study, we aimed to evaluate relationships between muscle strength in the body and functional disability in patients with DLSD.

**Method** Cross-sectional study was performed. A total of 67 female patients over 50 years old were enrolled, who complained chronic low back pain more than 3 months and whose lumbar spine X-ray showed degenerative changes such as disc space narrowing, osteophyte and facet hypertrophy. Their anthropometric data such as BMI, waist circumference and body fat percentage were collected. Oswestry disability index(ODI) survey and timed-up-and-go test (TUGT) were performed for evaluation of physical functional status. Muscle strength was measured in each body portion. Hand grip strength for upper extremity, sit-to-stand test for lower extremity. The core muscle strength was measured by using pressure gauge (Chattanooga Stabilizer Pressure Biofeedback, USA). It was placed behind lumbar area in a supine position and the maximal pressure was measured when the patients extend their trunk until the lumbar lordosis become flat on the floor.

**Result** Muscle strength and capability following age increase

The mean age of the subjects was 67.3±7.7 years old. The core muscle strength showed the strongest negative correlation with age ( $r=-0.46$   $p<0.05$ ). (Figure 1) Sit-to-stand test showed more negative correlation with age than hand grip strength. Also, it was found that high BMI and long waist circumference is correlated with weak core muscle strength.

Relationship of muscle strength with functional disability

The mean of ODI% score and TUGT was 28.7±14.0 and 10.9±3.0 sec, respectively. Core muscle strength only showed negative correlation with both ODI% scores ( $r=-0.38$ ,  $p<0.05$ ) and TUGT ( $r=-0.59$   $p<0.05$ ). (Figure 2) When patients were divided into 3 groups as ODI% score; Group A (ODI%: 0-20), Group B (ODI%: 20-40) and Group C (ODI%: 40-100), core muscle strength showed significantly lower in Group C than Group A by ANOVA ( $p<0.05$ )

**Discussion** The core muscle strength has been spotlighted as one of the important factors influencing not only sports-related activities but also daily-living activities, even in elderly people. In this present study, core muscle strength was getting weaker as age increased and significantly associated with functional disability measured by ODI% scores and TUGT in DLSD patients. With thoracolumbar spine, the core muscle is the key support structure keeping the body stand upright and balanced. Therefore, core muscle strengthening is necessary for better physical function in DLSD patients.

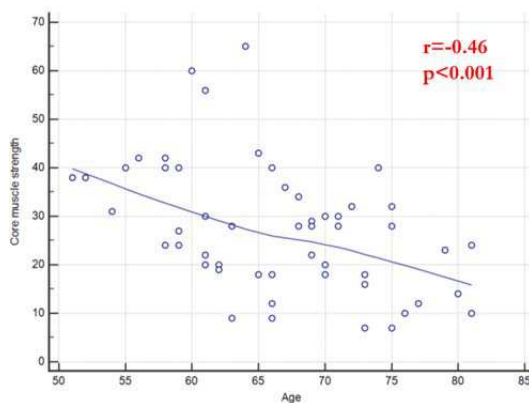


Figure 1. The core muscle strength showed negative correlation with age

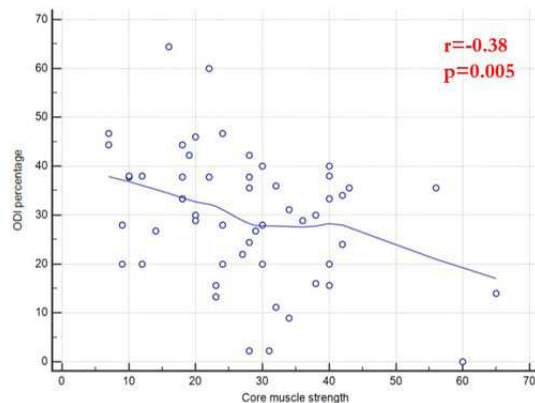


Figure 2. Core muscle strength showed negative correlation with both ODI% scores

## PARTICIPATION OF ORTHOPEDISTS IN HEMATOPOIETIC MALIGNANCIES

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**Introduction:** Hematopoietic malignancies such as multiple myeloma (MM) and malignant lymphoma (ML) sometimes initially present as low back pain, so patients are referred to orthopedists. However, few studies have investigated the physical examination findings and the involvement of orthopedists in diagnosing hematopoietic malignancies.

**Aim:** The object of this study was to investigate the participation of orthopedists in the diagnosis and treatment of hematopoietic malignant disease.

**Methods:** The subjects were 103 patients with MM (47 females and 56 males, average age 72 years) and 288 patients with ML (116 females and 172 males, average age 65 years) from 2004 to 2014 at our hospital. The rates of orthopedic involvement in the initial diagnosis and the correct diagnosis, as well as the chief complaint, diagnostic clues, frequency of skeletal metastases of unknown origin and treatment method were investigated.

**Results:** The rates of orthopedic involvement in the initial diagnosis and a correct diagnosis were 35% and 33% for MM and 5% and 36% for ML. Low back pain was the most frequent reason for visiting an orthopedist (MM: 41%, ML: 43%). The most frequently cited diagnostic clues were hyperproteineuria (46%) in MM and lymph node swelling on computed tomography (37%) in ML. The frequency of skeletal metastases of unknown origin was 13% in MM and 2% in ML. One MM patient underwent occipito-cervical fusion. One ML patient received a biopsy and another laminectomy.

**Discussion:** Most skeletal metastases of unknown origin are reportedly from breast, lung, renal, prostate and hematopoietic malignancies. We found that the frequency of skeletal metastases of unknown origin was 13% in MM and 2% in ML. Orthopedists should bear in mind the possibility of hematopoietic malignancies as a differential diagnosis when encountering skeletal metastases of unknown origin. Our study showed that the orthopedic intervention rates were 35% in MM and 5% in ML. During early diagnostic steady, orthopedists intervene the diagnosis of MM than that of ML. In both MM and ML, low back pain was the most frequently cited reason for visiting an orthopedist (40%). Orthopedists correctly diagnosed MM and ML only 30% of the time. These results show that many orthopedists delayed the diagnosis of MM and ML, which might affect the treatment, prognosis and the palliation of symptoms. This delay might have been due to orthopedists not considering the possibility of hematopoietic malignancies. Therefore, since orthopedists can play a prominent role in the initial diagnosis of MM and ML, they must be aware of the characteristics of these disorders and conducted detailed examinations in order to arrive at an accurate diagnosis. Although this study has several limitations, such as assessment bias associated with its retrospective nature and institutional bias, this study will help clarify the involvement of orthopedists in diagnosing hematopoietic malignancies and encourage orthopedists to consider hematopoietic malignancies in the differential diagnosis of back pain.



## CLINICAL EFFICACY OF PERCUTANEOUS ENDOSCOPIC LUMBAR ANNULOPLASTY AND NUCLEOPLASTY FOR TREATMENT OF PATIENTS WITH DISCOGENIC LOW BACK PAIN

Jung Hwan Lee<sup>1</sup>, Sang-Ho Lee<sup>1</sup>

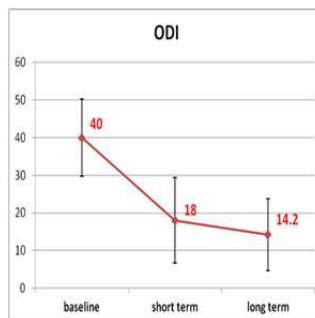
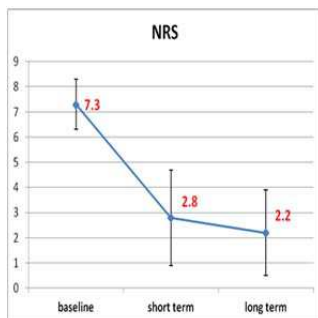
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**Introduction :** Discogenic low back pain (DLBP) caused by internal disc disruption accounts for approximately 40% of chronic low back pain. Conservative managements are performed but are not always successful. Therefore, surgeries such as fusion or disc replacement are considered but they are very invasive and occasionally results in severe complications. Various minimal invasive procedures have been introduced and among them, percutaneous endoscopic lumbar annuloplasty and nucleoplasty (PELAN) enables physicians to approach posterior portion of annulus, and to remove lesion site mechanically under direct visualization by endoscopy. This study was to investigate the clinical efficacy of PELAN to treat the patients with DLBP.

**Methods:** Clinical outcomes of PELAN were investigated in 47 patients diagnosed as DLBP who were refractory to conservative treatments including epidural injection. PELAN was performed using laser and forceps with endoscopy under fluoroscopic guidance. Outcomes were assessed using numeric rating scale (NRS) for back pain, Oswestry disability index(%) (ODI%), and modified MacNab's criteria at short term(2-3weeks) and long term follow up period(at least 12 months). Four patients underwent open surgery due to retractable pain so that 43 patients completed long term follow up.

**Results:** Mean back pain NRS was significantly reduced from  $7.38 \pm 0.87$  at pretreatment to  $2.81 \pm 1.87$  at short term and to  $2.19 \pm 1.74$  at long term follow up. ( $P < .001$ )(Fig.1) Also, mean ODI(%) was significantly improved from  $39.9 \pm 10.3$  at pretreatment to  $18.1 \pm 11.4$  at short term and to  $14.2 \pm 9.62$  at long term follow up. ( $P < .001$ )(Fig.2) In terms of proportion of successful outcomes, 29(61.7%) and 28(59.6%) obtained successful outcomes of NRS and ODI(%) respectively at short term follow up. Thirty-three(70.2%) accomplished successful results of NRS and ODI(%) at long term follow up. With regard to the modified MacNab criteria at short term, the global outcomes were excellent in 6 patients (12.8%), good in 18 patients (38.3%), fair in 17 patients (36.2%), and poor in 6 patients (12.8%). At long term follow up, the results were excellent in 9 patients (19.1%), good in 16 patients (34.0%), fair in 13 patient (27.7%), and poor in 7 patients (14.9%).(Fig.3) Before PELAN, all patients took oral analgesics for pain control. At long term follow up 25(53.2%) did not need analgesics at all. Twenty three(48.9%) patients fulfilled all of these criteria at the same time;  $\geq 50\%$  NRS reduction,  $\geq 40\%$  ODI(%) reduction, Good or Excellent in MacNab criteria, and no need for analgesics.

**Discussion :** PELAN provided favorable clinical outcomes in patients with DLBP who were refractory to conservative treatments. PELAN allowed the physicians to accomplish targeted tissue decompression in the posterior annulus, preserving the healthy disc tissues as much as possible. It mechanically removed pinched nucleus, granulation tissues, or damaged annular tissue as well as effectively reduce compressive force to nociceptors existing in torn annulus and posterior longitudinal ligaments. It could contribute to reduce necessity of extensive surgery including fusion or disc replacement and consequently avoid risk of complication associated with extensive surgery.





## SATISFACTION SCORES AND PATIENT REPORTED OUTCOMES FOLLOWING SPINAL SURGERY AND NON-OPERATIVE CARE.

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2. Canadian Spine Outcomes and Research Network, Toronto, Canada

**Introduction.** To compare patient satisfaction rates to clinical outcomes in two cohorts of patients: 1) one-year follow-up after elective lumbar spine surgery, 2) 3-month follow-up following spine-care physiotherapy and rehabilitation.

**Methods.** The surgery cohort (n=855) was drawn from the Canadian Spine Outcomes and Research Network (CSORN), a registry of 18 spine centres cross Canada. Those who had surgery for degenerative disc disease, disc herniation, spondylolisthesis or spinal stenosis between October 2008 and September 2015 were included. At 1-year follow up, patients were asked three 5-item Likert questions pertaining to satisfaction:

Are you satisfied with the results of your spine surgery? (Overall Satisfaction)

Compared to before your surgery, how do you feel now? (Feeling)

Would you have the same surgery again if you had the same condition? (Repeat)

The physiotherapy cohort (n=11720) was obtained from a clinical database of spine-care patients attending any one of 150 rehabilitation clinics across Canada between January 2008 and December 2011. At 3-month follow up, patients were asked a single 5-item Likert question pertaining to satisfaction: Overall, I am satisfied with the service I received at this clinic.

**Results.** In the surgical cohort, those who had surgery for degenerative disc disease had the least improvement in back pain ( $p<0.04$ ), leg pain ( $p<0.001$ ), disability score ( $p<0.04$ ) and physical component score of the SF-12 ( $p<0.001$ ); however, this group with lower specific measured scores had the same ratings for Overall Satisfaction, Feeling and Repeat surgery as patients undergoing the more successful procedures.

In the Physiotherapy cohort, there were no significant differences in satisfaction rates between those who had  $\geq 20\%$  reduction in pain compared to those with  $<20\%$  reduction in pain. Similarly, there were no significant differences in satisfaction rates between those who had  $\geq 30\%$  improvement in function compared to those with  $<30\%$  improvement.

**Discussion.** Despite recent emphasis on shared decision-making and similar definitions of success between clinicians and patients, high ratings of satisfaction did not equate to significant differences in improvements of pain and functional outcomes.

## DIAGNOSTIC CAPABILITY OF "Spine PainDETECT" TO SCREEN FOR NEUROPATHIC PAIN CAUSED BY SPINAL DISORDERS

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### Introduction

Spinal disorders often include neuropathic pain (NeP). However, using any screening tool to evaluate NeP caused by spinal disorders (NeP-SD) is considered difficult. We developed a tool called Spine PainDETECT (SPDQ) and a short-form SPDQ (SF-SPDQ) to distinguish NeP-SD from other types of pain. The present study aimed to verify the ability of SPDQ and SF-SPDQ to diagnose NeP-SD in general patient population.

### Methods

We recruited 250 patients with NeP-SD (NeP group) and another 250 with nociceptive pain due to joint diseases (NocP group) online. We calculated descriptive statistics for general scores in each group using SPDQ and SF-SPDQ. We also computed the sensitivities and specificities of SPDQ and SF-SPDQ to differentiate these types of pain. Total scores were calculated and preliminary obtained diagnostic criteria for NeP (total score  $\geq 0$ ) and NocP (total score  $< 0$ ) of the SPDQ and SF-SPDQ were used (table).

### Results and Discussion

The SPDQ scores were respectively,  $14.96 \pm 10.83$  and  $2.93 \pm 9.48$  and the SF-SPDQ scores were respectively,  $10.65 \pm 9.96$  and  $-1.64 \pm 9.15$  in the NeP and NocP groups.

The sensitivities of SPDQ and SF-SPDQ were 92.4% and 84.4%, respectively, indicating that both methods were sufficiently sensitive for screening applications. In contrast, the specificities were 38.8% and 61.2% for SPDQ and SF-SPDQ, respectively. Thus, SF-SPDQ was more specific than SPDQ.

### Conclusion

The sensitivities of SPDQ and SF-SPDQ were high, and both could function as screening tools for neuropathic pain in patients with spinal disorders. In addition, specificity was higher for SF-SPDQ than SPDQ, indicating potentially better screening capability.

PainDETECT Questionnaire	Pain course pattern	Radiating pain	Burning	Tingling	Pain by touch	Electric shock-like pain	Pain on cold/hot stimulation	Numbness	Pain by pressure	Constant term
SPDQ weight coefficient	-3	-3	1	2	-2	-3	-3	8	1	1
SF-SPDQ weight coefficient	0	0	0	0	0	-4	0	9	0	-7

## INTERPLAY AMONG PAIN INTENSITY, SLEEP DISTURBANCE AND EMOTION IN PATIENTS WITH NON-SPECIFIC LOW BACK PAIN

Zhaomin Zheng, hua wang, Jianru Wang, Hui Liu, Zemin Li

**Background:** Low back pain (LBP) is the most common orthopedic problem worldwide affecting both younger and older adults. There are several bad consequences of LBP, such as sleep disorder, work leave, disability, depression, anxiety, daily physical function, and poor quality of life. However, the relationship of pain, sleep disturbance and emotional status is conflicting. In this study, we designed to evaluate the prevalence of sleep disturbance in patients with Non-specific LBP(NSLBP), and cross-correlation among sleep disorder, anxiety, depression and pain intensity in patients with NSLBP.

**Methods:** A cross-sectional self-assessment questionnaire survey was carried out in outpatient clinic. Anonymous assessments was used to characterize the presence of NSLBP, Pittsburgh sleep quality index, Visual Analogue Scale, SF-36 form, Oswestry disability index, Beck anxiety inventory and Beck depression inventory. Cross-correlation among the severity of NSLBP and sleep disturbance, anxiety, depression and life quality were evaluated.

**Results:** Patients with NSLBP have higher incidence of sleep disorder, anxiety and depression, higher ODI score than healthy people without LPB ( $P < 0.01$ ). NSLBP patients with sleep disorders have more severe anxiety, depression, increased VAS score and poor daily living ( $P < 0.05$ ). NSLBP patients with anxiety have declined sleep quality, poor daily living, decreased work and social skills, increased LBP severity ( $P < 0.05$ ). NSLBP patients with depression have declined sleep quality, poor daily living, decreased work and social skills ( $P < 0.05$ ). Significant associations were found between the severity of NSLBP and sleep disorders, anxiety and ODI score. Spearman correlation analysis showed that VAS score was significantly correlated with PSQI, BDI, BAI and ODI ( $r=0.093$ ,  $p=0.029$ ;  $r=0.096$ ,  $p=0.024$ ;  $r=0.128$ ,  $p=0.003$ ;  $r=0.126$ ,  $p=0.003$ , respectively). PSQI was significantly correlated with BDI, BAI and ODI ( $r=0.317$ ,  $p<0.01$ ;  $r=0.276$ ,  $p < 0.01$ ;  $r=0.330$ ,  $p<0.01$ , respectively). BDI was significantly correlated with BAI and ODI ( $r=0.136$ ,  $p=0.001$ ;  $r=0.122$ ,  $p= 0.004$ , respectively). BAI and ODI were also significantly correlated ( $r=0.149$ ,  $p<0.01$ ).

**Conclusion:** Psychological and social factors play an important role in the development of NSLBP. NSLBP lead to sleep disorder, which decrease the sleep quality and increase the unpleasant emotions and memories in return, these can exacerbate the severity of LBP, the cycle repeat again to form a vicious cycle.

## THE TRACTION SPUR IS ASSOCIATED WITH INTERVERTEBRAL VACUUM PHENOMENON AND MODIC CHANGE

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**Introduction** Traction spurs, described as indicators of spinal segmental instability by Macnub, are well-documented. Although intervertebral vacuum phenomenon and Modic change have also been regarded as indicators of spinal instability, few studies have investigated the relationship between traction spurs and intervertebral vacuum phenomenon and Modic change. We evaluated the association between traction spurs and spinal instability.

**Methods** This study included 105 adult patients with 489 intervertebral spaces (60 males, 45 females; mean age, 67 years) who had undergone lumbar spine surgery at our institution. Patients with vertebral fracture (n=17), infection (n=10), lumber fusion (n=8) and inadequate images (n=12) were excluded. The degree of lumbago was assessed using the Numerical Rating Scale (NRS). Radiographs of the lateral lumbar spine were taken in the following positions: neutral, flexion, extension, supine and sitting. The disc height (DH), slip angle (SA) and slip distance (SD) were measured from these radiographs. The anterior vertebral osteophytes and vacuum phenomenon (VP) were evaluated based on the computed tomography findings, and the type of Modic change (MC) was evaluated based on the magnetic resonance imaging (MRI) findings. According to Kasai's classification, anterior spurs were classified as No spur, claw spur or traction spur. The correlations between the parameters were evaluated by a one-way analysis of variance and the chi-squared test. A p-value of <0.05 was considered to indicate statistical significance.

**Results** With regard to the breakdown of the anterior vertebral osteophytes, no spur was noted in 36%, claw spur in 21% and traction spur in 38%. The change in the DH from the supine to the sitting position was significantly larger in those with traction spurs than in those with no or claw spurs (p<0.05). The incidence of VP and MC in the traction spur group (61% and 35%, respectively) was significantly higher than that in the no spur group (9% and 6%, respectively) and claw spur group (25% and 15%, respectively) (P<0.05). With regard to the Modic type in the traction spurs, the incidence of type III (18%) was significantly higher than that of types I (6%) or II (11%) (p<0.05). There was no significant difference in the SA, SD or NRS of lumbago.

**Discussion** Our study had two main findings: 1) The change in the DH from the supine to the sitting position was significantly larger in the traction spur group than in the no spur and claw spur groups, and 2) traction spurs were more common as the VP and MC compared with no spur and claw spur. These findings suggest that traction spurs may be associated with spinal instability, VP and MC. Traction spurs were not associated with the NRS of lumbago, although we did not evaluate the subjects' quality of life. The clinical significance of traction spurs remains unclear.

## PREDICTIVE FACTORS FOR LOW BACK PAIN DEVELOPMENT IN HEALTHCARE STUDENTS: A SYSTEMATIC REVIEW

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### Introduction

Low back pain (LBP) is the leading cause of absenteeism and disability among healthcare professionals. Increasing evidence suggests that many healthcare professionals have experienced LBP since their training. Since a prior history of LBP in students may predispose them to future LBP, it is crucial to identify predictive factors for LBP development in healthcare students so that early prevention/management can be introduced. As such, the objective of the current systematic review was to summarize the evidence regarding factors that could predict future LBP in healthcare students.

### Methods

A systematic search through seven electronic databases was conducted from inception to March 2016. Studies were included if they were longitudinal studies reporting predictive factors for developing LBP in healthcare students. Two independent reviewers selected studies, extracted data from the included studies, and evaluated the quality of the included studies using the Quality in Prognostic Studies tool.

### Results

Eight out of 2,067 potential citations were included. Of seven prospective studies, four involved nursing students, one involved nursing assistant students, one involved dental students, and one examined dental hygienist trainees. One retrospective study evaluated medical students. The sample size of the included cohorts ranged from 33 to 694. While 20 demographic, 14 physical, and 15 psychological factors were evaluated, only 17 significant predictive factors were identified ( $P < 0.05$ ). These factors included: studying the second year of nursing (OR: 5.77), a history of LBP (OR: 2.48 to 15.97), headache (OR: 4.52), period pain (OR: 3.00 to 5.61), moderate physical activity (OR: 1.08 to 3.18), self-reported heavy physical workload (OR: 1.53), static loads (OR: 2.03), back muscle endurance (OR: 0.34), greater posterior pelvic tilt in slump sitting (OR: 1.08 to 2.7), high lumbar sitting repositioning error (OR: 3.33), self-reported fatigue (OR: 4.10), constant tiredness (OR: 5.90), low mood (OR: 3.12 to 5.07), stress (OR: 1.08 to 4.52), and high General Health Questionnaire score (OR: 1.36 to 3.95), life events score (OR: 1.05 to 1.09) and job dissatisfaction score (OR: 1.02). Although most of these factors were reported significant by a single study, three factors (a history of LBP, stress/mental pressure and moderate physical activity) were consistently found to be significant by three to four studies. As expected, some predictive factors reported conflicting results (e.g. smoking status, years in a given program, vigorous physical activity and anxiety). Quality assessments revealed that only two included articles provided clear inclusion and exclusion criteria, and all included articles did not describe the characteristics of dropout participants.

### Discussion

Our results highlight that a prior history of LBP and moderate physical activity are significant predictive factors for developing LBP in nursing/nursing assistant students. Additionally, stress is a significant factor for predicting LBP in nursing/medical students. Despite the high prevalence of LBP in healthcare students, only a few studies have been conducted to determine the predictive factors for LBP development in selected student groups. Future research should identify risk factors for LBP in students from all healthcare disciplines so that timely discipline-specific preventive measures can be provided.

## THE PREVALENCE OF SPINOPELVIC MISALIGNMENT IN INDIVIDUALS WITH REFRACTORY LOW BACK PAIN AND ASSOCIATION WITH MRI FINDINGS

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**Introduction:** The etiology of low back pain (LBP) is multifactorial. Morphological and postural factors can potentially affect the occurrence of LBP. A harmonious sagittal spinopelvic alignment is needed for a neutral posture, which is provided by balanced spinopelvic curves (lumbar lordosis (LL), pelvic incidence (PI), sacral slope (SS) and pelvic tilt (PT)). The effect of sagittal spinopelvic alignment on LBP is poorly understood. Thus, the aim of the present study was to determine the prevalence of sagittal spinopelvic misalignment in a cohort of patients with LBP, refractory to comprehensive non-operative treatment. Sagittal spinopelvic misalignment was also correlated with findings on lumbar magnetic resonance imaging (MRI) in order to explore possible relationship between degenerative changes.

**Methods:** This was a cross-sectional study conducted at a single urban, academic, tertiary spine center. Eighty-two consecutive patients with LBP who had failed to respond to comprehensive non-operative treatment were included. Comprehensive non-operative treatment included structured exercise programs, oral analgesic medication and spinal injections. Patients with scoliosis, spondylolisthesis, spinal canal stenosis, radicular pain/leg pain, concomitant hip joint pathology, tumor and fracture were excluded. After study enrollment, spinopelvic curves were measured using Surgimap® on lateral spine X-rays. Sagittal spinopelvic misalignment was defined as  $PI-LL \geq 10^\circ$ . Magnetic resonance images (MRI) findings recorded and correlated with SPM. Normal MRI was defined as not having degenerative disc disease, facet arthropathy, disc disruption or stenosis.

**Results:** Twenty-seven of 82 participants (32% 95% CI 22-42%) had sagittal spinopelvic misalignment. Patient characteristics were as follows: mean age= 43.9±10.6 years, female/male=15/12, body mass index (BMI)= 25.4±4.8. In 24 participants (89%), LL was higher than PI, which represented the greatest contribution to sagittal spinopelvic misalignment. Ten participants (37%) had a normal lumbar spine MRI. Participants with a normal MRI were significantly younger than patients without a normal MRI (38.6±9.43 vs 47.06±10.20 years, p=0.04). The groups were similar in gender, BMI (24.5±5.4 vs 25.8±4.6), PT (9.2±4.8 vs 10.7±7.8), PI (48.2±10.6 vs 47.9±12.4), SS (38.9±8.2 vs 37.2±9.2) and LL (62.6±11.8 vs 57.9±10.9).

**Discussion:** The present data demonstrated a 32% (95% CI 22-42%) prevalence rate of sagittal spinopelvic misalignment in a cohort with refractory LBP. Of these patients with sagittal spinopelvic misalignment, 37% had a lumbar spine MRI without evidence of degenerative disc disease, facet arthropathy, disc disruption, or stenosis. Sagittal spinopelvic misalignment may represent a primary etiology of refractory LBP in a subgroup of patients. While larger prospective study is needed to confirm the present findings, sagittal spinopelvic misalignment could be considered as a modifiable factor in patients with refractory LBP.

## EFFICACY OF ANKLE BRACHIAL INDEX IN DETERMINING PERIPHERAL ARTERIAL OCCLUSIVE DISEASE IN PATIENTS WITH LUMBAR SPINAL STENOSIS

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**Introduction:** Lumbar spinal stenosis (LSS), one of the most common degenerative spinal diseases in old aged population, not only causes back pain and radiating pain to lower extremities, but it may also lead to gait disturbance. Peripheral arterial occlusive disease (PAOD) is another type of degenerative disease that brings about pain in involved lower extremity and gait disturbance as well. Two disease entities may coexist and they are sometimes hard to differentiate from each other. We evaluated efficacy of Ankle-Brachial Index (ABI) test in diagnosing PAOD in patients with LSS.

**Aim :** To evaluate prevalence of PAOD in patients with LSS using ABI.

**Materials and Methods:** This was a prospective study with 200 patients diagnosed with LSS. Demographic data, physical exam results, and severity and characteristics of gait disturbance were documented. Plain radiograms and magnetic resonance imaging (MRI) scans of lumbar spine were reviewed. ABI was measured using pulse wave velocity, and if there were any abnormality from ABI, computed tomography (CT) scan was performed in order to confirm the presence of PAOD. Then, we statistically analyzed the significance of clinical and radiological characteristics presented by those with PAOD.

**Results:** There were 67 males and 133 females, and their average age was 68.5. Twenty-one patients (10%) showed abnormality from ABI test, and thus were diagnosed with PAOD. Old age correlated with male (80%), smoking history (85%), DM (70%), and hypertension (88%), and aortic calcification from plain radiogram was often observed ( $p<0.05$ ). Physical exam results showed very low sensitivity and specificity.

**Conclusion:** About 10% of patients with LSS were accompanied with PAOD, but it is hard to diagnose PAOD based on physical exam as its symptoms coincide with that of lumbar stenosis. ABI test, which shows high sensitivity and specificity, is therefore useful in preventing inappropriate diagnosis. One should keep in mind that there is high probability of PAOD if gait disturbance is presented by someone with risk factors such as old age (greater than 70 years), male, smoking history, and chronic metabolic disease.

## QUALITY OF LIFE OF PATIENTS WITH OSTEOPOROTIC VERTEBRAL COMPRESSION FRACTURES

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### Introduction

Osteoporotic vertebral compression fracture is the most common type of osteoporotic fracture. Patients experience severe morbidities from the fracture, but morbidity in patients with healed fracture has rarely been evaluated. The purpose of our study was to analyze the quality of life of those patients using EuroQoL-5 dimension (EQ-5D) and to evaluate factors affecting quality of life in OVCF patients.

### Methods

This study was performed ambispectively, using questionnaire interviews after institutional ethics board approval. The study participants were over 50 years old who had osteoporotic vertebral compression fracture at least six months previously. Questionnaires were divided into 2 sets. The surgeon's questionnaires included demographic features, history of anti-osteoporotic medication and information of fracture. The patient's questionnaires included functional measures. Each patient's scale calculated into the EQ-5D index. And they were analyzed by several variables and dimensions. Statistical analysis was performed and factors related to quality of life were analyzed.

### Results

A total of 196 patients were included. Mean EQ-5D index was  $0.737 \pm 0.221$ . EQ-5D index was significantly correlated with ODI score (correlation coefficient 0.807,  $p < 0.001$ ). On univariate analysis, age (Spearman's  $\rho = -2.0$ ,  $p = 0.005$ ), treatment method ( $p = 0.005$ ), history of fracture ( $p = 0.044$ ), and on multivariate analysis, conservative treatment ( $p < 0.001$ ), and osteoporotic treatment ( $p = 0.017$ ) were correlated significantly with EQ-5D index.

### Conclusions

Osteoporotic vertebral compression fracture markedly lowers quality of life in several dimensions, even in patients with healed status. Treatment of osteoporosis and conservative treatment method are factors that affect quality of life.



## STRUCTURAL VERTEBRAL ENDPLATE NOMENCLATURE AND ETIOLOGY: A STUDY BY THE ISSLS SPINAL PHENOTYPE FOCUS GROUP

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**Introduction:** The vertebral endplate is an integral structure within the motion segment. Evidence suggests that endplate abnormalities on spine MRI may be associated with disc degeneration and perhaps pain generation. However, standardized agreed definition to describe the various different endplate findings does not exist, posing a challenge to compare findings between studies and ethnic groups. The following survey was created to identify the variation of interpretation of endplate structural findings with respect to nomenclature and etiology among the global spine community.

**Methods:** A working group within the ISSLS Spinal Phenotype Focus Group was established to assess the endplate phenotype. A survey was constructed based on discussion and agreement by the working group. The survey consisted of 13 T2-weighted sagittal MRIs of lumbar spine, illustrating the superior and inferior endplates. Images were chosen to represent common endplate findings by consensus. A list of nomenclature and etiological terms with historical precedence was generated. Participants were asked to describe the endplates of each image and select from 14 possible nomenclatures and 10 etiological terms along with the option of free text response. The severity of each endplate finding was also rated. The survey was conducted using the RedCap online data collection system and was circulated throughout the ISSLS membership for data capture. Participants' demographics were also gathered.

**Results:** The survey was completed by 49 participants (90% males; 86% above 45 years of age). There were 35 clinicians & 14 researchers. 75% of researchers reported more than 16 years of research experience, whereas 83% of clinicians completed their training more than 16 years ago. 65% of the respondents had conducted research on the endplate, yet 53% of the participants were not aware of any endplate classification scheme. Considerable variation existed in selection of name, etiology and degree of severity of the endplate structural findings (reliability coefficients for single measures in each case were 0.3, 0.1 & 0.2, respectively). The most common terms selected by respondents for structural findings were "Schmorl's node" (19%), "abnormality" (13%) and "defect" (9%). "Degenerative" (39%) and "developmental" (15%) were most commonly selected as possible etiologies. Disc degeneration was the phenotype most commonly believed to be associated with endplate findings (82%), followed by Modic changes (50%) and narrow disc height (41%). 65% regarded Modic changes as being a structural endplate finding. Approximately 82% of clinicians and researchers agreed that a standardized endplate nomenclature and understanding the etiology is clinically important.

**Discussion:** This is the first study that has assessed the interpretation and variation of structural endplate findings with respect to nomenclature and etiology. This study found that variations exist with respect to endplate nomenclature and etiology between clinicians and basic scientists. Findings from this study stress the need for a standardized nomenclature scheme to provide a common language to facilitate and maximize the effectiveness of future clinical work and research studies, provides the foundation for development of a future consensus statement.

## A STUDY ON THE DIFFERENCE OF CLINICAL RESULTS BETWEEN UNILATERAL AND BILATERAL LUMBAR SPONDYLOLYSIS IN ADOLESCENT PATIENTS

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**INTRODUCTION** :At 2015 ISSLS, we reported that bilateral lumbar spondylolysis were at more progressive stages than unilateral lumbar spondylolysis. However, we did not compare the difference of clinical results between these two types, and there are few reports about them. The purpose of this study was to investigate the difference of their clinical results.

**METHODS**: From 2012.4 to 2016.3, 172 adolescent patients (145 men and 27 women, mean age; 14.9 years, range 10 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 two groups; unilateral spondylolysis group (U-group) and bilateral spondylolysis (B-group). The decision of bone union was made with CT. We compared the stages of spondylolysis, the period and the percentage of bone union between two groups.

**RESULTS**: The number of patients we can follow was 116 (93 men and 23 women) and mean follow-up periods was 7.7months. U-group consisted of 48 and B-group 68. Their stages were: U-group; 1) n=11, 2) n=33, 3) n=4, 4) n=0, B-group; n=2,13,27,26, respectively. (If the stages were different between right and left, we adopted more progressive stages) B-group were more progressive stages than U-group( $p<0.01$ ). Forty-four patients of U-group selected conservative treatment with lumbosacral corset, and 41 (93.2%) of those achieved bone union in 3.1months and returned to sports activity. On the other hand, at B-group, only 20 patients (44%) of 45with corset achieved bone union in 5.1months. Especially, when the stages were different from another side and at progressive stage, only 5 cases(11%) achieved bone union even if concerned side was at very-early or early stage. There were significant difference between two groups about bone union rate and treatment period ( $p<0.05$ ). 4 non- treatment patients of U-group and 14 of B-group still had low back pain at final follow up.

**CONCLUSION**: In this study, we showed that bilateral lumbar spondylolysis were at more progressive stages, lower rate and longer period for bone union than unilateral spondylolysis. We thought we must diagnose and treat unilateral spondylolysis as soon as possible in order not to proceed to bilateral spondylolysis.

## HOW DOES THE SEXUAL FUNCTION CHANGE AFTER LUMBAR SPINAL FUSION?

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**【Objectives】** Lumbar spinal fusions have been common surgeries for lumbar degenerative disorders over the past years. Although sexual function is affected by lumbar degenerative disorders, physicians and patients tend to avoid that topic. The aim of this study is to evaluate the quality and frequency of sexual activity in patients with lumbar degenerative disorders before and after surgery.

**【Methods】** We performed a retrospective questionnaire study about sexual activities in patients who had undergone spinal fusion for lumbar degenerative disorders. After informed consent, 35 patients participated in this survey. They were 17 males and 18 females with a mean age of 47.4 years old (34-55). Twenty-nine patients received single-level lumbar fusion, and 6 patients received 2-level fusion. Duration of symptom was averaged 24.6 months. They answered the anonymous questionnaire concerning sexual desire, activity and satisfaction before and after surgery to evaluate sexual function.

**【Results】** 69% of the patients had sexual desire, and 75% achieved satisfaction during sexual activity in presick period. There was significant difference about sexual desire in males and females (males vs females; 89% vs 50%,  $p=0.015$ ). Frequency of sexual activity was about 2.2 times per month. Lumbar degenerative disorders decreased sexual desire in 40%, and frequency of sexual activity in 71% of this population. 47% of males and 50% of females felt discomfort in sexual activity. Satisfaction during sexual activity decreased in half of males and females. Adjustment of sexual position was required in 41% of males and 44% of females. Patients who needed adjustment had higher points in visual analog scale of lumbar pain ( $p=0.022$ ). Even after surgery, sexual desire and frequency of sexual activity were not regained in 77% and 63% of patients, respectively. Uncomfortable feeling in sexual activity remained in 50% of patients after surgery. 30% of patients had no sexual activities even after surgery. Satisfaction during sexual activity also unchanged in 50% of patients. Sexual activity resumed within 3 postoperative month in 50%.

**【Conclusions】** Lumbar degenerative disorders decreased sexual desire, activity and satisfaction, which were not regained in a majority of middle-aged population even after surgical treatment.

## INVESTIGATION ON PHYSICAL ACTIVITY PARTICIPATION, ATTITUDE AND PREFERENCE OF FEMALE PATIENTS 50 YEARS AND OLDER WITH DEGENERATIVE LUMBAR SPINAL DISEASE

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### Introduction

Although the association between exercise and degenerative spinal disease has not yet been fully elucidated, recent literature suggests exercise to alleviate symptoms and strengthen trunk muscles. It is important to understand the attitude and preference of patients with degenerative lumbar spinal disease (DLSD) toward the physical activity and exercise before we can optimize the therapeutic effects of exercise and physical activity.

### Method

A total of 67 female patients, over 50 years old, were enrolled, who complained chronic low back pain and whose lumbar spine X-ray showed degenerative changes such as disc space narrowing, osteophyte and facet hypertrophy. The questionnaire on exercise participation can evaluate the frequency and duration of mild-, moderate- and vigorous-intensity physical activity during the past week and METs were calculated. The attitude and preferences towards exercise used a self-administered survey.

### Result

#### **Patient characteristics**

67 questionnaires were analyzed, all female. The average age of all patients was 68.4 years of age and the body mass index (BMI) was 25.2 kg/m<sup>2</sup> and the average of body fat was 34.4%.

#### **Exercise participation**

Analysis of exercise participation showed that DLSD patients participate in an average of 83min of exercise per week (14.6±12.2MET-h/wk) including mild 227min of exercise per week (15.9±11.8 METs-h/wk), moderate 105min of exercise per week (17.7±7.9 METs-h/wk) and vigorous intensity 56min (22.0±15.9METs-h/wk).

#### **Attitude towards exercise**

When asked about their exercise plans, 91.7 % of patients agreed that they will exercise more than 3 times a week, and 93.8 % agreed that they will start regular exercise within a month.

#### **Exercise preferences**

Most DLSD patients answered that they would like to receive information regarding exercise programs (93.6 %) and they were physically able to participate in an exercise program (91.5 %). DLSD patients preferred exercising alone (23.2%), to working out with friends (19.6%), with family (16.1 %), and with exercise specialists (10.7 %). When DLSD patients were asked where they would like to exercise, the most common answers were 'doesn't matter' (44.6 %), 'at home' (23.2 %), and 'at a local fitness center' (8.9 %). DLSD patients felt that they would be able to participate in > 30 min (57.1 %) and 20–30 min (36.7 %) of exercise per session, more than 5 times (39.3%) and 3 times (35.7 %) per week. The survey showed that 38% of patients wanted to participate in aerobic exercises including walking; 15.2% of patients preferred anaerobic exercises; and 8.6% of patients answered stretching exercises.

### Discussion

Even though the majority of DLSD patients intend to feel that they are able to participate in exercise, there are no clear exercise guidelines considering their needs. This study indicated that 92% of the patients believed that exercise is needed for the prevention of and decrease in low back pain. However, only 33% of patients participated in more than 18 MET-hours per week of physical activity, which is known to be beneficial for adults with low back pain. To successfully develop evidence-based exercise programs that are specific to DLSD, we reflect patient's attitude and their preferences.

## INTRADISCAL APPLICATION OF A PCLA-PEG-PCLA HYDROGEL LOADED WITH CELECOXIB FOR THE TREATMENT OF BACK PAIN: A TRANSLATIONAL APPROACH

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### Introduction

Chronic low back pain is a common clinical problem in both the human and canine population. Inflammatory mediators such as prostaglandin E2 (PGE2) play a key role in IVD degeneration in both species, causing structural changes of the IVD and low back pain. Current pharmaceutical treatment often consists of oral anti-inflammatory drugs to alleviate pain. In severe cases, surgery can be performed. Novel treatments for degenerative disc disease focus on local application of sustained released drug formulations. Injectable formulations that enable local sustained release of anti-inflammatory drugs aim at decreasing inflammation and thereby inhibiting degeneration and pain. The aim of this study was to determine safety and feasibility of intradiscal application of a PCLA-PEG-PCLA hydrogel releasing celecoxib, a COX-2 inhibitor.

### Materials and methods

Biocompatibility was evaluated after subcutaneous injection in mice and safety of intradiscal injection of the hydrogel was evaluated in experimental dogs with early spontaneous intervertebral disc (IVD) degeneration. COX-2 protein expression was determined in IVD samples surgically obtained from canine patients. Client-owned dogs with low back pain were diagnosed by MRI with degenerative lumbosacral stenosis marked by mild to moderate IVD degeneration and protrusion. The dogs were surgical candidates but were offered intradiscal injection. The PCLA-PEG-PCLA thermogel, loaded with 0.013 mg/ml celecoxib, was percutaneously injected into the nucleus pulposus of L7-S1 under fluoroscopy guidance. Follow-up consisted of clinical examination, owner questionnaires, and objective gait analysis by measurement of ground reaction forces (GRFs) using force plate analysis at 6 weeks, and 3 and 6 months after injection. MRI was repeated after 3 months and included T2- and T1-weighted images and T2-mapping.

### Results

Biocompatibility of the hydrogel was confirmed after subcutaneous and intradiscal injection. COX-2 expression was increased in IVD samples surgically obtained from canine patients indicating a role of COX-2 in clinical IVD disease. Ten client-owned dogs with chronic low back pain related to IVD degeneration received an intradiscal injection with the celecoxib-loaded hydrogel. None of the dogs showed adverse reactions after intradiscal injection. Follow up MRI showed no worsening of the IVD degeneration and the hydrogel did not influence MRI signal at long term follow up. Clinical improvement was achieved by reduction of low back pain in 9/10 dogs, as was shown by clinical examination and owner questionnaires. GRFs did not significantly change throughout the follow up period. In 3/10 dogs, standard-of-care surgical treatment was performed due to recurrence of low back pain recurrence after 3 months.

### Conclusion

This study showed the safety and feasibility of intradiscal injections with a thermoresponsive hydrogel loaded with celecoxib. Ongoing studies concentrate on the long term clinical follow up of these patients. Future studies will determine the optimal loading dose of celecoxib for clinical efficacy. In this setup, the dog can be used as a model for the development of novel treatment modalities in both canine and human patients with chronic low back pain.

## IS CULTURE-NEGATIVE SPINAL INFECTION REALLY ONE OF THE SUPPURATIVE DISEASES?

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### Purpose

We encountered two cases of calcium pyrophosphate dehydrate (CPPD) deposition spondylitis, and think that some cases having been treated as pyogenic spondylitis were possibly caused by CPPD.

**Case1** A 63-year-old male was admitted complaining of low back pain and left knee pain. On physical examination, he showed 37.2 temperature, a stiffening pain in the lumbar region and swelling left knee with redness and localized inflammation. We performed knee joint puncture, and histological diagnosis revealed CPPD. Regarding magnetic resonance imaging (MRI), T1-weighted imaging showed iso-intensity between L4 and L5 vertebral bodies, whereas T2-weighted imaging showed hyper-intensity presumably suspected pyogenic spondylitis. A white cloudy fluid was removed from L4/5 intervertebral disc by a needle biopsy, which was culture-negative and found to contain CPPD in microscopic examination. We diagnosed as CPPD deposition spondylitis, and chose conservative treatment without antibiotics. After a while, his symptoms improved, moreover the abscess disappeared in MRI.

**Case2** A 68-years-old female was admitted complaining of deteriorating pain of lumbar region and lower extremities. She was diagnosed as having pyogenic spondylitis with epidural and iliopsoas abscess from lumbar MRI, and admitted to our hospital. After admission, cauda equina symptoms and bowel bladder disorder appeared, so we performed laminectomy urgently. In the surgery, a lot of white pus-like suspension spouted from L2/3 intervertebral disc. The cultivation test of this fluid was negative including a tubercle bacillus. After this surgery, inflammatory reaction still remained high. We performed abscess drainage to the iliopsoas abscess and drained similar fluid. This fluid was culture-negative, but CPPD was detected in histological examination. Finally we diagnosed as CPPD deposition disease and stopped antibiotics, then inflammatory reaction improved gradually. After confirmation of abscess disappearance in MRI, she was able to walk unassisted.



### Discussion

CPPD deposition to joints, tendons, or ligaments is commonly known as one of the diseases. However, CPPD deposition to the spine is rare. Crowned dens syndrome in cervical spine has been reported, but CPPD deposition in lumbar spine is less frequent. Because of the similarity with pyogenic spondylitis in clinical symptoms and imaging studies, it usually needs a histological examination to diagnose. We consider the possibility of an involvement with CPPD deposition spondylitis in some cases which show Modic type1 change in MRI and have been diagnosed aseptic spondylitis or low-virulent spondylitis. We emphasize the importance of considering this disease entity in the differential diagnosis of lumbar spondylitis, moreover not only culture test but also histological examination after a needle biopsy is necessary.

### Conclusion

We should consider the possibility of CPPD deposition spondylitis, when distinguishing the cause of spinal infection.

## THE COST IMPACT OF A PRECISE MECHANICAL DIAGNOSIS FOR LOW BACK PAIN: A COMPARISON WITH USUAL COMMUNITY CARE

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**Introduction:** The cost of treating low back pain (LBP) keeps increasing with little evidence of improved outcomes. A fundamental contributor is the inability to make a reliable, accurate diagnosis which results in a wide range of questionably effective treatments. However, considerable reliability and patient-reported outcome validity evidence documents that a "mechanical diagnosis" based largely on a directional preference finding identifies predictably-effective directional exercises and posture modifications for most. Until now, no study has looked at the cost impact of basing treatments on mechanical diagnoses compared with "usual" community care.

Analyzing employer's claims data offers the rare opportunity to identify initial and downstream care and costs regardless of where care takes place. A significant decrease in one-year downstream costs also reflects improvement in care quality in the absence of other cost-lowering factors.

This administrative claims data analysis evaluated for differences in costs and use of services between outcomes-driven McKenzie-type mechanical care (MC) and community care (CC) over one year. It was hypothesized that MC costs and use of services (imaging, injections, surgery) would be significantly lower compared to CC.

**Methods:** All care-seeking employees and dependents with low back complaints at a large U.S. manufacturer selected either community care (CC) or care within a company clinic. Each was first physician-examined and assigned a lumbar diagnostic code. Only patients with a fracture, dislocation, or infection code were excluded. Most who selected the company clinic were unaware they would undergo mechanical care (MC) based on a mechanical evaluation. Their mechanical diagnosis typically determined their treatment which, in most cases, focused on directional exercises and posture modifications that matched their evaluation findings.

CC providers were reimbursed using standard fee-for-service. MC providers agreed to risk-sharing reimbursement using a negotiated case-rate. All subsequent claims for one year were allocated to the baseline treatment group. The two groups were risk-adjusted using the company's claims-based risk score and patients' age and gender.

**Results:** During 2013, 434 subjects chose MC and 4,602 sought CC. After one-year follow-up and risk-adjustment, MC produced a 51.5% savings compared with CC, significant at  $p < .0001$ . Additionally, MC reduced the utilization of MRIs, injections, and surgeries by 61%, 75%, and 66% respectively, with relative risks within CC of 2.57, 3.97, and 2.95 respectively.

**Discussion:** The risk-sharing case-rate rewarded the MC provider for accepting allocation of all costs for each patient during the one-year follow-up. The 51.5% savings was largely related to substantial decreases in MC subjects' need for MRIs, injections, and surgeries. In the absence of any other cost-saving factors, e.g. payment denials, these substantial savings appear to reflect the benefit of making a mechanical diagnosis in determining patient-specific treatment. If diagnoses made at the outset of care are sufficiently precise to also identify a predictably-effective treatment, recoveries should be faster, treatments much simpler, and significantly less expensive.

It is widely accepted that indirect costs are 2-4 times greater than direct care costs. Our significant direct care savings with MC may therefore create a substantial indirect cost savings for the employer as well.

## PROGRESSION OF LUMBAR PARASPINAL MUSCLE ATROPHY FOLLOWING BILATERAL BOTULINUM TOXIN INJECTIONS IN A RABBIT MODEL

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**Introduction:** Paraspinal muscle weakness has long been thought to contribute to low back problems. As a result, minimally invasive surgical approaches have been implemented to reduce paraspinal muscle damage, and rehabilitation efforts often aim to improve paraspinal muscle function. Understanding the relationship between muscle function and spine health is essential to validate this current clinical rationale. Botulinum toxin type-A (BTX-A) injections have been shown to induce skeletal muscle weakness and subsequent atrophy and fatty infiltration, though this information is limited in the lumbar spine literature. In order to investigate the effects of induced paraspinal muscle weakness and spine health (e.g., disc and facet joints), characterizing the effects BTX-A injections have on paraspinal muscle atrophy and fatty infiltration is necessary. Thus, the aim of this study was to determine the effects of two different BTX-A injection dosages on paraspinal muscle atrophy and fatty infiltration using a well-controlled animal model.

**Methods:** Eighteen New Zealand White (NZW) rabbits were randomly divided into three groups: 1) 8.0 Units/kg dose of BTX-A (BOTOX®, Allergan Inc.) (n=7), 2) 3.5 Units/kg dose of BTX-A (n=6), and 3) Controls (n=5) injected with physiologic saline (0.9% NaCl). Magnetic resonance imaging (MRI) was serially performed using a pre-clinical 7-Tesla MRI system (BioSpec 70/30 USR, Bruker) weekly for a total of 8 weeks. Axial T1 (T1-FLASH) and T2 (T2-TurboRARE) images of the paraspinal muscles were acquired using a transmit and receive volume coil. OsiriX image processing software (version 8.0, Pixmeo) was used to analyze the MR images. Paraspinal muscle cross-sectional areas (CSA) were measured for left and right paraspinal muscles at the L3, L4 and L5 intervertebral disc levels. Left and right CSA values were averaged, as there was no significant difference between sides. Atrophy was quantified as diminished CSA with respect to the baseline CSA values. MRI and histological analyses were also performed on the paraspinal tissue following the final 8-week time point.

**Results:** Paraspinal CSA significantly decreased at each spinal level for both the 3.5 Unit/kg and 8.0 Unit/kg injection groups and was more pronounced in the higher dosage group ( $p < 0.05$ ). An example of the progression of paraspinal muscle atrophy at the L4 intervertebral disc level is displayed in Figure 1. In addition to decreased CSA, fatty infiltration was observed on the MR images in both BTX-A groups. Histological analysis confirmed the presence of adipocytes in the paraspinal muscles, validating the MRI fatty infiltration findings.

**Discussion:** Following BTX-A injections, there was progressive paraspinal muscle atrophy and fatty infiltration that was confirmed on both MRI and histological analyses. This well-controlled model demonstrates the potential to be used to investigate the effects of paraspinal muscle weakness on spine health. Additional studies investigating extended time points, repeated injections and anatomical (intervertebral disc and facet joint) changes are currently underway.

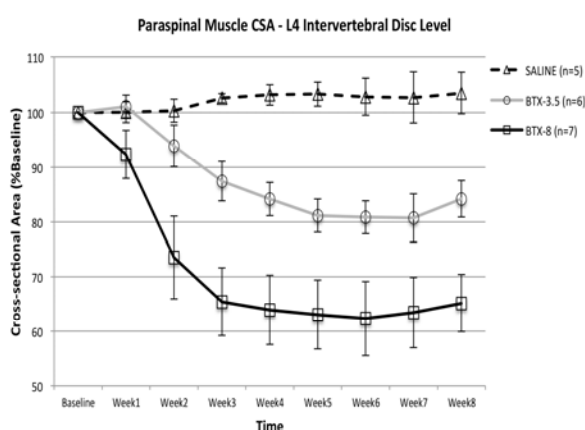


Figure 1. An example of the weekly progression of paraspinal muscle atrophy following BTX-A injections.



## THE PROFILE OF LOW BACK PAIN PATIENTS WHO ATTEND THE EMERGENCY DEPARTMENT AND THEIR REASONS FOR DOING SO.

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**Introduction:** Low back pain (LBP) is a common problem associated with considerable morbidity and cost. A significant portion of these burdens are thought to arise when persons with non-emergent LBP present in high-cost facilities such as a hospital emergency department (ED). With this in mind, the aim of this project was to determine the profile of LBP patients attending the emergency department and their reasons for doing so.

**Methods:** Between January 1, 2016 and March 31, 2016, persons seen at the University of Alberta Hospital ED with a diagnostic code related to LBP were identified from an electronic database. De-identified data available from the resulting records included: patient demographics, triage code, diagnostic code, procedure code, referral code and length of time in the ED. Following their presentation in the ED, each LBP patient was sent a survey by mail with the aim of understanding their motivation for attending the ED. Descriptive statistics were calculated and a non-parametric test (Mann-Whitney) used to determine if triage codes were significantly different (alpha 0.05) between peak hours (0800-1800) and off-peak hours (1801-0759).

**Results:** 194 males and 190 females (384 total) ranging in age from 18-95 (mean 46 years) attended the ED for low back pain over the study period. The most common assigned triage code from the 5 point Canadian Triage And Acuity Scale (CTAS) was 3 (227/384) which corresponds to a description of "Patients need to be seen by a physician within 30 minutes 90% of the time". The three most common diagnostic codes were "Dorsalgia, Unspecified Site" (118), "Low Back Pain" (67) and "Sciatica" (41) while the most common procedures were x-ray (156), and MRI (10). The most commonly requested referral was orthopaedic surgery (10) followed by neurosurgery (9) then family practice (9). Of the 384 patients, 311 were dismissed to their homes without support, 38 left without being seen or receiving treatment and 30 were admitted to another area, critical care or the operating room (8%). The average length of stay in the ED was 6 hours. Of the 384 surveys mailed, 52 persons responded (14% response rate to date). When asked by survey why they attended the ED, 67% reported unmanageable pain followed by diagnostic uncertainty (49%). Top factors influencing this decision were 1) the ED did not require an appointment and 2) the ED was perceived to have a high quality of care. No significance difference was observed in triage codes between peak hours and off-peak hours.

**Discussion:** A low admission rate combined with a majority of LBP patients being discharged to their home suggest inappropriate patient usage of the ED at the University of Alberta. Further, the lack of difference in triage codes between peak and off-peak hours suggest that the ED is not acting to absorb more severe cases when other facilities are closed or unavailable. This data suggest that most ED presentations of LBP could be seen in the community if those services provide, and are perceived to provide, easy access and high quality care.

## HUMAN CARTILAGINOUS ENDPLATE DISCONTINUITIES: FLASH MRI FOR POTENTIAL CLINICAL DIAGNOSTICS

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### Introduction

The cartilaginous endplate (CEP) is important for both nutrient transfer and mechanical function of the intervertebral disc, but with degeneration both CEP permeability<sup>1</sup> and tensile modulus decrease.<sup>2</sup> CEP discontinuities (focal changes in shape) are sometimes present. These structural defects may contribute to disc degeneration, perhaps via altering permeability and nutrition to the nucleus pulposus. CEP discontinuities may also be related to pathological changes to the vertebral endplate (e.g. Modic Changes) or low back pain, although this study focuses solely on the CEP. We recently developed a FLASH MRI sequence that enhances CEP contrast<sup>3</sup> and provides the means to study CEP discontinuities in the context of disc degeneration. The objective of this study was to quantify CEP discontinuities across lumbar levels and the degenerative spectrum using an MRI sequence that is designed for translation to a clinical setting.

### Methods

Sagittal plane MR images were acquired of intact cadaveric lumbar spines using a Siemens 3T magnet and two Siemens large flex coils at a resolution of  $0.4 \times 0.4 \times 2.5 \text{ mm}^3$  in under 2 min. A FLASH sequence was used (TR = 9 ms, TE = 3.6 ms, flip angle  $20^\circ$ ). Four intact lumbar spines (L1-S1) were imaged via this method yielding 20 discs (5 from each spine), and 15 additional discs from a previous study<sup>4</sup> were included. The total sample set ( $n=35$  discs, age 50-75) ranged in degenerative grade from 1-4 based on the Pfirrmann grading scale. The mid-sagittal image was examined for CEP discontinuities (Figure 1). Discontinuities were identified as a focal loss of signal or an abrupt change in shape (Figure 1 inset). Hypothesized effects of degeneration, spine level, and age on number of CEP discontinuities were tested using multifactor ANOVA and post-hoc Tukey tests with significance set at  $p < 0.05$ .

### Results

The total number of discontinuities tended to be greater in more degenerative discs ( $p=0.07$ , Figure 2). When including only the superior CEP, there were more discontinuities in more degenerative discs ( $p<0.05$ ) and grade 4 discs had more discontinuities than grade 2 discs ( $p<0.05$ ). Spine level and age did not significantly influence the number of CEP discontinuities.

### Discussion

We found that the number of discontinuities in the superior CEP increases with disc degeneration. This finding is similar to prior work that found an increase in osseous superior endplate lesions post-discectomy, but no significant changes in the inferior endplate<sup>5</sup>. Additionally, we have improved the FLASH MRI sequence previously used *in vivo* by our group<sup>3</sup>, halving the slice thickness while keeping scan time short enough for *in vivo* use. This cadaver study demonstrates that the scan visualizes the CEP well enough to detect pathology. Future work will apply this scan *in vivo* to evaluate the CEP's potential role in degeneration and low back pain.

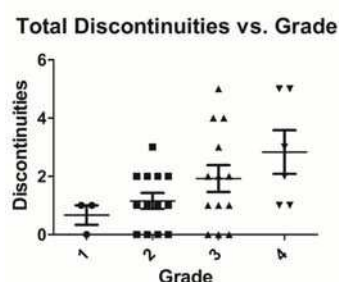
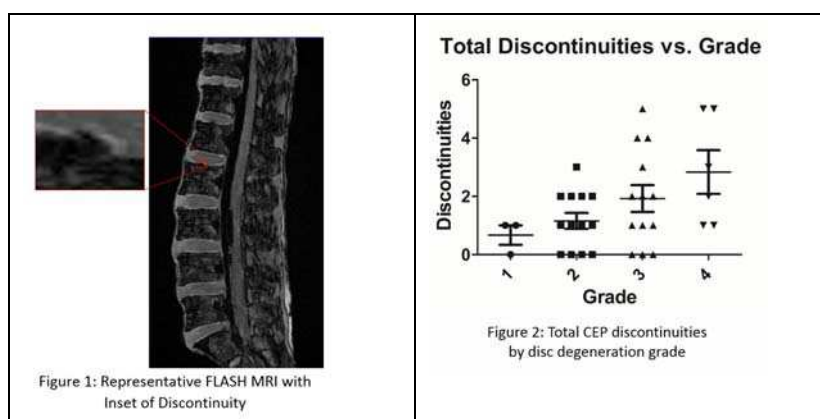


Figure 2: Total CEP discontinuities by disc degeneration grade

- [1] DeLucca et al. J Biomech 2016
- [2] Fields et al. J Orthop Res 2014
- [3] Moon et al. Eur Spine J 2013
- [4] DeLucca et al. J Orthop Res 2016
- [5] Weiner et al. Eur Spine J 2015

## THE NATURAL HISTORY OF IDIOPATHIC SCOLIOSIS DURING GROWTH: A META-ANALYSIS.

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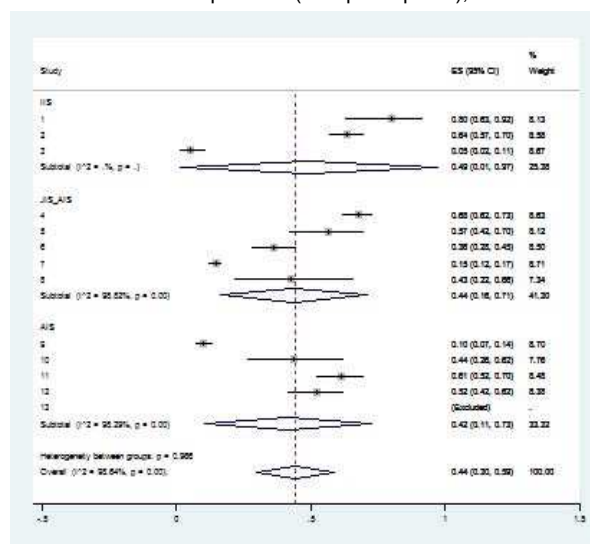
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**Introduction:** The real risk of progression of idiopathic scoliosis is considered to vary during different growing phases, but so far data concerning this issue refer only to few studies and narrative reviews. Today no systematic reviews or meta-analysis are available to group the results of different studies. The aim of this study is to provide a systematic review and a meta-analysis of the current literature concerning the natural history of idiopathic scoliosis during growth.

**Methods:** We searched the MEDLINE, EMBASE and SCOPUS databases up to November 2016 to retrieve articles reporting about natural history of scoliosis during growth. Eligible studies were prospective or retrospective studies that enrolled patients with infantile, juvenile or adolescent idiopathic scoliosis followed up without any treatment from the time of detection. The studies were included only if they reported the progression rates during growth of untreated patients. Two authors independently reviewed each article for data extraction and quality assessment. The main outcome measure was the rate of progression. For the meta-analysis, the studies were grouped according to diagnosis: Infantile Idiopathic Scoliosis (IIS), Juvenile Idiopathic scoliosis, (JIS) and Adolescent Idiopathic Scoliosis (AIS). Due to expected heterogeneity, we applied a random effect model to pool data together.

**Results:** Of the 1797 citations screened, we assessed 61 full-text articles and included 13 of these (2301 participants). Three studies included IIS patients (347 participants), 5 studies included a mixed population of JIS and AIS (1330 participants), 5 studies included AIS patients only (624 participants). The random pooled estimated progression rate was 49% (95CI: 1-97%) for IIS; 44% in a mixed group of patients affected by juvenile or adolescent IS (95CI: 16-71%) and 42% in AIS (95CI: 11-73%). The criteria to define progression were slightly different among studies, being this a change of 5, 6 or 10° Cobb, or a progression over the threshold of 50° Cobb. Risser, age and clinical features varied among studies.



**Discussion:** During growth, idiopathic scoliosis tends to progress in a high percentage of cases. The progression rate varies according to the age at diagnosis, with infantile scoliosis being the most unpredictable. There are many confounders like age, Risser sign and baseline Cobb angles that were not consistent among studies, and this makes the data quite heterogeneous as reported in our analysis. These features, together with the different definitions of progression can explain the variability of results among different studies. We suggest that future research about natural history looks in a more detailed way at the clinical parameters that can predict progression, and give more homogeneous definition of progression.

## PEAK SCOLIOSIS BRACE CAN REDUCE PAIN IN ADULTS WITH PAINFUL SCOLIOSIS: SIX MONTHS RESULTS FROM A PROSPECTIVE COHORT PILOT STUDY

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**Introduction:** Adult scoliosis is sometimes associated to back pain and severe curves can progress over time. The main approach for these patients is the surgical one, however surgery is not appropriate for all patients, and certain patients do not accept surgery. Despite scoliosis has been estimated to affect up to 68% of the population over 60, there is scant literature about conservative treatment for adult scoliosis. A recent paper showed the possibility for braces to reduce scoliosis progression during adulthood, but no data about pain control and quality of life were published. Recently we tested a new brace (Peak™ Scoliosis Brace - Aspen Medical Products) designed to alleviate pain for adult patients with chronic pain secondary to scoliosis showing some pain relief at one month, but no longer follow up are available.

The aim of the present study is to test the efficacy of the Peak™ Scoliosis Brace in reducing pain in adult scoliosis patients at six months.

**Methods:** Design: follow up of prospective experimental cohort study.

Population: 20 adults (age  $67.8 \pm 10.5$ , curve  $61.9 \pm 12.6^\circ$  Cobb) with back pain secondary to Idiopathic Scoliosis. The sample size calculation was based on unpublished data collected in clinical practice.

Inclusion criteria: Adults affected by Idiopathic scoliosis of  $30^\circ$  Cobb or more and chronic low back pain (cLBP). Exclusion criteria: secondary scoliosis.

Outcome measures: GRS, Oswestry Disability Index (ODI), Roland Morris Questionnaire (RM), COMI.

Statistical analysis: paired t-test and non parametric tests.

Protocol: patients were evaluated at baseline immediately before starting with the brace and after 1 month. The brace must be worn for at least 2 hours per day.

**Results:** All parameters showed a short term improvement at one month. At six months, worst pain, leg pain and back pain were significantly improved: from 7.15 to 5.60, from 5.65 to 4.35 and from 6.55 to 5.25 ( $p < 0.05$ ). Sixty five percent of patients achieved the minimal clinically important difference of 2 points for worst pain and leg pain, 55% for back pain. RM and COMI improved ( $p < 0.05$ ), no differences for ODI.

**Conclusion:** The Peak Scoliosis brace showed a significant improvement at 6 month of worst, leg and back pain in the majority of patients in a group of adult women with scoliosis and cLBP. Some changes were noticed at one month, but at long term this effect was increased. The quality of life didn't change in a clinically significant way even if the patients reported satisfaction with the treatment. It's possible that a higher dosage would guarantee a better effect, and it would be important to determine the features of responders with respect to non responders in a larger study

## SCOLIOSIS-SPECIFIC EXERCISES REDUCE BRACING RATE IN ADOLESCENTS WITH IDIOPATHIC SCOLIOSIS. END GROWTH RESULTS OF AN EVERYDAY CLINICS' PROSPECTIVE COHORT CONTROLLED STUDY

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**Introduction.** Adolescent idiopathic scoliosis (AIS) is a three-dimensional deformity of the spine and trunk. Recently, 3 randomized controlled trials (RCTs) showed the efficacy of specific exercises for treating AIS, prescribed with the aim to avoid bracing or reaching a spinal curvature of 30° Cobb. To check the generalizability of these results, a large observational cohort study in everyday clinics is needed. The aim of this paper is to verify the effectiveness of specific exercise for AIS in everyday clinics to avoid bracing or reaching a curvature measurement of 30°.

**Methods.** Design: an observational and controlled cohort study nested in a prospective database started in March 2003. Setting: outpatient tertiary referral clinics. Participants: consecutive patients from start of the database to September 30, 2010. Inclusion criteria: IS; Risser sign 0-2; 11° to 20° Cobb; age 10 years or older; first evaluation. Exclusion criteria: consultations only; immediate prescription of a brace. Groups: physiotherapeutic specific scoliosis exercise (PSSE), according to the scientific exercise approach to scoliosis (the SEAS school); control (CON); usual physiotherapy (UP). End-of-treatment (EOT): medical prescription, bracing, Risser sign 3. Failures: bracing for scoliosis; EOT measurement above 30°. Statistics: intent-to-treat (ITT) and efficacy (EA) analyses were performed; relative risk (RR), number needed to treat (NNT), and 95% confidence interval (95CI) have been calculated.

**Results.** Of 327 patients, 34 (10.4%) were excluded due to a prescription of bracing at the first evaluation. We included 145 PSSE, 95 UP, 53 CON with no differences at baseline. Physicians prescribed bracing without differences among the groups. Intent-to-treat: exercises RR 0.73 (0.58-0.92) with NNT 5.7 (3.1-33.0) ( $P < .01$ ). Efficacy analysis: exercise RR 0.68 (0.50-0.93) with NNT 5.5 (2.9-46.0) ( $P < .05$ ); PSSE RR 0.66 (0.48-0.90) with NNT 5.9 (3.4-20.7) ( $P < .01$ ); UP were not statistically significant.

**Conclusion.** PSSE reduces bracing rate in AIS not only during RCTs but also in everyday clinics. Provided that patients accept treatment, PSSE (SEAS school) is more effective than UP. Specific exercises are another tool to be included in the therapeutic toolbox of the AIS treatment community.

## VERTEBRAL ENDPLATE ABNORMALITIES ARE HIGHLY ASSOCIATED WITH THORACIC DISC HERNIATIONS IN SYMPTOMATIC PATIENTS

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**Background:** Lumbar disc herniations are common. Endplate abnormalities (e.g. Schmorl's node) have been noted to occur throughout the lumbar spine, with or without disc herniation. However, disc herniations of the thoracic spine are often associated with neurological sequelae, frequently necessitating surgery which has a high incidence of complications. Unlike the lumbar spine, the mechanism of thoracic disc herniations is not well understood. Recently, a much thorough understanding of the endplate phenotype has been proposed that provides insight into the etiology and risk of disc changes. The following large-scale study was performed in a cohort of symptomatic thoracic disc herniation patients to determine the relationship between such lesions and the role of endplate abnormalities as well as other MRI phenotypes.

**Methods:** A retrospective review of a prospectively collected cohort of 161 adult patients who were diagnosed with symptomatic thoracic disc herniation and myelopathy requiring surgery from 2008 to 2012 at a single institute were assessed. Preoperative T2-weighted MRIs were assessed of the thoracic spine. Imaging phenotypes of black disc, disc space narrowing, disc herniations, Modic changes, endplate abnormalities, osteophytes and ossified longitudinal ligament were assessed from T1-L1.

**Results:** There were 49% males and 51% females. Black disc was noted in 75% of patients, most prevalent at T8/9 (32%), T7/8 (29%) and T6/7 (27.3%). Disc space narrowing was noted in 31% of the patients, mainly occurring at T11/12 (6.8%), T8/9 (8.1%) and T6/7 (7%). Disc herniation was more prevalent at T11/12 (60%), T12/L1 (55%), T10/11 (50%), T8/9 (42.9%) and T9/10 (37%). Endplate abnormalities were noted in 84% of the patients, occurring primarily at T11/12 (48%), T9/10 (33%), T12/L1 (32%) and T10/11 (44%), and strongly associated with levels of disc herniation. Modic changes were noted in 32% of patients, primarily occurring at T6/7 (11%), T7/8 (11%), and T8/9 (10%). Osteophytes occurred in 4% of the patients and were more common at the lower thoracic spine at T10-L1. Ossified longitudinal ligament was noted in 20% of the patients, mainly noted at T6-T9.

**Discussion:** This study represents one of the largest cohort of patients with symptomatic thoracic disc herniation and the imaging assessment of additional spinal phenotype patterns. Findings from this study have noted that endplate abnormalities are highly associated in patients with symptomatic thoracic pathology, mainly occurring at levels of disc herniations. Secondary degenerative phenotypes were also noted, mainly occurring in the lower thoracic spine but presenting with unique topographical and morphological patterns. Having a better understanding of the endplate phenotype and the occurrence of thoracic disc herniation may shed light into the etiology and mechanism of endplate and disc pathology, which may also shed light upon the prediction of future spinal conditions of the thoracic spine.

## THE PREVALENCE OF SPINOPELVIC MISALIGNMENT IN INDIVIDUALS WITH DEGENERATIVE DISC DISEASE AND REFRACTORY LOW BACK PAIN

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**Introduction:** Low back pain (LBP) is a common and challenging issue. While many patients with LBP respond to treatments such as physical therapy, oral analgesics, and spinal injections, others continue to experience symptoms, yet those with degenerative disc disease (DDD) in the absence of significant disc disruption or herniation, scoliosis, stenosis, or spondylosis are poor surgical candidates. Recent investigation has revealed spinopelvic misalignment (SPM) as a potential etiology of chronic refractory LBP in individuals without surgical pathology on lumbar magnetic resonance imaging (MRI). Thus, the aim of the present study was to determine the prevalence of SPM in a cohort of patients with refractory LBP and findings of degenerative disc disease (DDD) but no surgical or significant structural abnormality on MRI. The prevalence of Modic changes, a phenomenon thought to be associated with symptomatic DDD, in patients with SPM was also determined.

**Methods:** This was a cross-sectional study conducted at a single urban, academic, tertiary spine center. Patients with LBP and MRI findings of DDD but no surgical or significant structural abnormality, who had failed to respond to comprehensive non-operative treatment, were included. Comprehensive non-operative treatment included physical therapy, oral analgesic medication, and spinal injections. Patients with scoliosis, spondylolisthesis, spinal canal stenosis, radicular pain/leg pain, concomitant hip joint pathology, tumor, and fracture were excluded. After study enrollment, spinopelvic curves were measured using Surgimap® on lateral spine X-rays. Spinopelvic curves (lumbar lordosis (LL), pelvic incidence (PI), sacral slope (SS) and pelvic tilt (PT)) were assessed and SPM was defined as  $PI-LL \geq 10^\circ$ .

**Results:** Eighty-two patients were screened for possible study inclusion, of which, fifty-three met criteria and were enrolled. Patient characteristics were as follows: mean age=  $46.6 \pm 12.3$  years, female/male=37/16, body mass index (BMI)=  $25.0 \pm 4.2$  kg. Nineteen patients (36%, 95% CI 23-50%) out of 53 had SPM. Age and gender distribution were similar between the patients with SPM and those without SPM ( $47.8 \pm 13.3$  vs  $44.5 \pm 10.4$ ,  $p=0.365$ ). LL was significantly higher ( $51.1 \pm 9.7$  vs  $57.8 \pm 11.3$ ,  $p=0.03$ ) and PT was significantly lower ( $15.5 \pm 6.1$  vs  $10.7 \pm 7.6$ ,  $p=0.01$ ) in patients with SPM compared to those without SPM. There were significantly fewer patients with Modic changes in the group with SPM compared to the group without SPM (29 vs 10 patients,  $p=0.041$ ). In the group without SPM MODIC changes were as follows: MODIC I changes in 24 (70%) patients, MODIC II changes in 2 (6%) patients and MODIC I-II changes in 3 (9%) patients. In the group with SPM MODIC changes were as follows: MODIC I changes in 7 (41%) patients and MODIC I-II changes in 3 (16%) patients.

**Discussion:** The present study demonstrated SPM in 36% (95% CI 23-50%) of participants with refractory LBP and only DDD on MRI. Further, Modic changes were less common on participants with SPM, suggesting that the etiology of pain symptoms may be related to SPM rather of primary discogenic origin. These results support previous study that SPM may be the root etiology of refractory LBP in a subset of patients. Larger prospective study is needed to confirm these findings

## INHIBITION OF CYCLOOXYGENASE-2 PATHWAY MODULATES COLLAGEN SYNTHESIS OF CYTOKINE-STIMULATED FIBROBLASTS FROM LIGAMENTUM FLAVUM

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### Introduction

Hypertrophy of ligamentum flavum (LF) induces narrowing of spinal canal which develops neurogenic claudication. Several mechanisms of LF hypertrophy have been suggested. Among them inflammatory cytokine play a crucial role in LF hypertrophy by increasing collagen synthesis. Cyclooxygenase-2 (COX-2) pathway shares inflammatory reaction from infection and arthritis. Selective COX-2 inhibitor (COX-2si) might modulate collagen synthesis via suppressing inflammatory pathway. Hence, the current study examined the effect of COX-2si in collagen synthesis of inflammatory cytokine induced LF cells.

### Method

Fibroblast and LF cells were harvested and cultured. Inflammatory cytokines (IL-1, TNF- $\alpha$ ) were utilized to stimulate collagen synthesis of LF cells. Then COX-2si was administered to stimulated fibroblasts and LF cells. Collagen synthesis, RT-PCR for COX-2 and various collagens, were performed.

### Result

Fibroblasts and LF cells stimulated by inflammatory cytokines showed increase in collagen synthesis in translational and transcriptional level. Stimulated fibroblasts and LF cells with COX-2si demonstrated down-regulation of COX-2, various collagens mRNA, and finally collagen synthesis.

### Discussion

In stimulated fibroblasts and LF cells, COX-2si provided therapeutic mechanism in reducing collagen synthesis. Hence COX-2si might be useful in preventing LF hypertrophy, which opens new therapeutic, preventive measures in symptomatic lumbar spinal stenosis.



## ANATOMICAL FLOW PATTERN OF CONTRAST IN LUMBAR EPIDURAL SPACE: A HUMAN STUDY WITH A TRANS-LATERAL RECESS APPROACH UNDER FLUOROSCOPY

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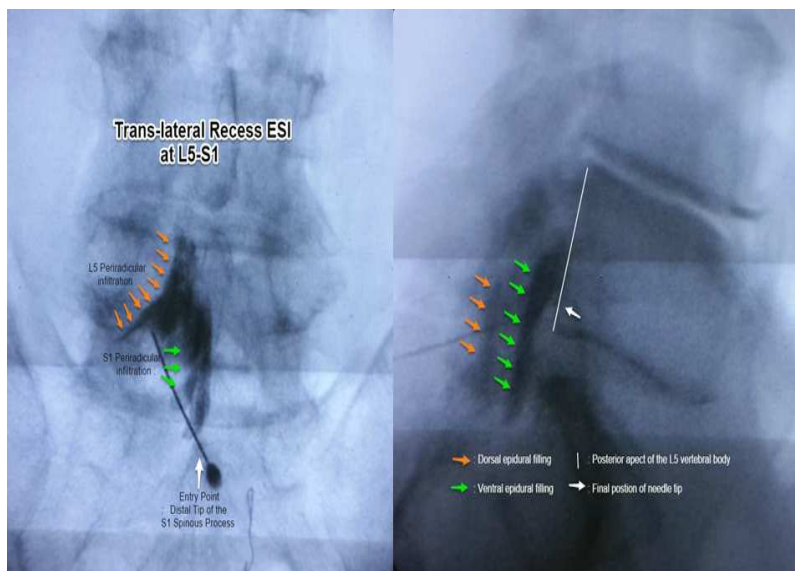
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**Introduction:** The ventral epidural space as well as lateral recess of spinal canal contains potential spinal pain generators. Targeted ventral epidural steroid injection with transforaminal approach has been widely used for the treatment of lumbar degenerative disc disease. However, there have not been studies regarding the direct simultaneous approach to the lateral recess and ventral epidural space without the use of additional catheter system.

**Methods:** This study is a prospective analysis of 50 consecutive patients with axial back and leg radicular pain treated with the TLR epidural injection. TLR epidural injection was performed with 20G Tuohy needle which was inserted into the distal tip of lower spinous process of the target segment then advanced toward the center of upper pedicle. And, Tuohy needle was inserted as possible to parallel to the upper lamina of the target segment. Then, 0.5 mL of contrast was injected through the needle tip placed at the dorsal epidural space below the Ligamentum flavum to determine the epidurographic pattern. After confirming that the needle tip was placed outside the posterolateral margin of thecal sac, Tuohy needle was gently advanced until it touched posterior aspect of the vertebral body or intervertebral disc. Then, a 1 mL of contrast was injected to determine the epidurographic pattern.

**Results:** With 0.5 mL contrast injection, all patients showed filling in the dorsal epidural space. While Tuohy needle was placed at the ventral epidural space, there was no reported case of dural puncture. After 1 mL contrast injection, it showed rostral spread to the foramen of target segment in 48/50 (96%) patients, caudal spread to the foramen of lower segment in 45/50 (90%) patients. All patients showed excellent filling in the ventrolateral epidural space of target level. None of the patients showed intravascular injection, and no neural complications were reported.

**Discussion:** The data showed excellent spread of contrast into the lateral recess and the ventral epidural space in all patients. There are various potential pathologies that can stimulate the nerve roots in the ventral epidural space and lateral recess of spinal canal, such as herniated intervertebral disc, epidural edema, facet synovitis, and facet instability. TRL approach allows direct access to spinal pain generators present in the ventral epidural space and lateral recess. TRL epidural injection can be performed more safely and is relatively familiar with conventional lumbar interlaminar epidural injection. As well as, TRL approach can deliver a relatively large amount of injectate in target-specific. Therefore, in lumbar degenerative disc disease patients with a relatively clear aggravating factor, this modality may increase a safety and efficacy of the therapeutic effect.



## EXPRESSION OF PROTEIN KINASE C (PKC) ISOFORMS IN THE INTERVERTEBRAL DISC CELLS

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### Introduction

Intervertebral disc degeneration(IDD) is caused by imbalance in the homeostasis of the extracellular matrix, including type II collagens and proteoglycan in the nucleus pulposus(NP) and leads to low back pain. It has been demonstrated that the activation of protein kinase C(PKC), a family of serine/threonine protein kinases, plays a role in cell growth and differentiation on the intervertebral disc area. Also, PKCs may mediate crosstalk with other major signaling pathways including wnt canonical and non-canonical. However, it is not identified that relevance of the Wnt signaling and the non-canonical Wnt signaling in the homeostasis of intervertebral disc(IVD). Therefore, the objective of this study is to identify relation between PKC isoforms and b-catenine expression on chondrocyte-like cells

### Method

Human disc tissues were collected during surgery from patients and cultured. The IVD cells were seeded at a cell density of 70 cells cm<sup>-1</sup> for protein and RNA isolation in condition treated with Phorbol 12-myristate 13-acetate(PMA, 200nM) for 24 hours. Western blot was performed to detect expressions of PKC  $\alpha$ ,  $\delta$ ,  $\epsilon$ ,  $\zeta$ , and phospho-PKC, b-catenine and RT-PCR was used to confirm aggrecan, type II collagen, GLUT-1, GAPDH, SOX9 and HIF-1 $\alpha$  at the mRNA.

### Result

The expressions of PKC  $\alpha$ ,  $\epsilon$ , and  $\zeta$  increased in condition treated with PMA comparing with condition without PMA. Furthermore, the expression of b-catenine at protein level was decreased in condition treated with PMA.

### Discussion

The activation of PKC induces the expression of PKC isoforms on the chondrocyte-like cells in the IVD. Therefore, the activation of PKC on chondrocyte-like cells affects senescence and dedifferentiation, which provides the possibility of turnover for degenerated chondrocyte-like cells. It is considered more observations on the relationship between Wnt signaling and their inhibitors and the signal of PKC downstream

## A SURVEY OF THE ATTITUDE ABOUT OSTEOPOROSIS AMONG PATIENTS WITH OSTEOPOROTIC VERTEBRAL FRACTURE

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**[Introduction]** Osteoporotic vertebral fracture (OVF) impairs the daily activities of the patient, resulting in sequential problems such as new fractures, pneumonia, and pressure ulcers. Accordingly, treatment of OVF is often difficult due to such problems. Although OVF has become a serious social problem because of its frequent occurrence, few studies mentioned about prevention of primary OVF. This study aimed to clarify the problems related to prevention and treatment of OVF through a survey of attitudes about osteoporosis among patients with OVF.

**[Methods]** In total, 17 patients suffering from OVF (OVF group) undertook a questionnaire regarding osteoporosis between June 2016 and October 2016 at our institute. The mean age at the time of injury was 75 years, 4 patients were male and 13 were female. Of these, 10 patients had primary osteoporosis, 5 had a potential of secondary osteoporosis, and 2 had previous OVF. Additionally, 7 patients without OVF or other fracture after falling, all female with an average age of 75 years, participated as the control group. The questionnaire consisted of 5 questions: whether the patient had an awareness of osteoporosis before injury, whether the patient had undergone examination for osteoporosis, whether the patient had been diagnosed with osteoporosis, whether the patient had been treated for osteoporosis, and whether they were actively trying to prevent osteoporosis.

**[Result]** In the OVF group, 14 patients (82%) were unaware of osteoporosis or the potential of osteoporosis. Among these 14 patients, 8 patients (57%) had undergone examination for osteoporosis, and only 2 patients were diagnosed with osteoporosis. The other 6 patients (43%) had never been examined for osteoporosis. 2 patients had no awareness of osteoporosis despite past treatment for osteoporosis. In patients without fracture after falling, no patient had awareness of osteoporosis; however, 6 patients (86%) were examined for osteoporosis and osteoporosis was not diagnosed. In the OVF group, 8 patients (47%) were participating in one method of osteoporosis prevention, 4 patients (24%) were participating in two methods, and the other 5 patients (29%) were not actively engaged in osteoporosis prevention. In the control group, 2 patients (29%) were participating in one method of osteoporosis prevention, 4 patients (57%) were participating in two or more methods, and only 1 patient (14%) was not actively engaged in osteoporosis prevention.

**[Discussion]** Patients with OVF had less awareness of osteoporosis or the potential of osteoporosis, and fewer patients underwent examination for osteoporosis before injury compared with patients without OVF. Among the OVF patients with awareness of osteoporosis following medical examination, fewer were actively trying to prevent osteoporosis compared with patients in the control group. To prevent OVF, diffusion of awareness about osteoporosis for more patients is necessary; furthermore, it is necessary for patients without osteoporosis to be educated regarding osteoporosis and actively participate in preventive measures.

## DIFFERENCE BETWEEN RHEUMATOID ARTHRITIS PATIENTS WITH DEGENERATIVE LUMBAR SCOLIOSIS AND NON-RHEUMATOID ARTHRITIS PATIENTS WITH DEGENERATIVE LUMBAR SCOLIOSIS IN WEDGING SEGMENT AND NON-WEDGING SEGMENT - MATCHED COHORT STUDY

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### Introduction

The lumbar lesion in rheumatoid arthritis (RA) have been paid less attention, but some previous studies demonstrated the high prevalence of degenerative lumbar scoliosis (DLS). The lumbar lesion accompanied with RA is often difficult to treat, and it is important to know the characteristics of lumbar lesion in RA patients. In ISSLS 2014, we reported the degree of osteophyte formation was less in DLS patients with RA. In this study, we focused on the extent of DLS and the degree of endplate and facet joint, and we evaluated these parameters in DLS patients with RA and without RA using plain X-ray and MRI.

### Material and Methods

A total of 54 patients (44 women and 10 men,  $69.4 \pm 5.4$  years, Cobb angle:  $14.6 \pm 5.9$ ) with scoliosis (Cobb angle of  $> 10^\circ$ ) who fulfilled the revised criteria of the American Rheumatism Association were included in this study. As control, age, sex, and Cobb angle matched 54 patients without RA were selected and also included. We evaluated the extent of DLS, superior/inferior end vertebra, apical vertebra and on plain X-rays and the degree of erosion in endplate and facet joint on MRI from L1/2 to L5/S using Yamada's classification. (Yamada et al. J Spinal Disord Tech 2014;27:E128-8211;E135) These parameters were compared between RA group and non-RA group.

### Results

The extent of DLS was greater in RA groups (RA group:  $5.0 \pm 1.3$  levels, non RA group:  $3.6 \pm 0.6$  levels). The level of apical vertebra located significantly upper in RA than non-RA group. The level of superior end vertebra located also significantly upper in RA group, but there was no significant difference in the level of inferior end vertebra between two groups. The degree of erosion in endplate and facet joint at L1/2 were significantly more severe in RA group.

### Discussion

The present results showed the extent of DLS was greater, the level of superior end vertebra and apical vertebra located upper level, and the degree of endplate and facet joint erosion were severe in RA patients. On the other hand, the degree of endplate and facet joint erosion from L2/3 to L5/S was not significantly different in two groups. From these results, injured endplate and facet joint at upper level might affect great extent of DLS in RA patients.

**PUBLICATION RATES OF ABSTRACTS PRESENTED AT A SCIENTIFIC SPINE MEETING: A RETROSPECTIVE ANALYSIS OF FOUR CONSECUTIVE MEETINGS BETWEEN 2009 AND 2012**

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**Introduction:** Publication rates of the presented abstracts are the recent point of interest in the literature. We aimed to make a follow-up study to depict the trend in publication rates of the abstracts presented at the annual meetings of the EUROSPINE between 2009-2012, including the EUROSPINE section of the Spineweek 2012.

**Methods:** We retrieved 962 abstracts from the corresponding published conference proceedings. The abstract titles and contributing author names were searched using Pubmed/MEDLINE and Google Scholar engines. For each published abstract we compared the content of the presented abstract in the proceedings with that of published abstract in the journals.

**Results:** Publication rate of the abstracts (oral presentations, special posters or short communications, posters) presented between 2009-2012 was 33%. Publication rates were the highest for the abstracts presented as oral presentations, and the rates were higher for the abstracts presented as special posters or short communications comparing to those presented as posters (40%, 30%, 26%;  $p= 0.0002$ ). Three hundred fourteen abstracts were published in 77 different journals, mostly in European Spine Journal (29%), and Spine (21%). Among those 314 published abstracts 56% were from Europe, 31% were from Asia, 9% were from North America, and 4% were from other continents.

**Discussion:** The publication rates of the abstracts presented at the annual meetings of EUROSPINE between 2009-2012 are comparable to the other international scientific meetings.

## CAN PREOPERATIVE ADMINISTRATION OF PROCHLORPERAZINE MALEATE PREVENT POSTOPERATIVE NAUSEA AND VOMITING AFTER SPINAL SURGERY?

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**[Introduction]** The mean frequency of postoperative nausea and vomiting (PONV) has been reported to be 20%. PONV causes discomfort to patients, prevents early ambulation, and thus, decreases patient satisfaction. Here, we investigated whether preoperative oral administration of prochlorperazine maleate prevents PONV after spinal surgery.

**[Methods]** In this retrospective study, we included 195 patients who underwent spinal surgery under general anesthesia at our hospital between April 2014 and September 2016. The patients were divided into two groups: 87 patients not receiving prochlorperazine (untreated group: April 2014 to May 2015) and 108 patients receiving prochlorperazine (treated group: June 2015 to September 2016). Patients in the treated group received oral administration of prochlorperazine at 6:00 am before surgery or at bedtime after surgery on the day of surgery. We compared the incidence of PONV, the number of patients receiving an intravenous injection of metoclopramide, and its dosage between the two groups. In addition, we assessed the patient sex, age, operative time, Apfel score, and use of intravenous patient controlled analgesia (IV-PCA).

**[Results]** The incidence of PONV was 35% in the untreated group and 25% in the treated group. Although not statistically significant, the incidence of PONV was lower in the treated group. The number of intravenous metoclopramide injections per patient with PONV was 1.41vial in the untreated group and 1.11vial in the treated group, which was not significantly different. Although the incidence of PONV was significantly high in patients with an operative time of 120 min, no significant differences were observed in Apfel score or sex. Among patients who received IV-PCA combined with droperidol, the incidence of PONV in the untreated group, 38%, was significantly lower than that in the treated group, 20%.

**[Discussion]** The incidence of PONV in patients undergoing spinal surgery is approximately 35%, which is not a low rate for a surgical complication. Prochlorperazine has a long half-life, and thus, oral administration of prochlorperazine before surgery may prevent PONV. Oral administration of prochlorperazine showed a decrease in the incidence of PONV; however, this decrease was not statistically significant. Moreover, prochlorperazine was effective in patients using postoperative IV-PCA, which suggested an alleviation of PONV, which is an adverse reaction to opioids. Our results indicate that preoperative administration of prochlorperazine may prevent PONV associated with spinal surgery. Further, when IV-PCA is used for postoperative pain control, preoperative administration of prochlorperazine is effective.

## ACUTE VERTEBRAL LOW COMPRESSION FRACTURES: AN EARLY SURGICAL TREATMENT BY KYPHOPLASTY ALLOWS QUICK FULL RECOVERY

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### Background

The treatment of traumatic low degree vertebral compression fracture (VCF) remains in a wide range between functional treatment, bracing, vertebroplasty, kyphoplasty, even surgical fixation. A transpedicular cemented titanium expansible implant for kyphoplasty (Spinejack, VEXIM) was an option that we systematically proposed to our patients under 70 years old.

### Objectives

The goal of our study was to check for the achievement of immediate stabilization (pain relief with avoiding the morbidity of using a brace) and for the restoration of the vertebral anatomy (assessment of the endplates and sagittal balance).

### Study Design & Methods

A continuous series of twenty-nine patients (thirty-two fractures) was followed starting January 2013. There were 16 women and 13 men. The type of fracture in the Magerl classification was A.1.1 in 10 cases, A.1.2 in 8 cases, A.1.3 in 8 cases and A.3.1. in 6 cases. We excluded patients with abnormal neurological status. Preoperative and postoperative Oswestry score and Visual Analogic Scale (VAS) were recorded as well as duration of hospital stay and radiological outcomes.

### Results

26 patients were operated in 7 days which followed the fracture, 3 between day 10 and 1 month. All patients got out of bed the first day after surgery except one who presented an epileptic stroke day 1 after surgery. The mean pain was 8/10 on the VAS, reduced to 3/10 the day following surgery. The average preoperative vertebral kyphosis was 14.7° reduced to 11,9° at last follow-up. Thirteen patients had a full recovery in six months (45%), eight in three months (28 %) and five in six months (17%). The mean stay in hospital after surgery was 1.5 days. None neurological event occurred during and after the surgery and none adjacent vertebral fracture was listed.

### Conclusions

The main benefit of this procedure is the immediate and lasting pain relief, the short stay in hospital, with no bracing or bed rest and quick return to daily life including professional activities. The good clinical result was associated to a radiological stable restoration of the vertebral anatomy.

## OVER 3-YEAR FOLLOW UP STUDY CONCERNING THE RETURN-TO-PLAY AFTER POSTERIOR LUMBAR INTERBODY FUSION FOR HIGHLY COMPETITIVE (NATIONAL OR PROFESSIONAL LEVEL) ATHLETES

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**Introduction:** To the best of our knowledge, there have been few studies regarding the clinical outcome and the state of return-to-play, and the adjacent segment disease after posterior lumbar interbody fusion (PLIF) for highly competitive (national or professional level) athletes with the long-term follow-up. The purpose of the present prospective study was to evaluate the minimum 3-year outcomes and the state of return-to-play after PLIF for highly competitive athletes (HCA).

**Methods:** Between 2005 and 2012, 5 consecutive patients met the criteria for inclusion in the study. They were HCA (2 gymnasts, kendo, basketball, and tennis players) with symptoms that had been unresponsive to an adequate trial of non-operative treatment. All patients underwent PLIF using pedicle screws and interbody cages. We used cannulated pedicle screws via percutaneous approach in one patient. They were 2 men and 3 women, and the mean age at surgery was 28.2 (18~53) years. All patients were prospectively followed, and we investigated the intervals between the surgery and return-to-play, the degrees of athletic activities, and the adjacent segment degeneration using the UCLA grading scale. Clinical outcomes were evaluated according to the criteria of Henderson. The mean duration of follow-up was 54.2 (36~92) months.

**Results:** At the time of return-to-play, the mean interval between the surgery and return-to-play was 5.5 (3.5~7) months. A highly competitive male kendo player could return to the lower athletic activity than his original athletic activity, and the other 4 HCA could return to their original athletic activities. Six months after the surgery, a female gymnast returned to her original athletic activity. However, 10 months after the surgery, radiographs showed a breakage of the 6.5 mm cannulated screw in the right pedicle of S1 (Fig.). At the most recent follow-up, 3 HCA could return to their original athletic activities, and 2 HCA could return to the lower athletic activity than their original athletic activity. Seventy-one months after the L4/5 PLIF, radiographs showed the L2 end plate sclerosis (Grade IV) in a female professional basketball player, and 92 months after the L4/5 PLIF, radiographs showed the L5-S1 osteophytes (Grade III) in a female professional tennis player, however, these were symptom-free and the clinical outcomes were not affected. The adjacent segment disease, which was required pain management postoperatively, was not observed in any athlete. Clinical outcomes were excellent in 1, good in 3, and fair in 1.

**Discussion:** We have been treated many athletes with symptoms that had been unresponsive to an adequate trial of non-operative treatment by PLIF. However, we have been treated not so many HCA by PLIF. The findings of the present small study suggest that our PLIF is a useful surgery that can lead to return-to-play and a good clinical outcome without the adjacent segment disease for HCA. We think this is because of their strong low back and abdominal muscles. However, the 6.5 mm cannulated screws were not enough to strong for HCA, and this problem could be resolved by the use of the thick and strong pedicle screws.

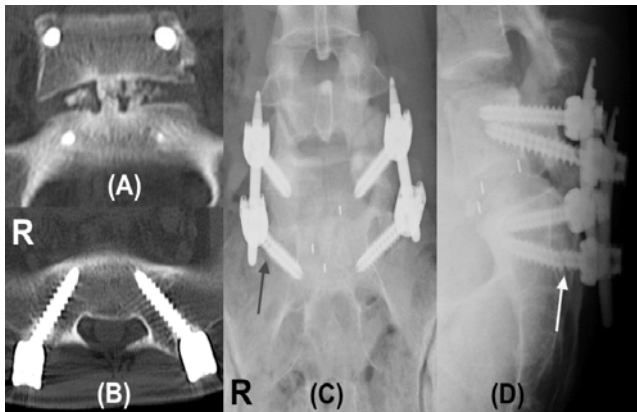


Fig. An eighteen-year-old highly competitive female gymnast. Preoperative myelogram showed the total block at the L5-S1 level due to the L5 spondylolytic spondylolisthesis. After L5-S1 decompressive laminotomy and posterior lumbar interbody fusion, the pain in the low back and left leg disappeared. Six months after the surgery, bone union was observed (A), and the position and length of the cannulated screws in the pedicles of S1 were not so bad (B). Therefore, she returned to play gymnastics. Ten months after the surgery, anteroposterior (C) and lateral (D) radiographs showed a breakage of the screw in the right pedicle of S1. Forty months after the surgery, she still has low back pain and mild pain in the legs.



## MAGNETIC RESONANCE IMAGING AND COMPUTED TOMOGRAPHY (CT) VS CT ALONE IN THE EVALUATION OF CERVICAL SPINE INJURY: A PROPENSITY MATCHED ANALYSIS

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**Introduction:** The optimal evaluation protocol (computed tomography [CT] alone vs CT and magnetic resonance imaging [MRI]) for patients with suspected cervical spine injury in the setting of blunt trauma remains controversial. Most prior research is impaired by the potential for selection and indication bias to confound results. We endeavored to evaluate the utility of CT-MRI in the diagnosis of cervical spine injury using propensity matched techniques.

**Methods:** This study included adult patients who received CT alone or CT-MRI for the evaluation of cervical spine injury between 2007-2014. The primary outcome was the identification of a cervical spine injury, with decision for surgery and change in management considered secondarily. A propensity score was developed based on the likelihood of receiving evaluation with CT-MRI and this score was used to balance the cohorts and develop two groups of patients around whom there was a degree of clinical equipoise in terms of the imaging protocol. Logistic regression was used to evaluate for significant differences in injury detection in patients evaluated with CT alone as compared to those receiving CT-MRI.

**Results:** In the time period under study, 8,060 patients were evaluated using CT and 693 with CT-MRI. Following propensity score matching, each cohort contained 668 patients. There were no significant differences between the two groups in baseline characteristics. The odds of identifying a cervical spine injury were significantly higher in the CT-MRI group, even after adjusting for prior injury recognition on CT (OR 2.6; 95% CI 1.7, 4.0;  $p < 0.001$ ). However, only 53/668 patients (8%) in the CT-MRI group had injuries identified on MRI not previously recognized by CT. Only a minority of these patients ( $n=5/668$ , 1%) necessitated surgical intervention.

**Conclusion:** In this propensity matched cohort, the addition of MRI to CT alone identified missed injuries at a rate of 8%. Only a minority of these were serious enough to warrant surgery. This speaks against the standard addition of MRI to CT-alone protocols in cervical spine evaluation after trauma.

## DESCRIPTION AND RESULTS OF A COMPREHENSIVE CARE PROTOCOL FOR OVERNIGHT-STAY LUMBAR SPINE SURGERY IN ADULTS

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### Introduction

Qualifying criteria for ambulatory or overnight-stay adult spine surgery are not well defined in either the spine or anesthesia literature. Most reports go simply to ASA risk classification or issues of surgical technique and do not thoroughly present a comprehensive defined management protocol.

We have designed a standard care protocol and applied it to a consecutive series of 83 adult patients with a large variety of common degenerative spine disorders, and report a high probability (98%) of successful morning-after discharge after adult spine surgery with this protocol.

### Methods

A standardized protocol of patient preparation, preoperative comorbidities optimization and perioperative care was applied in a prospective cohort of 126 patients. Office and hospital chart records were reviewed for relevant outcomes.

### Results

Fully 81 of 83 appropriately selected cases were able to successfully achieve uneventful same-day discharge without any need for readmission, unscheduled early ER or clinic visits, or other major complications. Both discharge failures were related to urinary retention in senior males, and both were resolved and discharged after a single-day admission to the inpatient ward.

### Discussion

The available literature to date on ambulatory and short-stay spine surgery is largely limited to presentations of ASA risk categorization and surgical technique alternatives as limiting or indicating such care but presents little discussion of details in case selection and management. We demonstrate that a wide variety of common degenerative lumbar spinal pathology in adults including limited instrumentations can be routinely managed on an overnight-stay basis without requirement for formal hospital inpatient admission.

## COMPARISON OF CLINICAL RESULTS AND FUSION RATES IN PLIF BETWEEN PLATE SYSTEM AND ROD SYSTEM

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### Background Context:

For instrumentation of PLIF, we have used plate system (Stefee: Depuy) until 2010, and after 2011 we have changed to rod system (Expedium: Depuy) with the increase of elderly patients. There was no report of surgical outcomes of PLIF regarding comparison for plate and rod system.

### Purpose:

The purpose of this study was to compare clinical and radiological outcomes of PLIF between plate and rod system.

### Materials and Methods:

The patients who underwent L4/5 single PLIF for L4 degenerative spondylolisthesis from 2010 to 2011 were included in this study. Plate group was 35 patients in 2010, and Rod group contains 33 patients in 2011. Follow up rate was 91.2%. Average age was 66.9 years old in Plate group and 69.1 years old in Rod group, respectively. There was no significant difference in age between two groups.

As for clinical assessment, pre and postoperative JOA score and recovery rate were investigated. In terms of radiological assessment, pre/postoperative % slip, fusion rate and loosening of pedicle screw (PS) were evaluated by XP. Fusion was defined as a radiographic condition in which bony continuity between graft bone and vertebra was detected by plain radiographs or reconstructed CT, without apparent motion at the fused segment on flexion and extension lateral radiographs.

### Results:

Pre and Postoperative JOA scores were 12.8 and 24.5 in Plate group and 13.5 and 24.4 in Rod group, respectively. Recovery rate was 73.9 % in Plate group and 71.7 % in Rod group, respectively. Pre and postoperative % slip in Plate group were 16.9 % and 3.6 %, while those in Rod group were 15.6 % and 8.8 %, respectively. Average reduction of % slip were 13.3% in Plate group and 6.8% in Rod group, respectively ( $P<0.05$ ). Fusion rate was 97.0% in Plate group and 96.6% in Rod group, respectively. The average fusion term was 12.8 months in Plate group and 8.6 months in Rod group, respectively. Loosening was observed in 35 PS (26.5%) of Plate group and 8 PS (6.8%) of Rod group ( $P<0.05$ ). The average term of PS loosening was 4.7 months in Plate group and 12.3 months in Rod group, respectively ( $P<0.05$ ). There was no statistical difference in clinical outcomes, fusion rate and fusion term between each group, while reduction of % slip was larger, PS loosening rate was more often, and loosening term was earlier in Plate group than Rod group. With regard to PS loosening, average age was older and fusion term was longer in patients with PS loosening overall each group.

### Conclusions:

In the present study, PS loosening rate was more often and loosening term was earlier in Plate group than Rod group, although plate system had an advantage in reduction. We speculated that plate system specific rigidity of the construct might affect the early PS loosening, especially in elderly patients. In fact, average age was older and fusion term was longer in patients with PS loosening. These results suggested that rod system should be recommended for elderly patients.

## PRECEPTS OBTAINED FROM OUR PATIENTS WHO UNDERWENT SPINE SURGERY DURING RECENT 15 YEARS SUGGESTED PREVENTION AND CONTROL OF HEMATOMA FOLLOWING SPINE SURGERY

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**Introduction:** Hematoma following spine surgery HFSS, one of the serious complications, is associated with severe pain and paralysis. While several precautions were taken, HFSS has not been completely prevented yet. The purpose of this study was to analyze HFSS rate in our hospital, to clarify its pathological condition, to consider how to prevent developing hematoma.

**Methods:** The subject is all 2,546 spine surgeries carried out by the same operator for 15 years. The patients with HFSS were selected from the subjects. The patient's condition and the causes inducing HFSS were investigated retrospectively. Furthermore the precaution for HFSS was considered based on the results.

**Results:** There were 20 cases (female 6, male 14) that hematoma was removed after spinal surgery. HFSS rate was 0.8% in our hospital. The details of the patients are as follows, median age 65 years old, (min. 36 years old, max. 81 years old), the part of spine (cervical 3 cases, thoracic 2 cases, lumbar 15 cases), and the area of surgery (one segment 11 cases, two segments 5 cases, more than three segments 3 cases). The cases with HFSS were various.

The patients' condition of HFSS was classified into two types, the fulminant type (14 cases) and the prolonged type (6 cases). The fulminant type developed within 24 hours after surgery, due to acute painful lesion and paralysis in the leg. The main symptoms of the prolonged type were persisting discomfort and slight paralysis in the legs, and hematoma was removed more than 24 hours later, maximum 24 days later.

The causes of hematoma were identified in 8 cases that included a failure in hemostasis; blood was oozing out from the bone marrow of the vertebral body and the epidural vessels in 5 cases and the intramuscular blood vessel in one case. In those cases, high blood pressure was associated with oozing. Blood gushed out into the surrounding tissues by anticoagulant drugs in 2 cases. The remaining 12 cases included a failure in drainage by clogging drain.

**Discussion:** In almost all patients with HFSS, mishap such as insufficient hemostasis in the end of surgery, blood pressure control, or drain management in addition to both the hemorrhagic diathesis and the thrombophilia of the patients involved developing HFSS. We considered the prevention and control of HFSS from the results. During spine surgery, the coagulation to the vessels (especially segmental artery) against the bleeding from the intervertebral foramen should be enforced and the hemostatic agent against oozing in the surgical site of the patients with hemorrhagic diathesis due to anticoagulant drugs should be used without exception. After spine surgery, clinicians should not let the drain clog up against the patient with thrombophilia. Clinicians including anesthesiologist should manage to keep blood pressure within the normal range in the recovering period of spine surgery.

## SPINAL CANAL DIAMETER IN CAUDA EQUINA SYNDROME PATIENTS IS SMALLER THAN IN THE AVERAGE HERNIATED DISC PATIENT: AN MRI STUDY.

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**Introduction** The correlation between clinical and imaging features in cauda equina syndrome (CES) has not been studied before. The aim of this study is to evaluate 1) the association between clinical features of CES and magnetic resonance imaging (MRI) at presentation, 2) the predictive value of MRI for CES outcome and 3) differences in sagittal spinal canal diameter on MRI in herniated disc patients with and without CES.

**Methods** Consecutive patients presenting with a CES in our clinic were radiologically evaluated (n=75). MRIs were assessed by a neurosurgeon, who was blinded for clinical presentation or outcome, for: level of herniated disc; degree of cauda equina compression; type of compression (uni- or bilateral); sagittal spinal canal diameter (at each disk and mid-vertebral level). Lumbar herniated disc patients without CES, operated in the same center, acted as a control group for spinal canal diameter. Baseline characteristics (age; gender; micturition/defecation/sexual dysfunction, sensory changes of the saddle area and sciatica at presentation; duration of complaints of herniated disc at presentation; duration of complaints associated with CES at presentation), time to decompression and follow up data (micturition/defecation/sexual dysfunction, sensory changes of the saddle area and sciatica at discharge from the hospital [follow up moment 1, FU 1]) were extracted from the existing database and used for regression.

**Results** Twenty-seven MRIs could not be retraced; therefore, 48 patients were included (47% male; mean age 43 years). Lesion at MRI was most common at L5S1 (49%), followed by L4-L5 (39%). Eighty-two percent displayed bilateral compression at MRI. Sixty percent of patients displayed 100% compression of the cauda equina at MRI. All patients were surgically decompressed. Two FU moments served as outcome points, with a median of 48 hours postoperatively (FU 1) and a median of 56 days postoperatively (FU 2). MRI did not correlate with clinical features at presentation nor with outcome. In the evaluation of patient characteristics, women were found to have more defecation dysfunction at presentation (p=0.036; OR 10.3). A shorter time to decompression was associated with less sciatica at FU 1 (p=0.022 OR 2.83), which effect was not seen anymore at FU 2. In 26 CES patients, morphometrical data of the spinal canal could be obtained; the control group consisted of 31 herniated disc patients. At all levels (both disc and intervertebral levels), CES patients displayed significantly smaller diameters than the control group, largest p-value =0.002 (Table 1.1). When compared to standardized measurements from literature<sup>1</sup>, diameters of all levels were significantly more often below average in CES patients than in the control group (Table 1.2).

**Discussion** This is the first study to reveal a difference in spinal canal size between herniated disc patients with and without CES. This finding implies that lumbar herniated disc patients with a relative small spinal canal should be approached differently in managing complaints of herniated disc, to prevent progression to CES. Since the number of studied patients is relatively small, further (multicenter) research should be conducted before clinical consequences are considered.

Table 1.1: Mean sagittal spinal canal diameter in mm

	CES patients (n=26)			Controls (n=31)			P value
	N not measured*	Mean ±SD	Minimum-maximum	N not measured**	Mean ±SD	Minimum-maximum	
L1	0	14.06±1.99	10.0-18.0	0	16.10±1.40	14.0-18.0	<0.001
L1-L2	0	12.92±3.19	6.0-20.0	0	15.58±1.52	12.0-18.0	<0.001
L2	0	12.90±2.60	7.0-18.0	0	15.26±1.37	13.0-18.0	<0.001
L2-L3	1	11.88±2.40	6.0-16.0	0	14.55±1.77	11.0-18.0	<0.001
L3	0	11.54±2.16	7.0-16.0	0	14.32±1.72	11.0-17.0	<0.001
L3-L4	3	10.91±2.01	6.0-15.0	1	13.23±1.63	10.0-16.0	<0.001
L4	0	10.58±2.02	7.5-14.0	0	14.13±1.77	11.0-18.0	<0.001
L4-L5	8	10.06±2.30	5.0-14.0	11	12.75±2.51	9.0-20.0	0.002
L5	2	9.94±1.60	7.0-14.0	0	13.87±2.17	10.0-20.0	<0.001
L5-S1	15	9.09±2.35	5.5-14.0	22	15.56±2.40	12.0-20.0	<0.001

\*not measured due to: herniated disc (n=27; 1 patient had a double lesion), quality too poor at specific level for measurement (n=2, at L5).

\*\*not measured due to: herniated disc (n=33), quality too poor at specific level for measurement (n=1, at L5S1).

Table 1.2: Proportion with smaller than average sagittal diameter of the spinal canal in %

*	CES patients (n=26)	Controls (n=31)	P value
L1 (<14.1mm)	53.8	16.1	0.003
L1-L2 (<15.6mm)	84.6	54.8	0.016
L2 (<13.2mm)	50.0	12.9	0.002
L2-L3 (<15.1mm)	96.2	64.5	0.004
L3 (<12.6mm)	65.4	16.1	<0.001
L3-L4 (<13.8mm)	84.6	51.6	0.001
L4 (<12.4mm)	80.8	19.4	<0.001
L4-L5 (<12.9mm)	61.5	35.5	0.021
L5 (<12.4mm)	88.5	32.3	<0.001
L5-S1 (<11.6mm)	38.5	29.0	<0.001

\*cut off values derived from Chatha et al

- Chatha DS, Schweitzer ME (2001). MRI Criteria of Developmental Lumbar Spinal Stenosis Revisited. Bulletin of the NYU Hospital for Joint Diseases;69(4):303-7.

## EFFECTIVE REPAIR OF DURAL TEAR USING BIOABSORBABLE SHEET WITH FIBRIN GLUE

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### Background context

Cerebrospinal fluid (CSF) leakage caused by dural tear can often be difficult to manage even after repair when the same materials are used in a similar manner.

### Purpose

This study aimed to compare the techniques of surgical repair of dural tear using bioabsorbable material and fibrin glue.

### Study Design/Setting

Basic Science

### Methods

Burst pressure was measured for repaired porcine dura with holes of different diameters using spray of combined fibrinogen and thrombin solution (fibrin spray) alone as a control and the 5-mm hole following different methods using fibrinogen and thrombin solutions plus polyglactin 910 sheet (PGS). For group 1, fibrinogen was applied on the dura followed by PGS and thrombin. For group 2, thrombin followed by PGS and fibrinogen. For group 3, fibrinogen followed by PGS and fibrin spray. For group 4, thrombin followed by PGS and fibrin spray. Microscopic observation was conducted for each specimen.

### Results

Repair using fibrin spray alone was successful for the 0.3-mm diameter pinhole (breakdown pressure:  $27.8 \pm 8.6$  mmHg), but was not able to cover the 2.7- and 5-mm holes. For a 5-mm diameter hole, the breakdown pressure was  $54.4 \pm 38.8$  mmHg in group 1,  $26.3 \pm 19.4$  mmHg in group 2,  $147.7 \pm 65.0$  mmHg in group 3, and  $35.5 \pm 23.4$  mmHg in group 4 ( $p < 0.001$ ). There was little fibrin glue in the burst layer between the dural surface and PGS with thrombin on the dural surface (group 2 and group 4) (Fig. 1).

### Conclusions

Use of fibrin spray with PGS was effective in resisting burst pressure of the repaired dura. However, application of thrombin on the dura inhibited it. Suppression of CSF leakage could be successful by performing several cycles of the group 1 method, followed by the group 3 method, with thrombin solution wash each time.

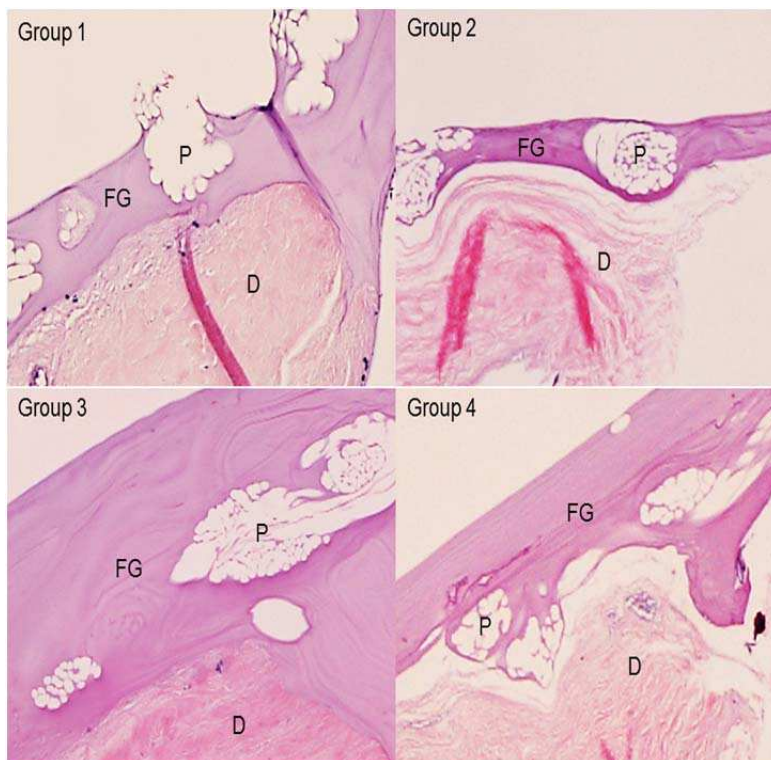


Fig. 1 Microscopic observation of dura augmented by fibrin glue and polyglactin 910 sutures sheet

## ASSESSMENT OF PELVIC OBLIQUITY IN NEUROMUSCULAR SCOLIOSIS USING THE EOS-CHAIR® PROTOCOL

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### Introduction

Scoliosis with pelvic obliquity (PO) is the most common deformity especially in patients with trunk hypotonia and quadriplegia. The development of a severe trunk deformity associated with the inherent neurological disorder can significantly restrict the patients' functional capacities and maximize the need for nursing care. Scoliosis with pelvic obliquity (PO) could be investigated with the EOS-CHAIR protocol as the most common deformity especially in patients with trunk hypotonia and quadriplegia. However, the intra-observer and inter-observer reliability of various angles assessing PO was not investigated with this new imaging protocol.

### Methods

A retrospective cohort of 36 EOS frontal full-spine acquisitions made in sitting position was used. PO was assessed using three different angular measurements (Figure 1):

- The Sacro-Iliac Pelvic Obliquity Angle (SIPOA) was measured by defining a sacroiliac line between the inferior edges of both sacroiliac joints on the frontal radiograph, the perpendicular to this line and the spinous process of T1 to the middle of the sacroiliac line (Figure 1A).
- The Iliac Crest Pelvic Obliquity Angle (ICPOA) was measured by defining a iliac crest line between the upper part of both iliac crests on the frontal radiograph, the perpendicular to this line and the spinous process of T1 to the middle of the iliac crest line (Figure 1B).
- The Ischiatic Pelvic Obliquity Angle (IPOA) was measured by defining a ischiatic line between the lower part of both ischiatic bones on the frontal radiograph, the perpendicular to this line and the spinous process of T1 to the middle of the ischiatic line (Figure 1C).

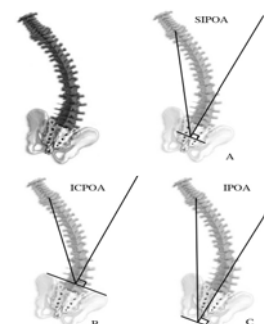
These three angles were assessed in a intra-observer and inter-observer study. Computer-assisted measurements of the three different angles were made in the 36 cases by two different observers (JR and RA), on 2 separate occasions, in random order using the same software. For all comparisons, the reliability between the two series of measures was assessed using Spearman's rank correlation test, a t test and intraclass correlation coefficient (ICC) and the limits of agreement by Bland and Altman.

### Results

The use of the EOS-CHAIR protocol was implemented satisfactory with a high acceptance rate by all caregivers, patients and their families. Intra-observer and inter-observer reliability was excellent for the three tested angular measurements.

### Conclusions

As for idiopathic scoliosis, we postulate the EOS system as being superior to standard radiographs to assess 3D spinal deformities in neuromuscular conditions. The EOS-CHAIR protocol improve preoperative comprehension of the lumbosacral junction anatomy in patients with poor standing or sitting postures. Our results show a very high reliability of three different angular measurements of the frontal pelvic obliquity in sitting position. Then it is possible to use one of these three angles as well as the others to assess frontal pelvic obliquity in neuromuscular patients. This frontal Pelvic Obliquity protocol in sitting position with the EOS-CHAIR is a validated measurement technique that needs to be used now to measure PO as a critical parameter of the global trunk balance in neuromuscular patients.



## TEN-YEAR FOLLOW-UP OF PATIENTS ENROLLED IN THE FDA-REGULATED TRIAL FOR SINGLE-LEVEL LUMBAR TOTAL DISC REPLACEMENT: ONE SITE'S EXPERIENCE

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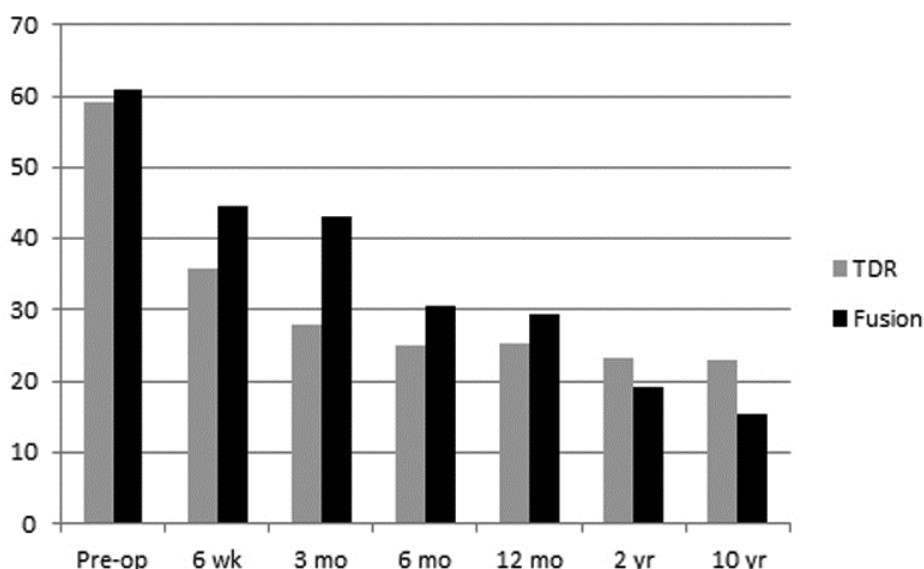
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**Introduction:** There have been several prospective studies evaluating lumbar total disc replacement (TDR) with up to 5-year follow-up reporting stable outcomes from early post-operative visits. The purpose of this study was to evaluate outcomes of patients enrolled in the FDA-regulated trial evaluating safety and efficacy of a lumbar total disc replacement 10 years after the study surgery.

**Methods:** This was an additional follow-up evaluation made at least 10 years after surgery of patients enrolled at one site participating in the prospective, randomized, controlled FDA-regulated trial for ProDisc-L (mean follow-up 11.4 yr).

129 patients were identified who enrolled in the trial (TDR n=34 vs. combined anterior/posterior fusion n=17) or the continued access study arm (all received TDR n=78). Questionnaires patterned after those used for the original study were mailed to patients. After two mailings, telephone contact was attempted. Online search services and other records were used to try to get current addresses. To date, 10 year follow-up data have been collected for 56 TDR patients, 5 fusion patients, and 5 patients are deceased (none related to surgery). Outcome measures included a modified Oswestry Disability Index (ODI), visual analog scale (VAS) assessing pain and also satisfaction, and any subsequent lumbar spine surgery. Self-reported outcomes data were analyzed for patients with minimum 10 year follow-up available, making comparisons to earlier time periods more relevant.

**Results:** Statistically significant improvements achieved as early as 6-week to 3-month follow-up were maintained throughout 10-year follow-up. The mean scores on the ODI are shown in Figure 1.



**Figure 1.** Mean ODI scores improved significantly early after surgery and the scores remained stable throughout 10-year follow-up.

VAS pain scores followed a similar pattern to the ODI scores. Satisfaction scores remained stable throughout follow-up. At least 80% of the TDR and fusion groups had a minimum 15 point improvement in their ODI scores when comparing pre-operative to the 10-year follow-up scores.

None of the 5 fusion patients and 12 of the TDR patients for whom 10-year follow-up was available underwent reoperation. Reasons for early re-operations were to reposition a polyethylene core that had been placed incorrectly, removal of a spinal cord tumor, spinal cord stimulation for severe pain, one patient underwent fusion at the TDR level due to bilateral pars fracture that was later identified as present but not recognized at the time of TDR, which is a contra-indication for TDR. The majority of remaining re-operations were at an adjacent segment.

**Discussion:** These results indicate that outcomes for this subset of patients for whom minimum 10 year follow-up could be collected remained stable from early postoperative scores. Significant improvements in mean scores noted within 3 months of surgery were maintained through 10 years. Of note, there were no indications of mechanical device failure during this long-term follow-up such as procedures to remove the devices and/or stabilize the TDR level. The clinical outcomes in this study parallel those from European studies with follow-up of 10 or more years after TDR.



## THE OUTCOME OF PEDICLE SCREW INSTRUMENTATION REMOVAL FOR ONGOING LOW BACK PAIN FOLLOWING POSTEROLATERAL LUMBAR FUSION

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**Introduction:** Our aim was to determine whether patients derived benefit from removal of pedicle screw instrumentation for axial pain without other cause using our surgical technique and patient selection. A secondary aim was to investigate factors that were associated with poorer outcomes for this procedure as well as complication rate in this cohort.

**Methods:** Theater records from a single spinal surgeon's practice were reviewed to identify patients that had undergone lumbar fusion for discogenic back pain with subsequent pedicle screw instrumentation removal (Expedium, DePuy Synthes) in the preceding 3 years with a minimum of 18 months follow-up. Inclusion criteria were persisting midline axial back pain with computed tomography (CT)-confirmed solid fusion with non-radicular symptoms and nil other potential causes found, e.g., infection. Case note review along with pre- and post-operative Oswestry disability index (ODI) questionnaires and visual analog scores (VAS) were assessed for all patients. Surgical technique included re-use of previous midline posterior incision and the Wiltse approach with removal of implants, confirmation of a solid fusion mass, washout and bone grafting of removal sites.

**Results:** From 50 consecutive patients who underwent removal of posterolateral instrumentation for an index elective lumbar fusion for discogenic back pain, 34 patients were identified that met the criteria with a mean follow-up of 25 months (range, 18-36 months). The VAS and ODI improved in 22/34 (65%) of participants. The mean cohort VAS score was 6.6 pre-surgery and 4.3 post-surgery ( $P=0.04$ ). Preoperative and postoperative mean Oswestry disability scores were 64 and 41, respectively ( $P=0.05$ ). There was a statistically significant difference in the proportion of patients with poorer compared to satisfactory outcomes with regards to compensable status, preoperative grade II opioid use and shorter time between fusion and removal procedure. Complications were one postoperative hematoma and one superficial wound infection, both of which settled without re-operation.

**Discussion:** Approximately two thirds of patients were satisfied with removal of instrumentation for treatment of residual low back pain (LBP) following elective lumbar fusion and recorded reduced VAS and grade II opioid use. A subset of patients remained that did not derive benefit and were associated with compensable status, preoperative grade II opioid use and a shorter time between fusion and removal procedure. A prospective cohort study with preoperative diagnostic injections and standardized imaging and microscopic techniques would strengthen future studies. However, this study suggests that removal of instrumentation is safe and provides modest benefit as a palliative procedure for a subset of patients with significant disability from chronic LBP without an underlying cause following lumbar fusion.

## ADMINISTRATION OF TERIPARATIDE AFTER BALLOON KYPHOPLASTY TO TREAT OSTEOPOROTIC VERTEBRAL FRACTURES PREVENTS SUBSEQUENT VERTEBRAL FRACTURES.

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**[Objective]** Balloon kyphoplasty (BKP) is useful for treating osteoporotic vertebral fractures (OVF), but the postoperative outcomes worsen when subsequent vertebral fractures occur. There are reports indicating that the administration of teriparatide (PTH) prevents the onset of post-BKP vertebral fractures and in the present study, we compared the postoperative clinical course for one or more years between subjects who received PTH after undergoing BKP (PTH group) and subjects who did not (non-PTH group).

**[Subjects and Methods]** Of 66 patients who received BKP for OVF between February 2012 and September 2015, 43 patients (2 men and 41 women) who could undergo follow-up assessments for at least a year postoperatively were included in this study. Their mean age at the time of surgery was 79.4 years and mean duration of postoperative follow-up observation was 23 months. The injured vertebral bodies were in the thoracolumbar (T10 - L2) in 34 subjects and in the middle to lower lumbar (L3 - L5) in 8 subjects. After deciding to perform BKP, we provided patients with an explanation regarding PTH, and PTH was administered either daily (group D: 15 subjects) or weekly (group W: 15 subjects) based on the patient's wishes. PTH was started prior to surgery and continued for at least 12 months. For the remaining 13 subjects (group C), PTH was not used and as a rule, bisphosphonates were given. Subjects wore a Damen corset for two months postoperatively. The items investigated were preoperative bone mineral density (BMD), the injected volume and filling pattern of the intravertebral cement, visual analog scale (VAS)-based scores for lower back pain before, immediately after, and six months after surgery and at the final follow up examination, and the incidence of post-BKP vertebral fracture. Scheffé's method was used for multiple comparisons to test intergroup differences.

**[Results]** Preoperative BMD (%YAM) was 64.2 in group D, 61.3 in group W and 63.6 in group C. The volume of cement injected (ml) was 5.4 in group D, 4.8 in group W and 5.2 in group C. There were no intergroup differences in these parameters. The VAS scores (preoperative→postoperative→six-month postoperative→final follow-up scores) in groups D, W, and C were 7.9→2.0→1.6→1.9, 7.9→1.4→1.9→1.7 and 7.5→1.8→1.4→2.5, respectively, showing significant improvements over the course compared with the preoperative scores, with no differences among the three groups. The incidence of post-BKP vertebral fractures was 6.7% in group D, 13.3% in group W, and 53.8% in group C, and was significantly higher in group C ( $p<0.05$ ) with no difference between groups D and W. The cement filling pattern was 'solid' in 9 of 10 subjects who experienced a vertebral fracture after BKP.

**[Discussion]** The incidence of post-BKP vertebral fracture was 23.3% in this case series, which was comparable to the rates documented in various previous reports and the rate of spontaneous occurrence of vertebral fractures. The incidence of post-BKP vertebral fracture in the PTH group (10%) was significantly lower than in the non-PTH group, suggesting that PTH is effective to prevent subsequent vertebral fractures from occurring after BKP.

## THE LONG-TERM CLINICAL EFFICACY OF SINGLE SEGMENT LUMBAR 4-5 FUSION AND ITS EFFECT ON THE LUMBAR-PELVIC SAGITTAL ALIGNMENT PARAMETER

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### Introduction:

The effect of lumbar fusion of single segment 4-5 (SL4-5) with lumbar healthy adjacent segments on the Lumbar-Pelvis Sagittal Alignment parameter, radiographic ASD (rASD) and its clinical efficacy was discussed according to lumbar types (Roussouly Type).

### Methods:

Between March 2008 and March 2012, 317 patients with lumbar fusion of SL4-5 were collected. 51 cases of them met the inclusion and exclusion criteria (25 males and 26 females, with an average age of 43.45). They were categorized to 4 types according to the types of Roussouly. We compared the VAS, ODI, and JOA scores, and the Lumbar-pelvic parameters, such as pelvic incidence (PI), sacral slope(SS), pelvic tilt (PT), lumbar lordosis (LL), UP arc and intervertebral lordosis of lumbar 4-5(IVA4-5), C7 plumb line /Sacro-femoral distance ratio (C7PL/SFD ratio), of the patients in the preoperative and postoperative and final follow-up. MRI was adopted to evaluate ASD before the surgery, and the UCLA Grading Scale and intervertebral stability criteria of lumbar degeneration were introduced to evaluate ASD after the operation. Changes of the parameters in different periods were statistically analyzed.

### Results:

Mean follow-up time was 42.58 months (36 to 67 months). The distribution of patients according to Roussouly types was high proportion: Type II: 15 cases (29.42%) and Type III: 20 cases (39.22%). In Type I group: There were significant improvement ( $P < 0.01$ ) in LL, UP arc, IVA4-5 and SS in Postoperative and final follow-up, compared with that in preoperative, but PT was decreased. In Type II and III: IVA4-5 significantly improvement ( $P < 0.05$ ) in the postoperative and final follow-up compared with that in preoperative, the LL in follow-up significantly increased ( $P < 0.05$ ) compared with that in preoperative, while the SS, PT, and PI showed no significant differences. In Type II UP arc was significantly increased in the final follow-up. In Type IV: The IVA4-5 ( $P < 0.05$ ) significantly increased with statistically significant differences to the preoperative, but there was no significant difference in LL, UP arc, SS, PT and PI between preoperative and postoperative. The ratio of C7PL/SFD was significantly decreased in the postoperative and final follow-up compared with that in preoperative in all types. Postoperative and follow-up of patients had significant improvement over preoperative in VAS, ODI, JOA scores. The general prevalence of rASD was 17.64% in all patients. Analysis of rASD risk factors found that: Age, follow-up time, PI, IVA4-5 is a major factor.

### Discussion:

SL4-5 can significantly increase IVAL4-5, but have different effects to spine-pelvis Sagittal Alignment parameters according to types of Roussouly. IVA4-5 is a significant risk factor, the greater the age, the longer follow-up time, higher PI values more prone to rASD. The view of select the appropriate intervertebral fusion angle is possible to change the adjacent segment degeneration process, reduce the incidence of rASD and improve patient prognosis.

## TREATMENT OF CHRONIC LOW BACK PAIN VIA ABLATION OF THE BASIVERTEBRAL NERVE: RESULTS OF THE SMART TRIAL

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**Introduction:** The INTRACEPT™ Intraosseous Nerve Ablation System is the first targeted therapy to relieve chronic axial low back pain in the presence of Modic type 1 or 2 abnormalities by denervating the nociceptive pain signaling within the vertebral body (VB). The Intracept System uses bipolar radio frequency (RF) energy to ablate the basivertebral nerve (BVN), delivered by a minimally invasive, transpedicular approach. The BVN is an intraosseous sensory nerve within the vertebral body, whose role in afferent pain transmission is thought to be a source of chronic axial low back pain associated with degenerative VBs or VB endplates.

**Methods:** 225 patients at 15 sites in the United States and 3 in Germany were enrolled in this prospective, double blinded, randomized, sham controlled SMART study. 147 patients were randomized to the Intracept System arm (received the treatment); 78 were randomized to the Sham arm (received sham surgery). Follow-up was at 2 and 6 weeks, 3, 6, and 12 months. Both the patients and the physicians providing postoperative care were unaware of the treatment assignment until the conclusion of the one year follow-up. Criteria for enrollment included chronic (>6 months), non-radicular low back pain failing 6 months of conservative care.

**Results:** Targeting success (assessed by postop MRI) was achieved in 300 of the 317 treated and evaluated vertebral bodies (94.6%); or in 129 of 145 patients (89.0%). Results of the primary end point analysis for the per protocol (PP) population at 3 months showed that the ODI improvement observed in the Intracept arm (LS mean = 20.5 points) was statistically superior (p=0.019) to the Sham arm (LS mean = 15.2 points). The mean improvement in ODI in the Intracept patients (PP population) at 3 months was twice the 10-point MCID for ODI as recognized in the published literature. This result was sustained through two years of follow-up. Furthermore, an analysis of ODI responder rates found that 75.6% of patients treated with the Intracept System demonstrated a greater than 10-point, clinically meaningful improvement in their low back pain and associated disability at 3 months. There were no unanticipated adverse device effects. There were no device related serious adverse events (SAE) and only one procedure related SAE. The rates of neurological events reported were minimal and comparable between treatment arms. MRI evaluations at the 6-week and 6-month follow-up time points found no evidence of any spinal canal abnormalities, avascular necrosis or accelerated disc degeneration.

**Discussion:** The Intracept System is safe, well tolerated, and effective for the treatment of chronic low back pain in this patient population. This conclusion is based on the results of the analysis of the primary study end point that showed a significantly greater improvement in ODI for the Intracept System arm over the Sham arm in the PP population. The majority of patients treated with the Intracept System reported improvement in their low back pain and associated disability throughout the follow-up period. BVN ablation with the Intracept System represents a new, minimally invasive, treatment for CLBP.

## SLIP REDUCTION IMPROVES GLOBAL SAGITTAL BALANCE AND SPINOPELVIC HARMONY IN LUMBAR DEGENERATIVE SPONDYLOLISTHESIS SURGERY

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**Introduction:** In the surgical treatment of lumbar degenerative spondylolisthesis (LDS), the main goal is to decompress the neural elements and stabilize the unstable spinal segment. However, the role of slip reduction in the surgical management of LDS remains controversial. Recently, the importance of restoration of global sagittal balance and spinopelvic harmony has been advocated, even in short-segment lumbar fusion surgery. In this study, we evaluated the impact of slip reduction on global sagittal alignment and spinopelvic parameters in LDS surgery.

**Methods:** To exclude the influence of surgery-related back muscle damage on spinopelvic parameters, 48 patients with single-level LDS (Meyerding grade I or II) and same-level stenosis, who underwent minimally invasive (MI) surgery from 2012 to 2015, were retrospectively reviewed. The reduction group consisted of 32 patients (mean age, 60.3 years) who underwent single-level MI posterior lumbar interbody fusion, where we attempted to reduce spondylolisthesis to the maximum extent possible. Sixteen other patients (mean age, 64.3 years) who underwent single-level endoscopic bilateral decompression via a unilateral approach without fusion served as a control group to exclude the influence of simple decompression on spinopelvic parameters. Radiographic parameters such as sagittal vertical axis (SVA), pelvic incidence (PI), pelvic tilt (PT), lumbar lordosis (LL), PI minus LL (PI-LL), %slip, and slip angle (SA) were measured preoperatively and 1-year postoperatively using standing full-length radiographs.

**Results:** Among 48 patients, preoperative %slip was significantly correlated with preoperative SVA ( $r = 0.47$ ), LL ( $r = -0.36$ ), and PI-LL ( $r = 0.46$ ). Between the 2 groups, preoperative SVA, PI, PT, LL, and PI-LL were not significantly different. SA increased significantly after surgery in both groups (reduction group:  $8.9^\circ \rightarrow 11.7^\circ$ ; control group:  $13.0^\circ \rightarrow 15.1^\circ$ ); however, the %slip decreased significantly only in the reduction group (reduction group:  $17.3\% \rightarrow 4.1\%$ ; control group:  $10.5\% \rightarrow 10.5\%$ ). Although PT and PI-LL significantly improved after surgery in both groups, there was a trend toward greater improvement in the reduction group compared to the control group. SVA significantly decreased and LL significantly increased after surgery only in the reduction group (reduction group:  $43.0 \text{ mm} \rightarrow 24.9 \text{ mm}$  and  $39.7^\circ \rightarrow 46.1^\circ$ ; control group:  $38.2 \text{ mm} \rightarrow 32.2 \text{ mm}$  and  $44.3^\circ \rightarrow 47.2^\circ$ , respectively). The change ( $\Delta$ ) in the %slip after surgery (postoperative value minus preoperative value) was significantly correlated with  $\Delta$ SVA ( $r = 0.35$ ),  $\Delta$ LL ( $r = -0.39$ ), and  $\Delta$ PI-LL ( $r = 0.43$ ). A prediction formula to calculate  $\Delta$ LL using stepwise regression analysis is as follows:  $\Delta$ LL =  $0.787 + 0.878 \times (\Delta$ SA) -  $0.254 \times (\Delta$ %slip).

**Discussion:** Decompression alone improved spinopelvic parameters after surgery; however, fusion with slip reduction further improved global sagittal balance and spinopelvic harmony in LDS surgery. Spinopelvic alignment is increasingly being recognized as important for long-term surgical success, even in short-segment lumbar fusion surgery, since spinopelvic alignment is reported to play a role in the development of adjacent segment pathology. The relationship between slip reduction and the development of adjacent segment pathology is an issue to be addressed in the future.

## A RETROSPECTIVE ANALYSIS OF SAGITTAL ALIGNMENT AFTER VERTEBROPLASTY WITH POSTERIOR INSTRUMENTATION FOR OSTEOPROTIC VERTEBRAL FRACTURES PRESENTING NEUROLOGICAL DEFICITS

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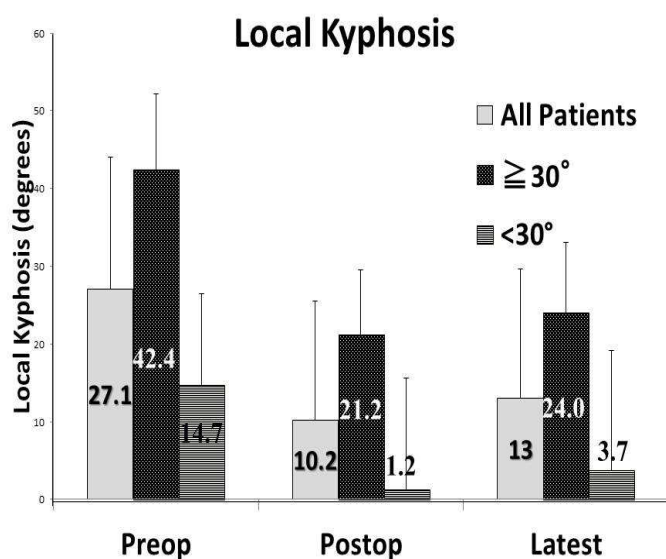
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**PURPOSE.** It has been reported that vertebroplasty with posterior instrumentation provides sufficient neurological recovery in patients with osteoporotic vertebral fractures with neurological deficits. However, the capability of this procedure in kyphosis correction remains uncertain. The purpose of this study was to investigate the effects of preoperative amount of local kyphosis and concomitant posterior decompression on postoperative sagittal alignment and fusion rate.

**METHODS.** Seventy-five patients who underwent vertebroplasty with posterior instrumentation for osteoporotic vertebral fractures with neurological deficits were reviewed. There were 58 female and 17 male patients with a mean age of 76.6 years. Follow-up period was minimum two years (2 to 8 years). Vertebroplasty was performed using calcium phosphate cement for fractures with intravertebral cleft, while HA block used for fractures without cleft. For myelopathy, 2-above 1-below instrumentation was performed using pedicle screws (PS) combined with lamina hook at the distal end. For cauda-equina or nerve root lesions, 1-above 1-below fixation with PS was performed. 43 patients underwent posterior decompression. Posterolateral local bone graft was done in all cases. Local kyphosis was evaluated preoperatively, postoperatively, and at the latest follow-up. Then, the patients were divided into two groups according to preoperative degrees of kyphosis. Large Kyphosis group was defined as 30° or more (n = 32), while Small Kyphosis as less than 30° (n = 43). Kyphosis correction and loss of correction were compared between the two groups. Also, all patients were divided into another two groups such as Decompression (+) group (n = 43) and Decompression (-) (n = 29). Effects of posterior decompression on postoperative kyphosis and fusion rate were evaluated.

**RESULTS.** Bony fusion was obtained in 72 of 75 patients (96%). It was 31 of 32 patients (97) in Large Kyphosis group, and 41 of 43 patients (95%) in Small Kyphosis group. Also, it was 98% in Decompression (+) group, and 94% in Decompression (-) group. As shown in Figure 1, average local kyphosis in all cases was 27.5° preoperatively, 10.7° postoperatively, and 13.6° at the latest follow-up. Mean loss of correction was 2.9°. In Large Kyphosis group, mean local kyphosis was 42.7° preoperatively, 21.2° postoperatively, and 24.0° at the latest follow-up. Loss of correction was 3.8°. In Small Kyphosis group, it was 14.7°, 1.2°, and 3.7°, respectively. Loss of correction was 2.5°. Posterior decompression did not affect loss of correction and fusion rate.

**DISCUSSION.** Degree of preoperative kyphosis did not affect fusion rate. In Small Kyphosis group, kyphosis correction was sufficient and loss of correction was little. Therefore, fractures with kyphosis less than 30° are the good indications for this procedure. In Large Kyphosis group, however, over 20° of kyphosis remained after surgery, indicating limitations of this procedure in kyphosis correction. Hence, this procedure can be indicated for the patients with severe kyphosis as long as the aim of surgery is to improve neurological deficits, however, different procedure should be considered if correction of severe kyphosis is required. Posterior decompression did not affect postoperative kyphosis and fusion rate, and may be performed if required.



## VERTEBRAL ARTERY LOOPS IN SURGICAL PERSPECTIVE

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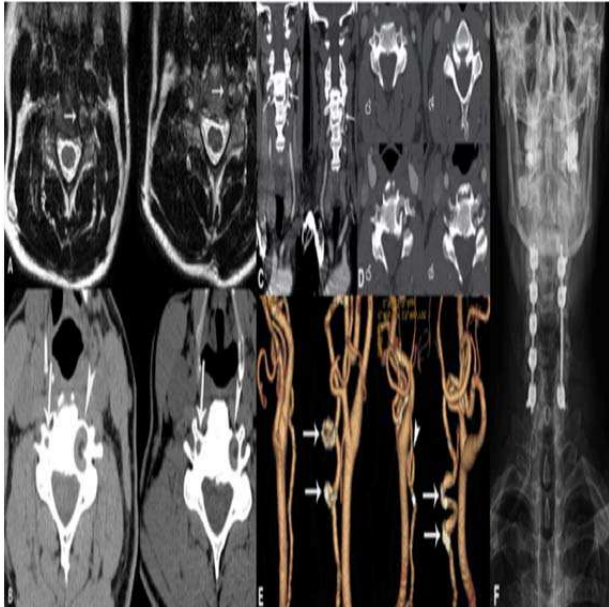
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**Introduction:** Vertebral artery loop is a congenital or acquired anomaly. Vertebral artery (VA) loops are incidentally diagnosed during evaluation of neck problems and trauma. We aimed to present the incidence of VA loops using magnetic resonance angiography in consecutive patients and discuss epidemiological data including the gender, age, location, signs and symptoms, treatment approaches and outcomes of VA loops via analyzing literature.

**Methods:** In the first leg of our two-legged study, consecutive patients were evaluated using magnetic resonance angiography to detect any medial loop of vertebral arteries. The study period was from October 2015 to March 2016. In the second leg, academic databases about medial loop of vertebral artery were screened. Case reports, case series, abstracts and references of relevant literature were searched manually to avoid any missing cases.

**Results:** We evaluated 239 consecutive patients using magnetic resonance angiography. Twenty-one patients were excluded from the study due to inadequate image acquisition, aplastic vertebral artery and/or concomitant vertebral artery stenosis. Medial loop of V2 vertebral artery was observed in 13 patients (5.9 %): 9 with left, 2 with right and 2 with bilateral medial V2 loop. Patients with medial V2 loop were significantly older than patients with straight vertebral arteries (70.30 vs. 62.36,  $p = 0.028$ ). In the literature analysis, VA loops were more commonly observed at V2 segment (90.5 %). Vertebral artery loops were mostly diagnosed at the 5th and 6th decades of life predominantly in females. The most common signs and symptoms were radiculopathy and/or neck pain, and signs and symptoms of vertebrobasilar insufficiency.

**Discussion:** Concise pre-operative evaluation of the vertebral arteries is essential to avoid the injury of undiagnosed VA loops during surgery, which might result in catastrophic circumstances. Further evaluation of the vertebral arteries using MR angiography is required, especially in elder age, before cervical spine surgeries.



## TEMPORARY PEDICLE SCREW FIXATION FOR THORACOLUMBAR BURST FRACTURES. - COMPARATIVE STUDY WITH OR WITHOUT VERTEBROPLASTY

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### Introduction

Short-segment posterior instrumentation for thoracolumbar burst fracture has its merit based on superior correction of kyphosis by indirect reduction technique. However, failure of this procedure in loss of kyphosis correction has been frequently reported in 1990's. Recently, there are some reports that additional vertebroplasty (VP) can prevent this failure. Meanwhile, we reported satisfactory results of temporary instrumentation for thoracolumbar burst fractures without augmentation. The purpose of this study was to compare the treatment outcomes in patients with thoracolumbar burst fractures with or without VP.

### Methods

A total of 62 consecutive patients with thoracolumbar burst fracture (T11-L3) who underwent surgery by ligamentotaxis procedure using Schanz screws in three institutions were included in this study. There were 42 men and 20 women, with an average age of 40 years (range 16–69). Thirty-three patients were treated without augmentation and 29 patients with VP. Their implants were removed around 1 year after operation. We have measured local vertebral body angle (VBA) and superior-inferior endplate angle (SIEA), 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 final follow up in lateral roentgenograms at standing position except before surgery. We also evaluated fracture severity according to load sharing classification.

### Results

Operation was performed 0 to 9 (mean 3.5) days after injury. Mean operating time was 101 minutes without VP and 153 minutes with VP. Mean blood loss was 152 ml without VP and 578 ml with VP. Load sharing classification score was 7.0 points without VP and 6.6 points with VP. Without VP, VBA was corrected 11.2° after surgery and loss of correction was 1° at final follow up. SIEA was corrected 12.5° after surgery and loss of correction was 9° at final follow up. Meanwhile, with VP, VBA was corrected 13.1° after surgery and loss of correction was 1° at final follow up. SIEA was corrected 12.6° after surgery and loss of correction was 9.4° at final follow up. Taken together, these results indicate that postoperative kyphotic change was related to disc level not fractured vertebra with or without VP.

### Conclusion

Fractured vertebra was reduced and maintained after surgery and kyphotic change was observed due to loss of disc height mostly after removal of implants with or without VP. Such change might be inevitable, as adjacent discs can be injured at the onset. Kyphotic change may thus be a limitation of this procedure.



## THE EFFECT OF CORRECTING THE INITIAL OLIF IN A TWO STAGE CORRECTIVE FUSION USING OLIF METHOD FOR ADULT SPINAL DEFORMITY

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**【Background】** Oblique lumbar interbody fusion (OLIF) is a minimally invasive procedure that involves the removal of damaged intervertebral disc and fusion of two adjacent spinal vertebrae. We have recently been performing two-stage corrective fusion using the OLIF method for adult spinal deformity (ASD).

**【Purpose】** This study investigated the corrective effect of the initial OLIF procedure in two-stage OLIF and posterior spinal fusion (PSF) for ASD.

**【Materials and Methods】** Between October 2015 and October 2016, eight patients (4 men and 4 women) underwent two-stage OLIF and PSF for ASD. Average age was  $68.5 \pm 6.0$  (range: 60-81) years. OLIF was performed between 23 intervertebrae (L1/2: 3 cases, L2/3: 7 cases, L3/4: 8 cases, L4/5: 5 cases). The average final number of fixed intervertebrae was  $10.3 \pm 4.2$ . Mean scoliotic angle and lordotic angle per intervertebra preoperatively / after initial OLIF / at final PSF were measured using sagittal reconstructive computed tomography. Cobb angle, lumbar lordosis (LL), sagittal vertical axis (SVA), pelvic tilt (PT), and pelvic incidence (PI)-LL were determined radiographically.

**【Result s】** The average scoliotic angle per intervertebra preoperatively / after initial OLIF / at final PSF was  $4.7 / 2.4 / 1.4$  degrees, respectively, and average lordotic angle was  $1.9 / 6.5 / 9.8$  degrees, respectively. Cobb angle was  $25.7 / 19.6 / 12.0$  degrees, LL was  $3.8 / 22.6 / 45.0$  degrees, and SVA was  $124.5 / 57.4 / -10.2$  mm, respectively. PT was  $30.5 / 18.3 / 15.8$  and PI-LL was  $54.0 / 21.2 / 0.4$  degrees, respectively. **【Discussion】** Although 2.3degrees of scoliotic angle and 4.6degrees of lordotic angle per intervertebra were achieved, a PI-LL mismatch remained after the initial OLIF procedure. This mismatch appeared to be corrected by facetectomy and compression force in the second PSF surgery.

**【Conclusion】** Initial OLIF procedure does not provide sufficient correction for ASD. An additional PSF is therefore necessary to obtain good final coronal and sagittal alignment.

## POSTOPERATIVE COMPENSATORY ACTION OF LOWER EXTREMITIES IN PATIENT WITH ADULT SPINAL DEFORMITY (ASD): IMPLICATION FOR THE POSTOPERATIVE SAGITTAL ALIGNMENT

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**INTRODUCTION:** Adult spinal deformity (ASD) patients recruit various compensatory mechanisms to maintain erect posture and keep the balanced sagittal alignment. Those compensations are observed in the spine, the pelvis and/or the lower limb areas however, postoperative change of lower limb mechanism of compensation remain poorly described. This study is based on the hypothesis that inadequate decompensation of spine and pelvis would lead to sustained compensatory action of lower extremity even if the patients achieve the balanced sagittal alignment.

**METHODS:** This is a retrospective cohort study of patients operated for adult spinal deformity from January 2011 to December 2013. Postoperatively, the patients who showed normal sagittal balance (sagittal vertical axis; SVA <5 cm) with completion of 1 year follow-up were classified into compensated balance (CB; femur inclination angle  $\geq 5^\circ$ ) group and uncompensated balance (UB; femur inclination angle  $< 5^\circ$ ) group. Radiologic parameters including SVA, femur inclination angle (FIA), T1 pelvic angle (TPA), T1 spinopelvic inclination angle (T1SPi), lumbar lordosis (LL), pelvic incidence (PI), pelvic tilt (PT) and sacral slope (SS) were measured for both groups. Clinical assessment was done using visual analog scale (VAS) and Oswestry disability index (ODI). Those parameters were compared between two groups and multivariate analyses were used to investigate a correlation with FIA.

**RESULTS:** Of the 105 patients included in this study, 27 patients were classified as CB group and 46 patients as UB group. With similar preoperative SVA between two groups, CB group showed higher FIA and T1SPi while PT was observed to be higher in UB group. Postoperatively, FIA was  $9.23^\circ$  in CB group and  $3.32^\circ$  in UB group ( $p = 0.00$ ). Under the acquisition of normal SVA, postoperative TPA was higher in CB group than UB group ( $25.93^\circ$  vs.  $19.03^\circ$ ,  $p = 0.02$ ) while there were similar LL, PT, SS and LL-PI ( $p = 0.17, 0.31, 0.22$  and  $0.42$ , respectively). The changes of parameters demonstrated that for the balanced sagittal alignment, the CB group used mainly thoracic spine  $\Delta$ T1SPi;  $5.83^\circ$  vs.  $4.23^\circ$ ,  $p = 0.04$ ) and lower extremity  $\Delta$ FIA;  $3.29^\circ$  vs.  $5.83^\circ$ ,  $p = 0.01$ ) while the UB group used tilted pelvis  $\Delta$ PT;  $3.52^\circ$  vs.  $10.62^\circ$ ,  $p = 0.00$ ). At the time of 1 year follow-up, the CB group showed both increased SVA, TPA and FIA ( $66.78\text{mm}$ ,  $28.34^\circ$  and  $11.28^\circ$ ) accompanied by worsened VAS and ODI scores. Correlation analysis revealed that  $\Delta$ FIA was positively correlated with  $\Delta$ TPA ( $R = 0.63$ ) while  $R$  was  $0.52$  with  $\Delta$ SVA.

**DISCUSSION:** The sustained postoperative compensation by lower extremity is related with the limited utilization of pelvis in patients with ASD. Although the balanced sagittal alignment (normal SVA) is achieved through corrective surgery, the patients with inclined femur (flexed knee) could go through with deterioration of clinical symptoms. This study suggest that TPA is more appropriate to evaluate the global alignment and the compensatory action by lower extremity.

**THE VALUE OF BONE SPECT/CT IN DIAGNOSIS OF PATHOLOGY CAUSING LOW BACK PAIN**

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**Introduction:** The exact cause of nonspecific low back pain (LBP) is known in only about 15% of cases. The use of diagnostic imaging with single-photon emission computed tomography/computed tomography (SPECT/CT), which combines scintigraphy and CT, has become widespread recently. However, little has been published about its diagnostic accuracy and usefulness in LBP.

**Aim:** This study aimed to assess the usefulness of bone SPECT/CT in localizing the pain site in LBP.

**Patients and Methods:** This study included 23 patients (10 men and 13 women; mean age, 68 years) with lumbar degenerative disease, who underwent preoperative bone SPECT/CT with <sup>99m</sup>Tc-MDP and a lumbar spinal fusion surgery between January 2014 and October 2016. They had moderate or severe LBP, along with a neurological symptom due to lumbar degenerative instability. We evaluated the following points: (1) concordance rate between the most integrated site on bone SPECT/CT and the lumbar level with instability that caused the clinical symptoms, as diagnosed by using radiography, magnetic resonance imaging, and clinical examinations; (2) numerical rating scale (NRS) of LBP score changes between pre and post operation; and (3) comparison of integrated enhancement and modic changes at the vertebral end plate of the fusion level.

**Results:** In all the cases except one, maximal integrated enhancement on bone SPECT/CT was consistent with the facet joint or end plate of the vertebra, which was clinically diagnosed as a LBP-causing lesion. All patients experienced significant improvement in NRS scores within 1 month after the surgery. In all 28 fusion levels, 17 showed integrated enhancement at the vertebral end plate. Modic changes were identified in 17 levels (type 1: 4, type 3: 11, and combination of types 1–3: 2) but not in the remaining 11 levels.

**Conclusion:** In this study, all patients who required a lumbar fusion surgery for degenerative instability, maximal integrated enhancement on bone SPECT/CT matched with the lesion clinically responsible for LBP. We also obtained good postoperative results by performing interbody fusion to that level. The lesion that showed integrated enhancement at the vertebral end plate showed modic changes, so we think that bone SPECT/CT is useful for identifying the lesions responsible for LBP in lumbar degenerative disease. In nonspecific LBP, the responsible lesion may be identified by using bone SPECT/CT with the same mechanism, which can provide information for guiding clinicians on the use of adequate treatment. Bone SPECT/CT can be a useful imaging study for identifying the lesion responsible for nonspecific LBP.

## PERCUTANEOUS VERTEBROPLASTY FOR OSTEOPOROTIC VERTEBRAL FRACTURE ASSOCIATED WITH DELAYED NEUROLOGIC DEFICIT IN THORACOLUMBAR SPINE

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**Introduction:** The number of cases of osteoporotic vertebral fracture (OVF) with intravertebral cleft with delayed neurologic deficit (DND) is increasing as the population ages. However, the cause of DND after OVF has been poorly understood, and no definitive treatment of the disease has been established. The purpose of this study was to clarify the radiographic parameters contributing to the occurrence of DND in thoracolumbar OVF, and to evaluate the efficacy and safety of percutaneous vertebroplasty (PVP) for this pathology.

**Methods:** PVP was prospectively performed for 291 patients with OVF with intravertebral cleft; 24 had DND in thoracolumbar spine (mean age: 78.1 years). DND was clinically diagnosed based on the following criteria: 1) neurologically intact immediately after vertebral fracture; 2) sensory and/or motor involvement appearing in an insidious and tardy process with progression of vertebral collapse; and 3) intractable pain of lower extremities in a sitting and/or standing position with improvement on lying down (postural leg pain). Radiographic parameters of percent spinal canal compromise and intravertebral instability were investigated for correlations to DND. Procedural outcomes were evaluated using visual analogue scale (VAS), Oswestry Disability Index (ODI), and modified Frankel grades.

**Results:** In the 24 patients with DND, 11 patients (46%) showed motor disturbance and 13 patients (54%) showed postural leg pain. In the 11 patients with motor involvement, 9 patients (82%) had T12 vertebral fracture and 6 patients (55%) had drop foot. The mean score for VAS and ODI were 8.0 and 71.8% before PVP, and 2.2 and 37.1% after PVP, respectively. Modified Frankel grades improved after PVP. Intravertebral instability improved significantly from 10.5 before PVP to 2.7 after PVP, respectively. However percent spinal canal compromise did not change significantly from 44.5% before PVP to 44.1% after PVP.

**Discussion:** In the patients with dropped foot in the elderly, we should pay attention to OVF with intravertebral cleft in thoracolumbar spine. Intravertebral instability is the dominant cause of DND in thoracolumbar OVF. PVP appears effective and safe in the treatment of OVF with intravertebral cleft with DND.

## RISK FACTORS PREDICTING CEMENT LOOSENING AFTER PERCUTANEOUS VERTEBROPLASTY FOR OSTEOPOROTIC VERTEBRAL FRACTURE WITH INTRAVERTEBRAL CLEFT: A RETROSPECTIVE ANALYSIS

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**Introduction:** Percutaneous vertebroplasty (PVP) is an efficient procedure to treat painful osteoporotic vertebral fracture (OVF) with intravertebral cleft. However, cement loosening occurs occasionally with poor outcome. The purpose of this study was to evaluate the primary outcomes and radiographic results of PVP between the groups with and without cement loosening and to investigate the risk factors of cement loosening after PVP.

**Methods:** We retrospectively analyzed the patients of single-level OVF with intravertebral cleft who underwent PVP. Six months after the procedure, the primary outcomes were evaluated using the visual analogue scale (VAS) and modified Oswestry Disability Index (ODI). Cement loosening was detected by computed tomography 6 months after PVP. Possible risk factors, such as age, gender, wedging angle of the fractured vertebrae, intravertebral instability, Parkinson's disease, spinous process fracture, ankylosing spinal hyperostosis, split vertebrae and vacuum of the adjacent intervertebral space, were assessed. Associations between loosening of cement and preoperative parameters were analyzed using multivariate logistic-regression analysis.

**Results:** A total of 195 patients with single OVF with intravertebral cleft were enrolled. There were 50 men and 145 women, and the mean age at the time of diagnosis was 77 years (range, 57–93 years). The mean duration from the onset of acute fracture to PVP procedure was 38 weeks. The mean score for VAS and ODI were 87mm and 59.1% before PVP, and 31mm and 37.0%, 6 months after PVP, respectively. Forty-nine patients (25%) had cement loosening 6 months after PVP. The mean VAS in the patients with and without cement loosening was 50mm and 26mm, respectively. The mean VAS in the cement loosening group was significantly higher than that in the non-loosening group ( $P < 0.01$ ). Cement loosening was closely associated with intravertebral instability (odds ratio [OR]=1.20; 95% confidence interval [CI]=1.04–1.40;  $P = 0.015$ ), presence of Parkinson's disease (OR=54.31; 95% CI=4.47–659.53;  $P = 0.002$ ), spinous process fracture (OR=7.11; 95% CI=1.65–30.60;  $P = 0.009$ ) and split vertebrae (OR=11.59; 95% CI=1.64–82.02;  $P = 0.014$ ).

**Discussion:** Patients with cement loosening showed substantial back pain compared with the patients without cement loosening. The important risk factors affecting cement loosening following PVP were large intravertebral instability, Parkinson's disease, spinous process fracture and split vertebrae.

## CLINICAL AND RADIOGRAPHIC ANALYSIS OF UNILATERAL VERSUS BILATERAL INSTRUMENTED ONE-LEVEL LATERAL LUMBAR INTERBODY FUSION

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### Introduction:

The lateral lumbar interbody fusion (LLIF) is a widely applied and useful procedure for spinal surgeries. However, posterior fixation in this procedure has not yet been decided. This study aimed to compare the radiographic and clinical outcomes of unilateral versus bilateral instrumented one-level LLIF for degenerative lumbar disease.

### Methods:

We conducted a prospective cohort study of 100 patients, who underwent unilateral or bilateral instrumented one-level LLIF for degenerative lumbar disease from May 2013 to April 2015 in our hospital. Forty-one patients (17 men and 21 women; average age, 60.1 years) in group U were undergoing unilateral pedicle screw fixation, and 59 patients (22 men and 30 women; average age, 63.2 years) in group B were undergoing bilateral pedicle screw fixation. Clinical characteristic and demographic data before surgery were compared between these groups. The intraoperative data, including operative time with the time of changes in positions, intraoperative blood loss, and X-ray exposure time, as well as the perioperative data, including postoperative hospital stay and clinical and radiographic data were compared between the groups.

### Results:

The mean follow-up period was 14.8 months. Group U required a significantly shorter operating time than group B (83.1 min vs 119.2 min;  $P < 0.01$ ); however, no statistical differences were identified in the amount of blood loss, X-ray exposure time, and postoperative hospital stay between the groups. The subsidence grade and fusion rates exhibited no significant differences in the postoperative radiographic evaluation between the groups. However, significant differences were observed in the requirement of additional surgery owing to complications. In group B, five patients required re-operations because of pedicle screw and cage loosening, whereas in group U, one patient required re-operation because of adjacent segmental disease.

### Discussion:

LLIF with unilateral fixation required a significantly shorter operating time than that with bilateral fixation; however, no significant differences in the subsidence grade and fusion rates were found between them. In addition, LLIF with unilateral fixation required significantly more re-operations because of pedicle screw and cage loosening than that with bilateral fixation. We may indicate that LLIF with unilateral fixation lead some kind of instability for the fixation.

## EVALUATION OF THE MINIMUM CLINICALLY IMPORTANT DIFFERENCES OF THE ZURICH CLAUDICATION QUESTIONNAIRE AFTER MICROENDOSCOPIC LAMINECTOMY IN PATIENTS WITH LUMBAR CANAL STENOSIS

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### 【Background】

The ZCQ is a self-administered tool used to evaluate symptom severity and physical function in patients with LCS. It has been used in many studies worldwide. However, MCIDs of the ZCQ have not yet been determined. To evaluate the minimally clinically important differences (MCIDs) of the Zurich Claudication Questionnaire (ZCQ) after microendoscopic laminectomy (MEL) in patients with lumbar canal stenosis (LCS).

### 【Methods】

The study sample consisted of 649 patients who underwent MEL for LCS at our hospital between March 2012 and May 2014. The ZCQ, which includes 7 items for symptom severity (scored from 1 to 5) and 5 items for functional disability (scored from 1 to 4), was administered preoperatively and 1-year postoperatively; higher scores indicate more severe LCS. Each MCID was calculated by the receiver operating characteristic curve using the outcome of the preoperative and postoperative ZCQ scores.

### 【Results】

We were able to follow up with 349 patients for 1 year and administer the ZCQ postoperatively. The ZCQ score statistically significantly improved 1-year postoperatively. The MCID for symptom severity was -1.0, area under the curve (AUC) was 0.81, sensitivity was 64.8%, and specificity was 86.8%. The MCID for functional disability was -0.6, ACU was 0.80, sensitivity was 79.8%, and specificity was 67.1%.

### 【Discussion】

This study showed that the MCID of the ZCQ for symptom severity was -1.0 and the MCID for functional disability was -0.6. Additionally each ACU was over 0.80, we indicate that MCIDs of the ZCQ were found to have a high diagnostic performance.

## THE CORRELATION BETWEEN SPINAL ALIGNMENTS WITH CLINICAL OUTCOME AFTER LUMBAR DECOMPRESSION/FUSION SURGERY IN PATIENTS WITH LUMBAR SPINAL CANAL STENOSIS

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### Objective

The object of this study was to investigate correlations between sagittal spinopelvic alignment and clinical outcomes after lumbar decompression surgery and fusion surgery.

### Subjects and methods

Thirty-nine patients who underwent lumbar decompression surgery (Group D) and 35 patients with posterior lumbar interbody fusion (Group F) were analyzed. Radiographic parameters of standing whole spine radiographs at preoperative and final follow-up were examined. Measured spinopelvic parameters were pelvic incidence (PI), pelvic tilt (PT), lumbar lordosis (LL), thoracic kyphosis (TK), C2-7 angle, T1 pelvic angle (TPA), and sagittal vertical axis (SVA). Clinical outcomes were evaluated using the JOA Back Pain Evaluation Questionnaire (JOABPEQ).

### Results

In both Group D and F, there were no significant differences in radiographic parameters between preoperative and final follow-up. However, amount of changes of LL, TPA, and SVA between preoperative and final follow-up were significantly different between Group D and F. Clinical outcomes (JOABPEQ scores) were significantly improved postoperatively both in Group D and F.

In Group D, compared to patients with preoperative normal sagittal balance (TPA < 26°), those with preoperative sagittal imbalance (TPA ≥ 26°) had significantly lower improvement on JOABPEQ score in terms of walking ability (preoperative walking ability: 33.5 vs 23.7,  $p = 0.6$ ; postoperative walking ability: 71.4 vs 21.7,  $p = 0.03$ ).

### Conclusions

Lumbar fusion surgery improved LL, TPA, and SVA compared with decompression surgery. Preoperative sagittal imbalance was significantly correlated with walking ability after lumbar decompression surgery.



**TARGETING SPINE SURGICAL CARE TO PATIENT NEED FOR OPTIMIZED OUTCOME WITH THE SOLUTION-FOCUSED SPINE PATIENT OUTCOMES QUESTIONNAIRE - A SOLUTION-FOCUSED SURVEY LOOKING INTO PATIENT OUTCOME EXPECTATIONS IN ADULT RECONSTRUCTIVE SURGICAL SPINE CARE**

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**Introduction**

There is an increasing appreciation of major disconnect not just between patient- and surgeon-perceived outcomes of surgery but also between patient- and surgeon-perceived expectations of surgery (1). This latter issue may be important in both defining the indications for operation, that is in making the go/no go decision for elective surgery, and in optimizing postoperative care and rehabilitation which might be optimally targeted to the patient's perceived needs.

**Methods**

A simple four-point questionnaire (the Solution-Focused Spine Patient Outcomes Questionnaire, or SFSPQ), suitable for administration in the office setting and addressing patients' perceptions of what benefit they would want from the surgery, was designed using the validated principles of Solution-Focused Brief Therapy. At an office visit scheduled immediately prior to scheduled surgery, this questionnaire was administered to a cohort of thirty elective adult spine care patients.

**Results**

The information collected was compared to the surgeon's perceived indications for surgery and found frequently to differ. The patients' wants in approaching elective care presents an opportunity to maximize benefit through guided postsurgical rehabilitation and care.

**Conclusion**

A simple four-point office questionnaire has potential to bridge the gap between surgeon and patient in both deciding on surgery and benefitting from it.

**Reference**

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## THE INCIDENCE AND THE RISK FACTORS OF INJURY TO THE LATERAL FEMORAL CUTANEOUS NERVE AFTER POSTERIOR SPINE SURGERY

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### Introduction

Most spinal surgeries are performed in a prone position using the frame such as Hall-frame.

As the whole body weight is loaded onto four posts(positioned at the patient's bilateral chest and pelvis), excessive pressure may cause compression on adjacent peripheral nerves such as the lateral femoral cutaneous nerve(LFCN).

LFCN injury was well-known complication of posterior spine surgery and the incidence of LFCN injury was reported 12-24%.

We investigated the incidence and risk factors of postoperative LFCN injury after posterior spine surgery.

### Methods

This study consists of consecutive 539 patients who had posterior spinal surgery in our institutions. All patients were examined before and after surgery for neurological symptoms of LFCN. We defined post-operative additional symptoms including numbness, pain or impaired sensation at the anterolateral aspect of the thigh as LFCN injury.

Thirty-nine patients were excluded, because of preoperative sensory deficit at anterolateral thigh or disturbance of consciousness.

The remaining 500 patients were the subject of this study(the cervical surgery in 90 patients, the thoracic in 30, and the lumbar spine in 380). All of them were followed until symptoms of LFCN had disappeared. Operations were performed using two type of frame(A: the conventional Hall frame, B: the frame which has four flat posts having a merit of distribution of the body weight) alternately.

Eleven parameters including age, sex, estimated blood loss, height, body weight, body mass index(BMI), time of prone position, time of surgery, surgical position(chest-knee position or not), comorbidity, and type of the frame were assessed. We evaluated the risk factors of LFCN injury by multiple logistic regression analysis.

### Results

The incidence of LFCN injury was 5.8 %(29 patients) overall, 7.3%(18 patients) with frame A and 4.4%(11 patients) with frame B.

Mean body weight, BMI, surgical time, and time of prone position of patients with and without LFCN injury was 67.9 vs 60.7kg, 25.9 vs 24.2kg/m<sup>2</sup>, 149 vs 114minutes, and 180 vs 142minutes.

Statistical analysis revealed body weight(odds ratio, 1.042; 95% confidence interval(CI), 1.015–1.070), time of prone position(odds ratio, 1.010; 95%CI,1.003–1.017), and the chest-knee position(odds ratio, 3.104; 95%CI,1.032–9.343) were the risk factors of LFCN injury.

Twenty-seven patients(93%) had recovered the symptoms completely within 3 days and the longest duration of recovery was 3 months. Twenty-five patients did not notice the symptoms until they were asked in detail. Remaining four patients did not complain of severe pain but a little numbness and hypesthesia.

### Discussion

LFCN injury has been reported to be a common complication during spine surgery and occurs in about 20% of the patients. The most symptoms of LFCN injuries are minor, but occasionally they are severe, such as burning pain. Therefore, we have to take care for LFCN injury. In our series, proper positioning of the patients and a little ingenuity using the buffer materials such as gel-pads may decrease occurrence of LFCN injury to 5.8%. Statistics analysis revealed that the longer time of prone position, the heavier body weight and chest-knee position were risk factors for the incidence of LFCN injury.

## A PROSPECTIVE COMPARATIVE STUDY OF CLINICAL OUTCOMES FOR LUMBAR SPINE SURGERY IN ELDERLY PATIENTS OLDER THAN 80 YEARS OLD EVALUATED WITH JOABPEQ AND PATIENT SATISFACTION

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### Introduction

For the evaluation of clinical outcome after lumbar surgery, JOA score has been widely used in Japan. However, a major problem of the JOA score is that it is not a patient-oriented measurement, but rather a physician based measurement. And recently, the patient's perspective is widely accepted to be essential for evaluating the results of interventions and making medical decisions. The JOA Back Pain Evaluation Questionnaire (JOABPEQ), as a new outcome measure for patients with LBP in order to solve the problems of the JOA score. With increased aging of the population in Japan, spine surgeons have more opportunity to treat elderly patients. In this study, we prospectively evaluated patient satisfaction and JOABPEQ score after lumbar surgery in elderly patients more than 80 years old compared those in patients from 65 years old to 79 years old.

### Method

One hundred patients more than 65 years who underwent lumbar surgery were enrolled in this study. The patients were divided into two groups according to age. Group A (more than 80 years) : n=28, mean age : 82.4±2.3 years, male : 12 female : 16. Group B (65-79 years) : n=72, mean age : 73.1±4.3 years, male : 28 female : 44. As clinical result, JOABPEQ score was evaluated at enrollment and at 1 year after surgery. JOABPEQ is an ensured and a validated method for evaluating the degree of LBP related ADL/QOL and includes the following five dimensions: pain-related disorders, gait disturbance, lumbar spine dysfunction, social life disturbance, and psychological disorders. The score is from 0 to 100; a higher score indicates a better health status. To evaluate patient satisfaction, an original questionnaire (1: satisfied 2: moderately satisfied 3: other) was used and evaluated at 1 year after surgery. The JOABPEQ score and patient satisfaction were compared in two groups. Between groups comparisons were made using the Mann-Whitney U test and the chi-square test.

### Results

JOABPEQ score at enrollment was not significantly different between two groups (P= 0.86 : pain-related disorders, 0.32 : gait disturbance, 0.15 : lumbar spine dysfunction, 0.15 : social life disturbance, and 0.80 : psychological disorders, respectively) , but gait disturbance and social life disturbance in JOABPEQ score at 1 year was significantly lower in group A (P= 0.45 : pain-related disorders, 0.32 : gait disturbance, 0.035 : lumbar spine dysfunction, 0.023 : social life disturbance, and 0.50 : psychological disorders, respectively). About patient satisfaction, 1: satisfied was 85.7%, 2: moderately satisfied was 10.7%, 3: other was 3.6% in group A. Patients satisfaction was not significantly different between two groups (P=0.28).

### Conclusion

Patient satisfaction in elderly patients more than 80 years after lumbar surgery at 1 year was not significantly different from that in patient from 65 years to 79 years. Gait disturbance and social life disturbance evaluated by JOABPEQ score was lower in elderly patients more than 80 years after lumbar surgery at 1 year.

## RADIOLOGIC FEATURES AND CLINICAL OUTCOMES OF JUXTAFACET CYST ASSOCIATED WITH DEGENERATIVE LUMBAR DISEASE

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**Introduction:** Juxtafacet cysts occur more frequently in the lumbar spine, especially at L4–5 level, than in the cervical or thoracic regions. The cause of juxtafacet cyst is still unclear. However, it underlies spinal instability, facet joint arthropathy and degenerative spondylolisthesis. It appears that the optimal approach for patients with juxtafacet cysts remain unclear resulting many controversial for treatment. The purpose of this study is to evaluate radiologic features of juxtafacet cyst and determine whether there was any correlation between these features and clinical outcome.

**Methods:** We analyzed 23 patients. The degree of facet joint degeneration was classified using Fujiwara method. Facet joint angles were measured with MRI to determine whether there was a difference between cystic lesion that was occupied and cystic lesion that was not occupied. Disc degeneration was measured by Pfirrmann classification. Clinical result was evaluated using Oswestry disability index score and Visual analogue scale.

**Results:** The level of juxtafacet cyst affected was mostly L4-5 as found in previous studies. Facet joint arthritis was more severe within the side with cystic lesion. Significant correlation was found between disc degeneration and juxtafacet joint cyst. All patients underwent wide decompression and fusion. Clinical result was excellent. No patient had signs of recurrence during the follow up periods.

**Discussion:** Juxtafacet cyst has significant correlation with facet joint degeneration. Therefore, aggressive surgical treatment, not just simple cyst excision, should be considered as treatment option for juxtafacet cyst associated with degenerative lumbar disease.

## DECOMPRESSION ONLY OR DECOMPRESSION WITH CONCOMITANT FUSION IN DEGENERATIVE SPONDYLOLISTHESIS: A SHORT- AND LONG-TERM OUTCOME

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**Introduction:** Patients with lumbar spinal stenosis and concomitant degenerative spondylolisthesis with predominance of back pain have been shown to have inferior outcome after decompression only. This study is to investigate the necessity and efficacy of stabilization or fixation after posterior decompression for lumbar degenerative spondylolisthesis at short- and long-term clinical outcome.

**Method:** Subjects were patients indicated for decompression for lumbar canal stenosis at the L4/5 due to lumbar degenerative spondylolisthesis. After providing informed consent, patients were divided into two groups: decompression only (D group); and decompression with concomitant fusion (DF group). A comparative study Japanese Orthopaedic Association (JOA) score, ODI, VAS, SF36 results, and X-ray, CT scan and MRI findings was performed at pre- and post-operative years 2 and 6.8.

**Result:** Fifty-six consecutive patients, 28 in D group and 28 in DF group, were followed. All patients were available in 2 years follow-up and only 47 patients were available at final follow-up. Clinical outcome of excellent and good was 89.8% in D group and 90.2% in DF group at 2 years follow-up respectively ( $P>0.05$ ), and the data was 76.5% and 84.2% at 6.8 years follow-up respectively ( $P<0.05$ ). Preoperative lower limb pain score was statistically decreased at 2 year and 6.8 year follow-up. Preoperative low-back pain was also decreased statistically at 2 year follow-up in both groups, but was reversed at 6.8 year follow-up in D group. There was no significant difference between pre- and post-operative radiographic evidence of spondylolisthesis degree, disc height and sagittal motion. Complications were observed in 3 cases, 2 in D group and 1 in DF group, all of them accepted reversed operation.

**Discussion:** At the two year follow-up no significant differences were observed between the D and DF patients in terms of pain and function. Patients with predominant back pain operated with DF group still maintained better outcomes in terms of pain at final 6.8 years follow-up. For present study, Although these differences are significant on a group level they may fail to reach minimal clinical significant difference. Patients with predominant leg pain showed significantly more improvement in terms of leg pain with both of D and DF group at short- and long-time follow-up. The present results showed that decompressive laminotomy alone is an effective surgical method in the management of lumbar degenerative spondylolisthesis with spinal canal stenosis. Long-term clinical outcome is correlated with surgical technique, progression of natural history and adjacent segment degeneration.

## CAUSE AND RATE OF REVISION SURGERY FOR ADULT SPINAL DEFORMITY PATIENTS: A SINGLE CENTER STUDY

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**Introduction:** Long spinal corrective fusion for adult spinal deformity (ASD) is a complex procedure, especially for elderly with osteoporosis. High revision rates were reported for this procedure. In order to avoid the revision surgery, we have been modified our surgical strategies, for example, 4 rods to prevent rod fractures, vancomycin to protect infections, lateral lumbar interbody fusion, instead of posterior lumbar interbody fusion (PLIF) to avoid excessive epidural bleeding. There were few studies investigating the cause and rate of revision surgery for the elderly spinal deformity patients. The purpose of this study was to investigate the cause and rate of revision surgery for ASD patients, with special reference to annual change in the single center.

**Methods:** Consecutive ASD patients who underwent long corrective fusion from thoracic to either lumbar or pelvis from March 2010 to October 2016 were analyzed. Patient demographics (gender, age, pathology), surgical methods, cause of revision surgery, and numbers of revision cases by year were investigated. Staged and/or planned surgeries were excluded.

**Results:** Among 354 consecutive ASD primary surgeries (75 males, 279 females, average age: 63 (18-84), 70s: 41%), 93 revisions in 71 patients (20.5% in total, 13 males (17.6%), 58 females (21.3%), average age: 67) were performed. There was no statistical difference of revision rate between genders ( $P=0.48$ ). The primary diagnoses were iatrogenic flatback (47.1%), Parkinson's disease (34.4%), congenital or syndromic deformities (31.3%), kyphosis with vertebral fractures (VFs) (25.4%), degenerative kyphoscoliosis (17.7%), kyphosis without VFs (14.3%), and adult idiopathic scoliosis (7.4%). Primary surgical procedures were pedicle subtraction osteotomy in 24 cases, Ponte osteotomies with rod rotation in 20 cases, vertebral column resection in 19 cases, LLIF and posterior corrective fusion in 5 cases, Ponte osteotomy and PLIF in 3 cases. Cause of revision surgeries were rod fractures (35), deformity progressions (24), infection (13), hematoma (10), skin troubles (5), screw malpositions (4), and neurologic deficits (2). Six revision surgeries were done in 2011, 13 in 2012, 12 in 2013, 18 in 2015, and 9 in 2016. Although the number of revision surgeries were significantly decreased, average duration from the primary surgery to revision were prolonged year by year (average 43 days (3-154) in 2011, 169 days (0-615) in 2012, 347 days (1-748) in 2013, 440 days (1-825) in 2014, 669 days (26-1,794) in 2015, and 691 days (14-1,444) in 2016). Average duration between primary to revision surgeries were 2.3 days in hematoma. Revision surgeries were performed on the rod fracture for 1 in 2012, 3 in 2013, 9 in 2014, 14 in 2015, and 8 in 2016. Average duration from primary to revision in the rod fracture cases was significantly longer in later years, 9.6 in 2012, 14.6 in 2013, 16.3 in 2014, 24.4 in 2015, and 30.9 months in 2016 cases ( $P<0.0001$ ).

**Discussion:** There were no hematoma cases, and no revision surgery within postoperative 2 weeks was done in these 2 years, suggesting that our surgical strategies to avoid revision surgery would help reducing the revision rate for elderly spinal deformity patients.

## ARE PEDICLE SCREW PERFORATION RATES INFLUENCED BY THE DISTANCE FROM THE REFERENCE FRAME IN MULTI-LEVEL REGISTRATION USING CT-BASED NAVIGATION SYSTEM IN THE SETTING OF SCOLIOSIS?

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**Background Context:** Pedicle screw fixation is commonly employed for the surgical correction of scoliosis but carries a risk of serious neurovascular or visceral structure events during screw insertion. To avoid these complications, we have been using a computed tomography (CT)-based navigation system during pedicle screw placement. As this could also prolong operation time, multi-level registration for pedicle screw insertion for posterior scoliosis surgery was developed to register 3 consecutive vertebrae in a single time with CT-based navigation. The reference frame was set either at the caudal end of 3 consecutive vertebrae or at 1 or 2 vertebrae inferior to the most caudal registered vertebra, and then pedicle screws were inserted into the 3 consecutive registered vertebrae and into the 1 or 2 adjacent vertebrae.

**Objectives:** This study investigated the perforation rates of vertebrae at 0, 1, 2, 3, or 4 or more levels above/below the vertebra at which the reference frame was set.

**Methods:** We evaluated 161 scoliosis patients (34 male, 127 female; mean  $\pm$  standard deviation age:  $14.6 \pm 2.8$  years) who had received pedicle screw fixation guided by a CT-based navigation system between March 2006 and December 2015. All patients routinely underwent CT reconstruction scans of instrumented vertebrae after surgery to assess screw position. Screw perforation rate was evaluated according to the distance of the instrumented vertebral level from the reference frame.

**Results:** A total of 2203 pedicle screws were inserted into T2-L5 using multilevel registration with CT-based navigation. The overall perforation rates for Grade 1, 2, or 3, Grade 2 or 3 (major perforations), and Grade 3 perforations (violations) were as follows: vertebrae at which the reference frame was set: 15.9%, 6.1%, and 2.5%; 1 vertebra above/below the reference frame vertebra: 16.5%, 4.0%, and 1.2%; 2 vertebrae above/below the reference frame vertebra: 20.7%, 8.7%, and 2.3%; 3 vertebrae above/below the reference frame vertebra: 23.8%, 7.9%, and 3.5%; and 4 vertebrae or more above/below the reference frame vertebra: 25.4%, 9.5%, and 4.1%, respectively. Fisher's exact test was performed to detect significant differences among the above 5 groups. Regarding Grade 1, 2, or 3 perforations, the rates of screw perforation for 3 and 4 vertebrae or more above/below the reference frame vertebra were significantly larger than that for vertebrae at the reference frame (both  $p < 0.01$ ). No significant differences were found for Grade 3 perforations (violations) among the groups.

**Conclusions:** In multilevel registration of 3 consecutive vertebrae, the accuracy of screw insertion into vertebrae at which the reference frame was not set was not significantly inferior to that in vertebrae at which the reference frame was set with regard to major perforation rate. Including minor perforations, however, a distance of 3 vertebrae or more above/below the reference frame vertebra produced significantly more frequent perforations.

## METASTATIC SPINE TUMOUR SURGERY: DOES PERIOPERATIVE BLOOD TRANSFUSION INFLUENCE POSTOPERATIVE COMPLICATIONS?

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**Introduction:** There have been numerous advances in surgical techniques for spinal metastases. Despite the advances, blood loss still remains a significant problem in surgery for spinal metastases. The substantial blood loss is presently addressed by transfusion of allogeneic blood products. The effect of allogeneic blood transfusion (ABT) in surgical oncology has been most studied and debated in colorectal and hepatobiliary oncological surgeries. This literature has raised the controversy regarding the adverse effects of ABT influencing survival and/or postoperative complications. Previous studies pertaining to surgery in spinal metastases investigated the influence of ABT on survival, but not on postoperative complications.

### Methods

We aimed to evaluate the influence of perioperative ABT on postoperative complications and infections in patients undergoing metastatic spinal tumour surgery (MSTS). This is a retrospective cohort study including 10-year data in a tertiary university hospital: A total of 247 patients who underwent MSTS. The primary outcome measures were postoperative complications including cardiovascular, neurological, respiratory, renal, infection, haematological and electrolyte imbalance within 30 days after MSTS. Postoperative infections which included surgical site infection, systemic sepsis, chest infection and urinary tract infection were also subsequently analyzed.

Variables recorded from electronic records and case notes included patient demographics, tumour characteristics, operative details and postoperative complications. Multivariate logistic regression analyses were performed to assess influence of blood transfusion on postoperative complications and infections. Further adjustment for potential confounders was made in these analyses. There are no funding source and any conflict of interest to be declared.

### Results

Of 247 patients, 133 patients (54%) received ABT. The overall median unit of blood transfused was 2 units (range:0-10units). The mean age at the time of surgery was 60 years (range: 25-87 years). The adjusted odds of developing any postoperative complication was 2.27 times higher in patients with transfusion (95% CI: 1.17-4.38, P=0.01) and 1.24 times higher odds per every unit increase in blood transfusion (95% CI: 1.05-1.46, P<0.01). Exposure to blood transfusion also increase the odds of having overall postoperative infections (OR: 3.58, 95% CI: 1.15-11.11, P=0.02) and there were 1.24 times higher odds per every unit increase in transfusion (95% CI: 1.01-1.54, P=0.04).

### Discussion

Hill and colleagues, who conducted a meta-analysis of 20 studies concluded that ABT is an associated but frequently overlooked risk factor, for the development of postoperative bacterial infection in the surgical patient).

In this study, the differences in the rate of each specific infection between transfused and non-transfused groups were not significant though there was a trend towards more patients in transfused groups. Other transfusion risks like transfusion error and transfusion transmissible infection were near zero in our cohort as our blood bank follows very stringent prerequisites for blood donation.

The current study adds evidence to the literature implicating ABT to be influential on postoperative complications and infections in patients undergoing MSTS. Appropriate blood management measures should, therefore, be given a crucial place in the care of these patients so as to reduce any putative effect of blood transfusion.



## PERIOPERATIVE BLOOD TRANSFUSION: DOES IT INFLUENCE SURVIVAL AND CANCER PROGRESSION IN METASTATIC SPINE TUMOR SURGERY?

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### Introduction

Despite advances in surgical techniques for spinal metastases, there is often substantial blood loss resulting in patients requiring blood transfusion during perioperative period. Allogeneic blood transfusion (ABT) has been the main replenishment method for lost blood. However, the impact of ABT on cancer related outcomes has been controversial in various studies. We aimed to evaluate the influence of perioperative ABT on disease progression and survival in patients undergoing metastatic spinal tumour surgery (MSTS).

### Methods

We conducted a retrospective study including 247 patients who underwent MSTS at a single tertiary institution from 2005-2014. The impact of the use of perioperative ABT (either exposure to or quantities of transfusion) on disease progression and survival was assessed using Cox regression analyses while adjusting for potential confounding variables.

### Results

Of 247 patients, 133 patients (54%) received ABT. The overall median unit of blood transfused was 2 units (range: 0-10units). Neither blood transfusion exposure nor quantities of transfusion were found to be associated with overall survival (Hazard ratio [HR]:1.15, P=0.35) & (HR: 1.10, P=0.11) and progression-free survival (HR: 0.87, P=0.18) & (HR: 0.98, P=0.11) respectively. The factors influencing overall survival were primary tumour type and preoperative ECOG while primary tumour type was the only factor having impact on progression-free survival.

### Discussion

Studies across various disciplines including colorectal lung, breast, and urologic malignancies have shown that patients who received ABT were associated with worse prognosis, decreased overall survival or increase cancer recurrence. However, these results have been disputed by other researchers who did not identify such an association. To our knowledge, this is the first study evaluating the impact of perioperative ABT on overall survival as well as disease progression in patients undergoing MSTS. We found that neither exposure to blood transfusion nor quantities of transfusion had significant influence on survival or disease progression.

In a recent study of 649 patients, Pereira et al concluded that blood transfusion did not decrease survival. Our findings were consistent with these studies. In our study, patients with spinal metastases from breast, prostate and myeloma/lymphoma had better prognosis compared to those with lung cancer. This may be explained by advancement in chemotherapeutic management of these tumours over lung primaries.

The concerns of disease progression and decrease survival related to allogeneic blood transfusion, as seen in other oncological surgeries, may not apply for MSTS. If there were any worse oncological outcomes in patients who received ABT, it could be due to a surrogacy effect, rather than a causal association. Non-inferiority regarding survival and disease progression in transfused patients undergoing MSTS opens doors for judicious use of allogeneic blood if circumstances dictate so while treating such high-risk patients. However, one must also be cautioned that allogeneic blood transfusion can have propensity towards developing postoperative infections including surgical site infection. Hence, utilization of patient blood management interventions would be worthwhile rather than relying solely on allogeneic blood transfusions for these patients, if and whenever possible.

## "ANNULONUCLEOPLASTY-DISCFX" A RADIO FREQUENCY TREATMENT MODALITY FOR TREATMENT OF AXIAL LOW BACK PAIN - 2 YEARS OUTCOME

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### **Introduction:**

Most patients with low back pain respond to non-operative measures such as physiotherapy and analgesia. Patients with chronic disabling pain are considered for surgical procedures such as spinal fusion. Options for management of low back pain to bridge the gap between non-operative measures and fusion procedures are sparse. DiscFx is a technique of annulo-nucleoplasty that utilises radiofrequency ablation of disc material in the treatment of low back pain. This reduces the intradiscal pressure. It also ablates the pain generating free nerve endings in the posterior annulus and results in shrinkage of the annulus fibrosus thus relieving neural impingement. We have previously presented our early results of DiscFx technique in the treatment of low back pain patients who do not respond to non-operative measures. We now present our 2 year results for his group of patients.

### **Methods:**

This was a retrospective review of prospectively collected patient data. Patients with low back pain with or without leg pain who failed non-operative management of at least 6 months were offered DiscFx as a treatment option. Patients who underwent the procedure between September 2010 and December 2014 were included in this study. We have a total of 52 patients who have a minimum follow-up of 2 years. Clinical outcome measures collected include visual analogue scale (VAS), Oswestry Disability Index (ODI) and MacNab criteria scores. These were collected pre-operatively, immediate post-operative and at 6-month, 1-year and 2-year post-operative. Paired *t* test was used to compare the mean of VAS and ODI scores. Proportion test was used to compare the proportion of patients with excellent/good MacNab outcomes.

### **Results:**

The VAS scores demonstrated significant improvement at every post-operative follow-up visit compared to the pre-operative status. Similar improvements in the ODI scores were seen at every stage of the post-operative period. Based on the MacNab scores, excellent outcomes were achieved in 26 patients (51%), good in 14 patients (27%), fair in 9 patients (18%) and poor in 2 patients (4%) at 2-year follow-up. 1 patient underwent reoperation for new onset leg pain.

### **Discussion:**

The DiscFX is an attractive alternative procedure to fusion for patients with low back pain due to degenerative disc disease. Our study shows that at 2 years the improvement in functional outcome measures that were demonstrated at 1 year are still maintained with a low rate of re-operation.

**SURGICAL AGGRESSIVENESS INDEX (SAI) FOR METASTATIC SPINAL DISEASE (MSD)**

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**Introduction:**

Spinal surgery for decompression and stabilization remain an integral part of the management of metastatic spinal disease (MSD). There is a broad spectrum of surgical intervention involved ranging from simple decompressive procedures to significantly more aggressive procedures such as corpectomies. Parameters such as blood loss and operative time are significantly influenced by these and other factors such as primary tumour types, pre-operative embolization etc. Given the multiple factors involved, comparison of various treatment options becomes very complex. This in turn makes clinical decision difficult for surgeons as well as patients. To analyse variables influencing surgical outcomes, compare data between institutions and balance the clinical options of treatment, a standardized scoring system that compares the extent of surgery with outcome variables will be useful.

**Methods:**

This was a retrospective review of 10-year data in a tertiary university hospital on patients who underwent open spinal surgery for MSD. ICD9 codes were searched via electronic records and variables recorded. A Surgical Aggressiveness Index (SAI) was devised based on number of levels of posterior decompression, number of levels of anterior and/or posterior instrumentation, degree of corpectomy if performed, posterior fusion and vertebroplasty. It was tested for correlation with outcome measures such as length of stay, duration of surgery, blood loss and complications using multivariate linear regression analysis. The system was validated by comparison to the outcome measures using 10-year data with 241 cases, taking into consideration other clinical variables. Blood loss was determined by the surgeon and the anaesthetist.

**Results:**

There were a total of 241 patients included in this study. The mean SAI was 7.6 and the median as 7 (range: 1-20). The mean blood loss was 851 ml (range: 50-5500). There was positive correlation with higher SAI, with primary tumour types such as renal, hepatocellular and thyroid tumours and with longer operating time. Mean operative time was 249 mins (range: 50-720). Operative time correlated with higher SAI and preoperative embolization.

**Discussion:**

SAI for MSD appears to correlate well with important surgical outcome measures. Use of this Index should allow better prediction of surgical complexity and outcomes, and facilitate research and communication. We hope that use of this tool will help standardise public health related research into MSD and help computation of measures such as cost per QALY (Quality Adjusted Life Years).

## EFFECT OF PREOPERATIVE HEMOGLOBIN A1C ON SURGICAL SITE INFECTION AFTER POSTERIOR LUMBAR SPINAL INSTRUMENTATION SURGERY IN DIABETES PATIENTS

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### Introduction

Surgical site infection (SSI) is one of the most serious complications after spinal surgery. SSI following spinal surgeries has been reported at rates ranging from less than 1.0% to 10.9%. The purpose of this study is to elucidate the effect of preoperative HbA1c on SSI after posterior lumbar spinal instrumentation surgery in diabetes mellitus (DM) patients.

### Methods

510 patients who had undergone posterior instrumented lumbar spinal arthrodesis from 2011 to 2015 were reviewed at a minimum of 1-year follow-up. They were 216 males and 294 females with a mean age of 70 years, and were divided into DM group (n=112) and non-DM group (n=398). SSI was diagnosed as deep wound infection which required surgical intervention. The rate of SSI was compared between the two groups. As well, the effect of preoperative HbA1c and control of blood glucose level were also investigated.

### Results

The rate of SSI was 5.3% in DM group (6 of 112 patients) versus 1.7% in non-DM group (7 of 398 patients). In the DM group, SSI developed in 2 of 80 patients (2.5%) with HbA1c<7.0, and 4 of 32 patients (12.5%) with  $7.0 \leq \text{HbA1c}$ . Although the rate of SSI was not statistically different between non-DM and DM with HbA1c<7.0 ( $p=0.112$ ), DM patients with  $7.0 \leq \text{HbA1c}$  showed significantly higher SSI rate compared with non-DM group ( $p<0.001$  in one-way ANOVA). The rate of SSI was equivalent in 24 patients with  $7.0 < \text{HbA1c} < 8.0$  and 8 patients with  $8.0 \leq \text{HbA1c}$  (12.5% in both groups). Regarding perioperative blood glucose level, except one DM patient, fasting blood glucose (FBS) was kept less than 200 mg/dl, and maximum blood glucose level was controlled to less than 300 mg/dl.

### Discussion

The current study showed that the rate of SSI after posterior lumbar spinal instrumentation surgery did not increase in DM patients when preoperative HbA1c was less than 7.0 and perioperative blood glucose level was under good control.

## VALIDITY AND RELIABILITY OF A LOWER EXTREMITY LATERAL SCANOGRAM AS ALTERNATIVE METHOD OF EOS™ IMAGING SYSTEM IN THE ASSESSMENT OF GLOBAL SAGITTAL BALANCE

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### Introduction

Global balance of human standing is analyzed as the geometric sum of the individual alignments extending from the spinal column to the pelvis, and to the lower limbs. The innovative EOS™ Imaging system (A biplane x-ray) has opened new perspectives for the global analysis of whole body alignment, but its use is very limited due to its high cost. The lateral scanogram is that a lower extremity lateral scanogram includes lower lumbar spine, pelvis and entire lower extremity bones in a standing position. The combination of a whole spine lateral radiograph and a lateral scanogram may be an alternative to evaluate the global sagittal analysis of whole body alignment. The aim of this study was to determine the validity and reliability of a lateral scanogram in the measurement of sacropelvic parameters.

### Methods

We randomly selected 100 sets of digital radiographs, both whole spine radiographs and lateral scanograms, from our database. Sacropelvic parameters, including pelvic incidence (PI), sacral slope (SS), and pelvic tilt (PT), were measured on all images by three independent examiners on three separate occasions. Agreement regarding the measurements on both image types was calculated to assess the validity of the lateral scanogram for use in whole body alignment determinations. Intra-observer and inter-observer reliabilities among the types of measurements were calculated.

### Results

The sacropelvic area on the lateral scanogram was not visible in 19 patients (19%). In the remaining 81 patients, the sacropelvic parameters on the lateral scanogram were similar to those on the whole spine lateral radiograph. Intra-observer and inter-observer reproducibilities for both modalities were good to excellent (Table 1).

**Table 1. Validity and reliability of whole spine lateral radiograph and lower extremity lateral scanogram**

P	Correlation coefficient		Intra-observer ICC		Inter-observer ICC					
	WR	LS	WR	LS	WR	LS				
PI	0.219	0.805	0.823	-0.846	0.753	-0.793	0.680	-0.802	0.657	-0.709
SS	0.079	0.764	0.801	-0.899	0.822	-0.901	0.776	-0.801	0.757	-0.807
PT	0.388	0.852	0.913	-0.938	0.830	-0.984	0.758	-0.884	0.812	-0.834

WR; whole spine lateral radiograph, LS; lower extremity lateral scanogram

ICC; intraclass correlation coefficient

### Discussion

Sacropelvic parameter measurements on lateral scanogram were reliable and similar to those measured on whole spine lateral radiograph. With the results of this study global alignment including sacropelvic parameters can be evaluated using the lateral scanogram in combination with the whole spine lateral radiograph as an alternative to EOS™ system.

## SACRAL FRACTURES FOLLOWING INSTRUMENTED LUMBAR FUSION

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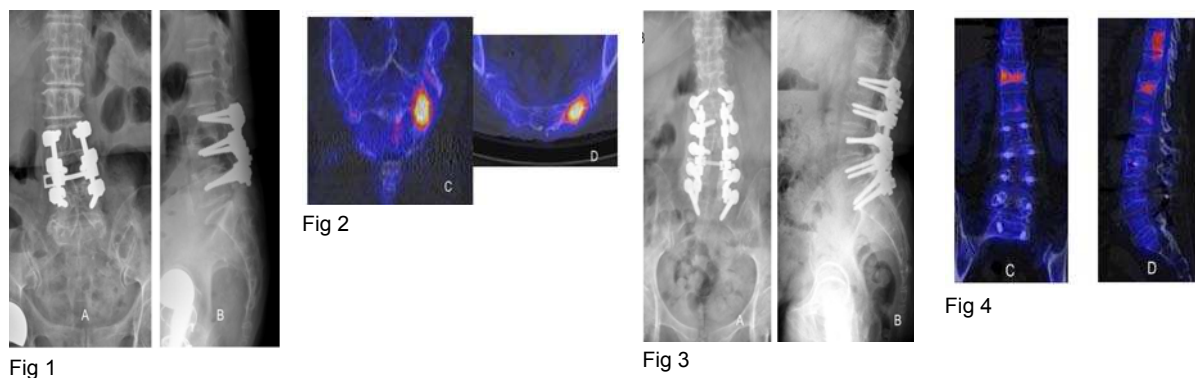
**Introduction:** Sacral fracture (SF) following instrumented spinal fusion is relatively rare. Lumbar or lumbosacral fusion alters spine biomechanics, supporting the possibility of a stress shielding effect on adjacent segments or insufficient SF. There were no reports including analysis of a matched cohort to compare risk factors between proximal adjacent segment fracture (ASF) and SF. The purpose of this study was to evaluate risk factors of SF following posterior instrumented lumbar or lumbosacral fusion, and to compare these patients with a matched cohort with proximal ASF, with a view to identifying risk factors.

**Methods:** 11 patients who showed SF following posterior instrumented fusion for degenerative lumbar diseases were identified and allocated to group 1. Among the patients showing ASF following posterior instrumented spinal fusion, 13 patients were selected after selective matching of demographic and descriptive data including age, gender, diagnosis, BMD, and BMI. These patients were allocated to group 2, and spinopelvic parameters were measured and compared between the two groups.

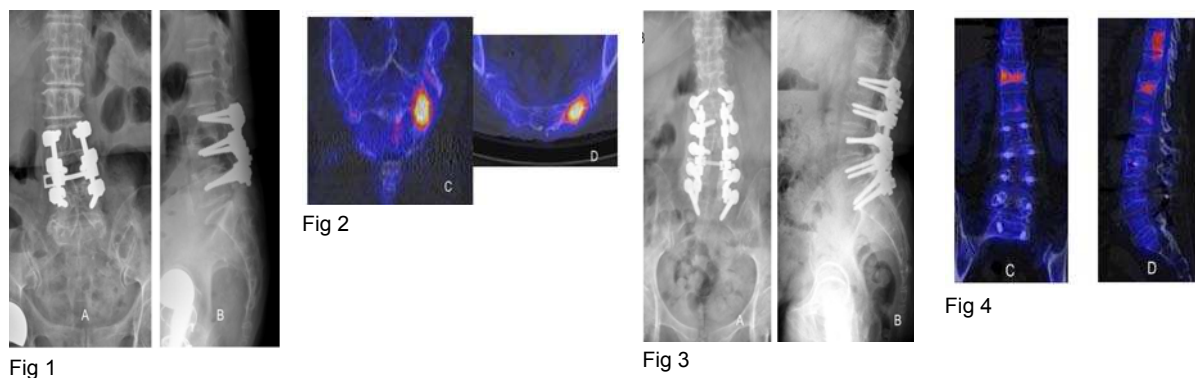
**Results:** In group 1, all patients were female and SF developed at an average of  $10.3 \pm 5.9$  years after surgery. The average number of fixed segments was  $2.7 \pm 1.5$ . All patients showed osteoporosis with T-scores of  $-3.4 \pm 0.8$ . 9 out of 11 patients had been receiving bisphosphonate as anti-osteoporotic treatment for an average of 9.4 years (range, 4-14 years). Proximal ASF developed at an average of  $32.4 \pm 34.4$  months after surgery. The average number of fixed segments was  $4.1 \pm 1.0$ , with average T-scores in Group 2 of  $-3.3 \pm 0.8$ . Compared with ASF, SF had statistical significance in pelvic incidence-lumbar lordosis (PI-LL) mismatch ( $p=0.007$ ).

**Discussion:** The risk factors of subsequent SF could be multifactorial. Osteoporosis with multisegmental fixation in elderly females is regarded as one of these risk factors. In our study, 9 (81.8%) of the 11 patients in group 1 had been taking bisphosphonates for an average of 9.4 years (range, 4-14 years), and among these, 2 patients had a history of a drug holiday during 1 year. In group 2, 7 (53.8%) out of the 13 patients had been taking bisphosphonates. However, we did not find any causal relationship between SF or proximal ASF and bisphosphonates, likely due to the small number of patients enrolled in this study. Similar to atypical femoral fractures associated with bisphosphonate use, however, it was assumed that SF can develop after long-term use of bisphosphonates. In group 1, under-correction of the sagittal alignment would cause SF due to the stooping posture with pelvic retroversion, causing tensile force of the sacrum, showing transverse fracture of the sacrum in group 1. Therefore, appropriate matching of PI-LL could be important to reduce SF. This matched cohort study demonstrates that osteoporotic elderly female patients with PI-LL mismatch following instrumented lumbar fusion could be considered at-risk for the development of SF.

**Figure 1 and 2. 78 year-old female who underwent lumbar fusion 19 years ago showing sacral insufficiency fracture**



**Figure 3 and 4. 65 year-old female who underwent lumbar fusion 5 years ago showing adjacent segment fracture**



## CLINICAL EFFICACY OF SHORT LEVEL BONY FUSION WITH LONG SEGMENT INSTRUMENTATION FOR UNSTABLE THORACOLUMBAR BURST FRACTURE ; A COMPARATIVE STUDY BETWEEN IMPLANT REMOVAL AND RETENTION

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### Introduction

Surgical treatment for unstable thoracolumbar fracture remained controversial due to many different surgical options. There is no consensus regarding the adequate fixation and fusion level. Long-level instrumentation and fusion provides more stability than short-level surgery but has weakness in morbidity. This study aims to investigate the clinical efficacy of short level bony fusion with posterior long-segment pedicle screw instrumentation by comparing implant removal and retention.

### Methods

We retrospectively analyzed the clinical and radiological outcome of 45 patients who had undergone an implant removal surgery after a posterior fusion (instruments two levels above and below injury and, bony fusion only at the fracture site posteriorly) for thoracolumbar fractures and had a minimum 2-year follow-up (R group). A control cohort of 38 consecutive patients with thoracolumbar fractures treated by the same posterior fusion methods without implant removal surgery (NR group) were enrolled. Subjects were evaluated with clinical parameters (VAS and ODI) and radiologic parameters (vertebral compression ratio, kyphotic angle, segmental motion, pelvic parameters, and adjacent disc degeneration).

### Results

The average age was  $47.3 \pm 17.5$  years in the R group and  $49.1 \pm 18.1$  years in the NR group ( $P=0.843$ ). There were 21 males in the R group and 29 in the NR group ( $P=0.756$ ). The mean follow-up duration was  $65.0 \pm 35.6$  months (range, 24~192 months). There was no significant difference between the two groups regarding the sex ( $P=0.756$ ), level of fracture ( $P=0.358$ ), type of fracture ( $P=0.209$ ), radiologic parameters at the injury (all  $P > 0.05$ ), compensation ( $P=0.429$ ), and follow-up duration ( $P=0.635$ ). Clinical and radiologic outcomes at the time of removal surgery in the R group were similar with those of the NR group. After 4-year follow-up from the index surgery, segmental motion in the R group was larger than NR group ( $P=0.022$ ). ODI was significantly lower in R group ( $14.9 \pm 9.8$ ) than NR group ( $22.1 \pm 14.0$ ) ( $P=0.042$ ). Hardware failure was 6 in the R group and 3 in the NR group ( $P=0.334$ ).

### Discussion

Short level bony fusion (at the fracture level) with posterior long-segment pedicle screw instrumentation and following implant removal provided reliable fracture site fusion and minimize the spinal segment stiffness without severe morbidity. For the aspects of spinal flexibility, this surgical method has more priority for the long instrumentation on the unstable thoracolumbar fracture.

## IS THE INTRADISCAL VACUUM PHENOMENON AT THE ADJACENT SEGMENT OF FUSION CLINICALLY IMPORTANT FOR THE ADJACENT SEGMENT PATHOLOGY? ; A COMPARATIVE STUDY WITH DISC DEGENERATION USING MINIMUM 5-YR FOLLOW-UP MRI

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### Introduction

In the studies of adjacent segment pathology after lumbar fusion, much attention has been focused on the adjacent disc degeneration(ADD) and disc pathology on MRI. Less has been documented about the intradiscal vacuum phenomenon at the adjacent level(AIVP) on radiographs. The aim of this study was to investigate the clinical importance of AIVP as the radiographical adjacent segment pathology after fusion by comparing the occurrence in fusion group with non-fusion group with the plain radiography and MRI.

### Methods

Seventy-five patients who had undergone spinal fusion (270° fusion 38, PLF 37) for lumbar degenerative diseases and had taken MRI at the time of index treatment and at least 5-year follow-up were included. The control cohort involved 66 patients with non-fusion (decompression 28, conservative treatment 38). ADD was evaluated using preoperative and follow-up MRI. AIVP was examined using lateral standing and dynamic radiographs.

### Results

The mean age was 51.9±14.6 years and the number of male patients was 31(41.3%). The mean MRI follow-up duration was 90.5±29.1 months(range, 60-164 months). The occurrence of ADD was 24% in the fusion group and 19% in the non-fusion group(P=0.692). The occurrence of AIVP was 10(13.3%) in the fusion group and 4(6.1%) in the non-fusion group(P=0.123). The AIVP was 4 at upper level, 5 at lower level, and 1 at both levels in the fusion group while 2 at upper level, 1 at lower level, and 1 at both levels in the non-fusion group (P=0.425). The occurrence of AIVP was not different between 270°fusion and PLF(P=0.745). The presence of AIVP was not associated with the occurrence of ADD(P=0.617).

### Discussion

AIVP occurred similarly at both fusion and non-fusion group. There was no difference regarding the occurrence of AVIP between fusion methods. The presence of AIVP was not associated with the occurrence of ADD. These results imply that the presence of intradiscal vacuum phenomenon may be natural course of spinal degeneration rather than spinal fusion.



## DOES THE PREOPERATIVE DIAGNOSIS OF DEGENERATIVE LUMBAR DISEASE DETERMINE THE CHARACTERISTICS OF CLINICAL ADJACENT SEGMENT PATHOLOGY?

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### Introduction

Adjacent segment pathology(ASP) includes various degenerative conditions such as degenerative disc disease, spinal stenosis, fracture, segmental instability, and spondylolisthesis. Although many risk factors for the ASP were evaluated, there has been no study regarding relationship between the characteristics of clinical ASP(CASP) and the preoperative diagnosis of degenerative lumbar disease. The aim of this study was to elucidate the relationship between the radiographical characteristics of CASP and the preoperative diagnosis of degenerative lumbar disease.

### Methods

This was a retrospective study of 111 patients who had undergone fusion for degenerative lumbar disease and re-evaluated due to clinical symptoms; 45 for spinal stenosis, 45 for spondylolisthesis and 21 for degenerative disc disease. All subjects were evaluated by lumbar radiographs and MRI at the time of index treatment and at the mean  $69.0 \pm 34.7$  months(range, 24-160 months) after surgery. Using preoperative and last follow-up lumbar radiographs and MRI, preoperative diagnosis and the radiographical characteristics of CASP were analyzed. CASP was defined by any changes in adjacent level of fusion which were closely related with clinical findings and divided into SS(moderate to severe SS), SLP(static and dynamic slip > 2mm), DDD(>2 Pfirman grade change, segmental instability, focal protruded, extruded, or sequestered HNP). Demographic factors were obtained from medical records.

### Results

There were no statistically significant differences regarding demographic factors except age(All  $P > 0.05$ ). The radiographical characteristics of CASP are shown in the below table.

	Age (Years) at fusion		Sex (M:F)		The radiographical characteristics of CASP	
	SS	SLP	DDD	SS	SLP	DDD
SS (N=45)	58.4 ± 9.7			11:34	7 (15.6%)	0 (0%) 2 (4.4%)
SLP (N=45)	50.1 ± 15.3			16:29	1 (2.2%)	5 (11.1%)
DDD (N=21)	45.5 ± 11.1			9:12	0 (0%)	4 (19.0%)
<b>P</b>	0.035*			0.279	0.018*	0.385 0.170

Among the patients with CASP, there was no significant difference of age between groups ( $P=0.313$ ). Only preoperative diagnosis was different significantly ( $P=0.026$ ).

### Discussion

There was a statistically significant difference of the radiographical characteristics of CASP among different degenerative disc disease. These results imply that the preoperative diagnosis degenerative disc disease may influence on the radiographical characteristics of CASP, and at the occurrence of CASP, the preoperative diagnosis must be reviewed and the treatment methods for CASP will be selected carefully.

## RISK FACTORS FOR SKIPPED ADJACENT SEGMENT PATHOLOGY AFTER SHORT INSTRUMENTED LUMBAR FUSION -DOES PRE-EXISTING DISC DEGENERATION MATTER IN ACCELERATING ADJACENT SEGMENT PATHOLOGY?-

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**Introduction:** Pre-existing disc degeneration may be accelerated by stress concentration after fusion. The condition of adjacent discs is important in the development of adjacent segment pathology (ASP). However, there is no report on risk factors for skipped adjacent segment pathology (SASP) that does not involve the juxta-proximal adjacent segment (JPAS). The purpose of this study was to investigate risk factors for SASP after instrumented lumbar fusion.

**Methods:** We reviewed 41 patients with SASP after posterolateral lumbar fusion with or without posterior lumbar interbody fusion. SASP was defined as collapse of the intervertebral cephalad disc space, without involvement of the JPAS. All patients underwent pre-operative magnetic resonance imaging (MRI); disc degeneration was graded at both the JPAS and the segment one level cephalad to the JPAS according to Pfirrmann's classification. The JPAS with less disc degeneration were considered as the control.

**Results:** Initially, 12 of 41 patients had grade II disc degeneration at the JPAS and 29 patients had grade III. At the cephalad segment, 21 patients had grade III, and 20 patients grade IV preoperatively. Fourteen patients had the same grade at both segments. In other 27 patients, the grade of disc degeneration was one (n=21, 51.2%) or two (n=6, 14.6%) levels higher at the cephalad segment than at the JPAS. None of spinopelvic parameters was correlated with degenerative changes at any segments. Follow-up MRI performed in 23 patients showed that the cephalad segment underwent more degenerative changes than the JPAS. Among them, 18 patients underwent revision surgery for new-onset neurological symptoms and axial low back pain.

**Discussion:** Clinically, the consensus is that pre-existing facet and disc degeneration may increase a risk of development of ASP. It is accepted that loss of disc space after instrumented lumbar fusion is caused by telescoping of the lumbar spine, attributable to the vertical configuration of facet joints, triggering up-down loading of intervertebral discs, and featuring stress concentration.

In conclusion, we found that instrumented spinal fusion accelerated pre-existing disc degeneration because of stress concentration, rather than natural age-related changes. ASP can develop more rapidly at the degenerative cephalad segments, skipping the adjacent segments without disc degeneration. Therefore, we provide clues to predict the fate of segments about development of ASP after instrumented lumbar fusion although we could not conclude whether all degenerative segments should be fused or not.



**Figure . 66 year-old female with degenerative lumbar spondylolisthesis.**

**A.** Preoperative radiograph. **B.** MRI Pfirrmann grade: II (juxta-proximal segment) and IV (cephalad segment). **C.** At postoperative 8 years. **D.** Follow-up Pfirrmann grade: V (juxta-proximal segment) and III (cephalad segment). **E.** Bone single-photon emission computed tomography/CT: hot uptake at the cephalad segment alone.

## LEARNING CURVE FOR RESIDENTS PLACING PEDICLE SCREWS WITH O-ARM NAVIGATION

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### Introduction

Pedicle screws (PSs) are widely used for various indications as an efficient method for spinal fusion; however, PS placement remains challenging because improper placement can injure nerve roots, spinal cords, and major vessels. Accurate placement requires substantial experience, thus senior surgeons are reluctant to let juniors insert PSs because of these complications. As a result, junior surgeons have little opportunity to gain experience using this technique. Multiple reports have suggested that an O-arm navigation system increases the accuracy of PS placement; however, it has not been established if junior surgeons can insert PSs as safely as experienced surgeons. The aim of this study was to evaluate the learning curve of residents placing PSs with an O-arm navigation system.

### Methods

The authors performed a retrospective review of 24 patients with lumbar disease who underwent percutaneous pedicle screw (PPS) fixation with an O-arm navigation system between April 2016 and November 2016 in our institution. In 12 cases, PS placement was performed by a resident with no experience using this procedure (group A), and an experienced senior surgeon performed the other cases (group B). In group A, the resident inserted PSs under direction of experienced surgeons. The pedicle breach rate and PS insertion time per screw were examined. The breach rate was assessed with CT scans 1 week after surgery. PS positions were classified into 4 grades based on the grading system described by Neo et al., as follows: grade 0, no perforation; grade 1, perforations < 2 mm; grade 2, perforations > 2 mm, but < 4 mm; and grade 3, perforations > 4 mm. Moreover, to assess the learning curve, patients in group A were divided into the first 6 cases (group A1) and the latter 6 cases (group A2).

### Results

In group A, 74 PSs were inserted at the Th10-S1 levels. The overall breach rate was 6.8% (n=5). Four PSs (5.4%) were grade 1 breaches and 1 PS (1.4%) was a grade 2 breach. No grade 3 or 4 breaches were noted. The average insertion time per screw was 6.3±1.7 min. There was a significant difference in the average insertion time between group A1 (7.4±1.7 min) and group A2 (5.3±1.0 min; p=0.035).

In group B, 66 PSs were inserted and the overall breach rate was 1.5% (n=1), which was not significantly different from the breach rate in group A (p=0.21). The average insertion time was 4.2±0.88 min, which was significantly shorter than the time in group A (p=0.0015).

### Discussion

The breach rate in group A (6.4%) was comparable to that in group B (1.5%). The present results suggest that residents also can safely insert PSs with an O-arm navigation system under supervision by a senior surgeon. The insertion time in group A was longer than in group B, and was shorter in group A2 than A1. Thus, there is a learning curve with PS placement, and resident skill has not plateaued. We conclude that O-arm navigation is a useful and safe method to teach PS insertions for junior surgeons.

## 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, 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; 1.78,  $p < 0.01$ ) and the location of component of SINS (OR; 0.387,  $p < 0.01$ ) 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  $109 \pm 104.8$  days from the first visiting. Whereas twelve of 88 patients with less than 9 points of SINS (13.6%) represented SSM at the mean  $139.5 \pm 186.8$  days.

### 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.

## COMPARISON OF COMPLICATIONS OF SPINAL SURGERY IN ELDERLY PATIENTS PERFORMED AT A TEACHING HOSPITAL AND AN AFFILIATED HOSPITAL

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### Introduction:

With the increasing number of elderly patients, the management of complications after spinal surgery becomes more important. Teaching hospitals are more fully equipped than affiliated hospitals. However, spinal surgery in elderly patients is increasing at poorly-equipped affiliated hospitals. The purpose of this study is to compare complications of spinal surgery in patients aged 80 years or older at a teaching hospital and an affiliated hospital.

### Methods:

From January 2014 to September 2016, a total of 123 spinal surgeries were performed in patients aged 80 years or older (mean age: 83.6±2.8) at a teaching hospital (TH) and an affiliated hospital (AH). Complications (surgery-related, systemic), morbidity, comorbidities, the number of medications, surgical site, operative time, blood transfusion, spinal instrumentation, operative procedure, and hospitalization duration were evaluated statistically for patient groups at TH (74 patients) and AH (49 patients).

### Results:

Surgery-related complications occurred in 19 patients (26%) at TH, and 11 (22%) at AH. The most common complication was delirium in both TH and AH. Systemic complications occurred in 6 patients (8%) at TH, and 5 (10%) at AH. Three patients (4.1%) died at TH, with acute cholangitis, pancreatic cancer, or acute cholecystitis as the respective causes of death; 1 patient (2.0%) died from brain hemorrhage at AH. Complication and morbidity rates did not differ significantly at TH and AH.

### Discussion:

No difference was found in complication rates for spinal surgery in elderly patients at TH and AH. However, unexpected complications can still occur.

## QUALITY MEASURES IN SPINE SURGERY

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### Background

Quality measures are tools for evaluating and improving healthcare through the measurement of healthcare processes, outcomes, patient perceptions, and organizational structures. Two systems commonly used classify measures are the Donabedian Framework and the United States (US) National Quality Strategy (NQS). The Donabedian model breaks down healthcare into three phases of delivery: structure, process, and outcome. The NQS model establishes six priorities that a well functioning healthcare system should address: patient and caregiver-centered experience and outcomes, patient safety, communication and care coordination, community and population health, efficient use of resources, and effective clinical care.

A balanced approach to quality assessment employs quality measures of all domains and addresses each of the NQS priorities, as the evaluation of one measure (e.g., attaining a specific outcome) may be predicated on another (having the processes in place to achieve this outcome). The purpose of this study is to assess the state of quality measures in spine surgery.

### Methods

We systematically reviewed MEDLINE/PubMed, Embase, the US National Quality Forum, the US Agency for Healthcare Research and Quality, and the US Physician Quality Reporting System, as well as clinical practice guidelines from the American Academy of Orthopaedic Surgeons, Congress of Neurological Surgeons, and the North American Spine Society for quality measures relevant to spine surgery. All measures were then categorized by clinical focus, NQS priority, and Donabedian domain.

### Results

We identified 76 quality measures relevant to spine surgery: 50 specific to the management of spine pathology, and 24 related to the general care of spine patients.

The majority of the spine-specific measures focused on the NQS priority of "Effective Clinical Care" 44 (88%), followed by "Efficient use of Healthcare Resources" 5 (10%), "Patient Safety" 2 (4%), and "Person and Caregiver Centered Experience and Outcomes" 1 (2%). Two measures covered more than one priority. Furthermore, 45 (90%) were process measures and 10 (20%) were outcome measures. Five measures covered more than one domain.

The majority of the general care measures addressed the NQS priority of "Patient Safety" 10 (42%), followed by "Communication and Coordination of Care" 7 (29%), "Person and Caregiver Centered Experience and Outcomes" 5 (21%), "Effective Clinical Care" 4 (17%), and "Community and Population Health" 1 (4%). Three measures covered more than one priority. Fourteen (58%) were process measures and 11 (46%) were outcome measures. One measure covered more than one domain.

### Conclusion

Spine surgery quality measures address both specialty specific as well as general care concerns. The majority of spine-specific quality measures were developed by national societies whose members practice spine surgery, and are focused on process measures relating to effective clinical care. General care measures, on the other hand, were all developed by national regulatory institutions and more broadly addressed NQS priorities and Donabedian domains. Additional measures, both specific to the spine, as well as to the general care of spine patients, are needed to ensure proper assessment of clinical practice and to identify areas for improvement.

## IMPROVEMENT OF SAGITTAL BALANCE AFTER MINIMALLY INVASIVE LATERAL LUMBAR INTERBODY FUSION FAVORABLY AFFECTS THE RISK OF FALL RELATED FUNCTIONAL MOBILITY TESTS AND QUALITY OF LIFE IN PATIENTS WITH LUMBAR SPINAL STENOSIS

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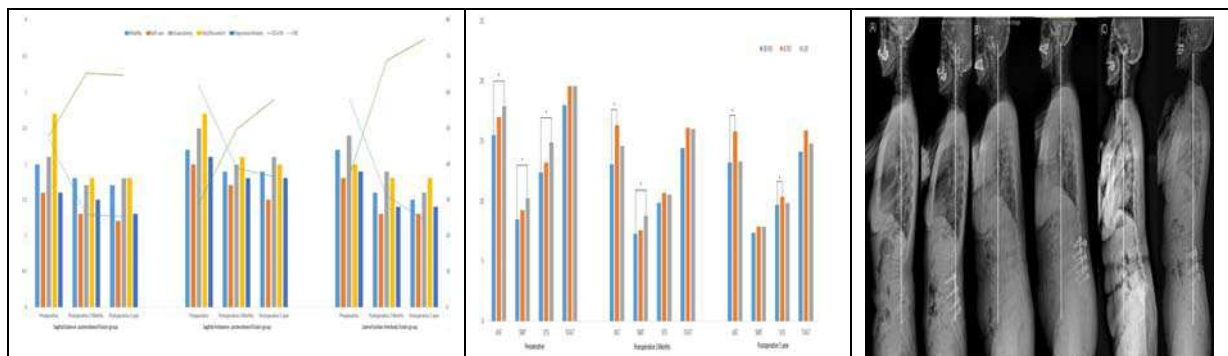
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**INTRODUCTION** Sagittal balance has become a major concern in the treatment of degenerative spine disease. However, the impact of sagittal balance in the surgical treatment of degenerative spinal disease is still controversial.

**METHOD** This is a prospective and retrospective matched cohort study. From November 2011 to March 2015, 56 patients who underwent minimally invasive lateral lumbar interbody fusion (LLIF) and 112 patients receiving decompression/postero-lateral fusion (PLF) *in situ* surgery for LSS were enrolled. Based on sagittal balance status and surgery type, patients were divided into three groups: sagittal balance(SB) PLF, sagittal imbalance(SI) PLF, and LLIF groups and their outcomes were compared using radiologic parameters related to sagittal profiles, functional mobility tests reflecting the risk of falling, a fall diary, the Oswestry disability index(ODI), and the Euro-QoL 5D(EQ-5D) visual analogue scale(VAS).

**RESULTS** The mean patient age was 70.6 years in the SB PLF group, 71.4 years in the SI PLF group, and 70.3 years in the LLIF group(not significant). The mean C7PL was  $6.2\pm 13.6$  mm in the SB PLF group,  $72.9\pm 33.8$  mm in the SI PLF group, and  $74.8\pm 38.2$  mm in the LLIF group preoperatively. Postoperatively, C7PL in only the LLIF group improved significantly( $p<0.05$ ). Patients in the LLIF group showed more improved scores than the SI PLF group for four functional tests during postoperative follow-up( $p<0.05$ ), but their performance was still worse than those in the SB group. The average number of falls during the follow-up period was  $0.4\pm 0.7$  in the SB PLF group,  $1.1\pm 1.4$  in the SI PLF group, and  $0.8\pm 1.0$  in the LLIF group( $p<0.05$ ). ODI and the EQ-5D VAS also showed a greater improvement in the LLIF group than the SI PLF group.

**CONCLUSIONS** Consideration of sagittal imbalance in patients with LSS and its surgical correction using combined minimal invasive LLIF and posterior surgery is encouraged in order to attain better surgical and functional outcomes and a lower incidence of actual falls after surgical treatment than when *in situ* PLF surgery is performed.



## SELECTIVE THORACIC FUSION TREATED BY ROD DEROTATION AND DIRECT VERTEBRAL ROTATION IN THE TREATMENT OF THORACIC ADOLESCENT IDIOPATHIC SCOLIOSIS

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**INTRODUCCION:** Determination of distal fusion levels and direction of rod derotation (RD) and direct vertebral rotation (DVR) are very important factors for deformity correction and preservation of motion segments in the treatment of adolescent idiopathic scoliosis (AIS). However, there are few long term follow-up studies regarding distal fusion level treated by RD and DVR following selective thoracic fusion (STF) with pedicle screw instrumentation (PSI) in the treatment of thoracic AIS. This study is to analyze the exact distal fusion level in the treatment of thoracic AIS using RD and DVR following STF with PSI.

**METHODS:** Sixty-five patients with thoracic AIS treated by selective thoracic fusion from neutral vertebra (NV) to NV or NV-1 with RD and DVR with a minimum 10-year follow-up were retrospectively analyzed. The patients were divided into two groups according to the radiographic outcomes based on adding-on, LIV tilt, and coronal balance (CB); satisfactory group (n =52) and unsatisfactory group (n = 13). An adding-on or a lowest instrumented vertebra (LIV) tilt of more than 10° or coronal balance of more than 15 mm were considered unsatisfactory results.

**RESULTS:** There were 13 cases of unsatisfactory results (10 cases of AD, 2 cases of CB progression, and 1 case of LIV tilt progression) and the overall prevalence of unsatisfactory results was 20% (13/65 patients). There was no significant difference in main thoracic (MT) curve between the satisfactory and unsatisfactory groups postoperatively ( $P = 0.218$ ) and at the last follow-up ( $P = 0.636$ ). Additionally, there was no significant difference in proximal thoracic (PT) and lumbar curve postoperatively (PT curve:  $P = 0.855$ , lumbar curve:  $P = 0.996$ ) and at the last follow-up (PT curve:  $P = 0.191$ , lumbar curve:  $P = 0.149$ ). However, MT and lumbar curve in the unsatisfactory group showed progression of deformity correction at the last follow-up. LIV tilt and LIV disc angle deteriorated during the follow-up in the unsatisfactory group, which showed relatively small gap difference (short fusion) between LIV (lowest instrumented vertebra) and NV and lesser correction of AV and EV rotation (insufficient DVR) compared with satisfactory group..

**DISCUSSION:** An unsatisfactory group had a significant influence on the progression of MT and lumbar curve which is closely correlated with the deterioration of LIV tilt and disc angle. Additionally, an unsatisfactory group showed relatively short fusion between LIV and NV and insufficient DVR. Therefore, distal fusion level which should be extended to NV or NV-1 and sufficient DVR which should be opposite to that of the vertebral rotation were inevitable to achieve satisfactory deformity correction and prevent a distal adding-on phenomenon in the treatment of thoracic AIS.



**FACTORS AFFECTING SEGMENTAL LORDOSIS OF LUMBAR SPINE AFTER XLIF**

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**Introduction**

XLIF (extreme lateral interbody fusion) surgery is very useful procedure for restoration of segmental lordosis in optimizing surgical outcomes. Recent studies had reported anterior placement results in achievement of larger lordosis. However, no study had reported whether posterior elements were affected after lumbar lordosis gain. The aim of this study was to analyze factors influencing segmental lumbar lordosis after XLIF surgery.

**Methods**

Thirty-six patients and 83 levels were studied. Segmental lordosis, lumbar lordosis(T12-S), lower lumbar lordosis (L4-S), and disc height were measured preoperatively and postoperatively on radiographs. Cage position and facet angle were analyzed using radiographs and CT scan image.

**Results**

Mean lumbar lordosis increased from 19.3 degree to 33.7 degree, but lower lumbar lordosis increased from 18.9 degree to 21.3 degree. The mean increase by spinal level was 16.6 degree at L1/2, 7.1 degree at L2/3, 6.4 degree at L3/4, 2.7 degree at L4/5. On the other hand, the average facet angle by spinal levels was 24.3 degree at L1/2, 27.2 degree at L2/3, 29.8 degree at L3/4, 41.5 degree at L4/5. The increase in lower lumbar spine was less compared to upper lumbar spine. Anterior cage placement resulted in largest lordosis gain (+7.3 degree per level) while posterior placement was less (+4.6 degree per level).

**Discussion**

We found increased in lumbar lordosis after XLIF were strongly affected not by anterior cage placement alone but also change in facet angle. Posterior element might influence the increased in lumbar lordosis after XLIF.

## DETERMINATION OF DISTAL FUSION LEVEL IN MAJOR THORACOLUMBAR AND LUMBAR ADOLESCENT IDIOPATHIC SCOLIOSIS TREATED BY ROD DEROTATION AND DIRECT VERTEBRAL ROTATION

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**INTRODUCION:** Determination of distal fusion level is a very important factor for deformity correction, maintenance of trunk balance, and preservation of motion segments in the treatment of adolescent idiopathic scoliosis (AIS). Fusion level may influence postoperative surgical outcomes, and improper fusion level may result in undercorrection or overcorrection of major and compensatory curves which could cause trunk imbalance and decompensation. However, the selection of distal fusion level remains debatable, and there has been no definitive criteria in AIS with major thoracolumbar and lumbar (TL/L) curve. Therefore, the present study aimed to analyze the exact distal fusion level in the treatment of major TL/L AIS using rod derotation (RD) with direct vertebral rotation (DVR) following pedicle screw instrumentation (PSI).

**METHODS:** AIS patients with major TL/L curves (n=64) treated by PSI with RD and DVR methods with a minimum 2-year follow-up were divided into AL3 (flexible) and BL3 (rigid) according to the flexibility and rotation by preoperative bending radiographs.

**RESULTS:** There was no significant difference in TL/L (major) curve between the AL3 and BL3 groups postoperatively ( $P = 0.933$ ) and at the last follow-up ( $P = 0.144$ ). Additionally, there was no significant difference in thoracic (minor) and compensatory (caudal) curve postoperatively (thoracic curve:  $P = 0.828$ , compensatory curve:  $P = 0.976$ ); however, there was a significant difference in compensatory (caudal) curve at the last follow-up ( $P = 0.041$ ). The overall prevalence of unsatisfactory results was 28.1% (18/64 patients), and the prevalence was 15.2% (7/46) in the AL3 group and 61.1% (11/18) in the BL3 group, which was significantly different ( $P < 0.05$ ).

**DISCUSSION:** The results of this study strongly support and validate Suk's classification guidelines for selection of distal fusion level in the treatment of AIS with major TL/L curves using RD and DVR following PSI. Unsatisfactory results occurred more often in the BL3 group than in the AL3 group, and unsatisfactory results had a significant influence on the progression of compensatory (caudal) curve and LIV disc angle in the BL3 group. LIV would be selected at L3 (end vertebra [EV]) when the curve is flexible; L3 crosses CSVL with a rotation of less than grade II in preoperative bending radiographs. However, if the curve is rigid, LIV should be extended to L4 (EV + 1) in order to prevent the adding-on phenomenon in the treatment of major TL/L AIS using RD and DVR following PSI.

## DISTAL ADDING-ON AND RISK FACTORS IN SEVERE AND RIGID SCOLIOSIS

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**Introduction:** Previous work has evaluated the challenges in the treatment of patients with severe and rigid scoliosis and the risks of complications. Furthermore, although several studies have investigated postoperative distal adding-on and attendant risk factors in Lenke type 1A scoliosis, very few have focused on distal adding-on in severe and rigid scoliosis. The aim of this retrospective study was to identify associated risk factors of distal adding-on in severe and rigid scoliosis.

**Methods:** In this study, 48 consecutive patients with severe and rigid scoliosis underwent posterior spinal fusion surgery. The parameters of preoperative, immediately postoperative, and minimum 2-year follow-up radiographs were evaluated. The patients were classified as positive or negative for distal adding-on at follow-up, and risk factors were comparatively analyzed in the two groups.

**Results:** The average Cobb angle and flexibility of the main thoracic curve (MTC) were 107.48° ± 15.98° and 16.4% ± 10.2%, respectively, before surgery. Distal adding-on was observed in 12 patients (25.0%) at follow-up. Univariate analysis identified several factors significantly associated with distal adding-on. Furthermore, significant independent risk factors identified by stepwise logistic regression analysis included the correction rate of the MTC immediately after surgery (odds ratio: 1.107, 95% confidence interval: 1.024 – 1.197, P = 0.011) and the difference between the lower instrumented vertebra (LIV) and last touching vertebra (LTV) levels (odds ratio: 0.121, 95% confidence interval: 0.028–0.518, P = 0.004).

**Discussion:** In severe and rigid scoliosis, a high correction rate of the MTC immediately after surgery and the LIV level above the LTV were significantly associated with distal adding-on.

## THE REOPERATION OF COFLEX INTERSPINOUS DYNAMIC STABILIZATION IN THE TREATMENT OF DEGENERATIVE DISEASE OF THE LUMBAR SPINE

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**Introduction:** To evaluate the rate of revision surgery after posterior Coflex interspinous dynamic stabilization for degenerative disorders of the lumbar spine, and to discuss its causes and management.

**Methods:** From Sept 2007 to July 2015, 295 patients with degenerative disorders of the lumbar spine were treated with decompression and Coflex interspinous dynamic stabilization in our hospital. In order to evaluate the rate of revision surgery among these patients, and to discuss its causes and management, a retrospective study was conducted and all revision patients were treated and followed up to evaluate the clinical outcome through patient's satisfaction.

**Results:** Among 295 patients in this study, there were 16 patients underwent revision surgery and the total rate of reoperation was 5.4%. The duration between revision procedure and primary procedure was  $15.1 \pm 23.4$  months (range, 0.1 - 60 months) in these patients. Among the 16 patients, 6 patients (37.5%) were underwent reoperation due to non-implant related complications such as infection of the wound or local hematoma. These 6 patients all healed with debridement or hematoma evacuation. Another 10 patients (62.5%) who underwent reoperation due to implant related complications. There were two patients who had topping-off procedure initially developed pedicle screw loosening or nerve root adhesion and were treated with reimplantation of the fixation or neurolysis. Another 8 patients who had single level Coflex dynamic stabilization developed symptoms related to the deterioration of the degeneration at previous segment or adjacent segment. Those patients were managed with decompression and fusion with pedicle screw fixation. None of the 16 patients who underwent revision surgery was directly related to the Coflex implant such as migration, loosening or dislocation of the Coflex implant and fracture of the spinous process. These revision patients were followed up for  $28.6 \pm 12.6$  months (range, 6-48 months) and 93.8% of the patients were satisfied with the revision surgery at the final follow-up.

**Discussion:** Coflex interspinous dynamic stabilization for the treatment of degenerative disorders of the lumbar spine was safe and the reoperation rate was low. The main cause of the revision surgery including wound infection, local hematoma, or degeneration at previous segment or adjacent segment was not directly related to Coflex implant itself.

## ANALYSIS OF CHARACTERISTICS OF SPINAL SURGICAL EMERGENCY EXCLUDING TRAUMA CASES

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### Introduction

Emergency spine surgeries excluding trauma has poor prognosis because of the development of paralysis compared to elective surgeries. The aim of this study was to evaluate the outcomes and analyze the characteristics of emergency spine surgeries.

### Methods

Patient's records from 2013-2016 were reviewed, total of 30 patients (22 male, 8 female) received emergency spine surgery in our hospital. Mean age was 60.0(24-81) at the time of procedure and mean follow-up time was 272 days (7-911). Fourteen patients (47%) were referred by other hospitals. Cases were 15 spinal metastatic tumors, 10 lumbar disc hernia, 3 extradural hematoma, 1 cervical myelopathy, and 1 postoperative hematoma. Primary lesions of metastatic tumor were lung : 4, prostate : 4, breast : 2, rectum : 2, and others : 3.

### Results

Eighteen patients (60%) were diagnosed before the onset of paralysis in which 7 patients (47%) were introduced from other hospitals. Five cases were diagnosed malignancy for the first time when paralysis developed. Eight cases (80%) with lumbar disc hernia underwent emergency treatment. Duration from the onset of paralysis to operation was 3.7 days in spinal tumor, 2.9 days in lumbar disc hernia, 2 days in cervical myelopathy, 0.3 days in extradural hematoma, and immediate surgery in postoperative hematoma. Minimum of 1 and progressive stage recovery by FRANKEL classification was detected in 6 (40%) patients with metastasis, 7 cases (70%) with lumbar disc hernia and 3 cases (100%) with extradural hematoma.

### Discussion

Emergency surgery in spinal tumor has poor prognosis. Despite of aggressive treatment, regular doctor might overlook spinal lesion. Orthopedic surgeon must inform other medical specialties to initiate early detection and intervention of spinal lesion to prevent emergency surgery, which has a poor prognosis.

**RISK FACTORS FOR ROD FRACTURE AFTER POSTERIOR CORRECTION SURGERY IN ADULT SPINAL DEFORMITY: MULTIVARIABLE LOGISTIC REGRESSION ANALYSIS**

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**INTRODUCTION:** The corrective surgery for adult spinal deformity (ASD) has wide spread use among the procedures of spinal surgery. A favorable result would be obtained unless the morbidity and/or mortality occur. Implant-related complications include rod breakage, hook dislodgement, and pullout of pedicle screws. Rod fracture (RF) is one of the most common complications in ASD surgery, and it influences on the surgical results. The purpose of the current study was to determine what are the risk factors for RF after the correction surgery for the patients with ASD.

**METHODS:** A retrospective review of clinical records was conducted on consecutive surgical cases with ASD in April 2011 to March 2015. Thirty patients (28 female, 2 male; an average age of 64.3 years) met strict inclusion/exclusion criteria with a minimum 1-year follow-up. Inclusion criteria are based on SRS-Schwab adult spinal deformity classification: the cases with PI minus LL > 10 degrees or SVA > 45mm or PT > 20 degrees. The sagittal vertical axis (SVA), T1 pelvic angle (TPA), lumbar lordosis (LL), pelvic tilt (PT), pelvic incidence (PI), PI-LL, sacral slope (SS), sacrofemoral angle (SFA) were measured on the whole spine standing X-P before surgery, immediate after surgery, and at the final follow-up. The number of instrumented segments, correction rate, presence of XLIF and any osteotomies, bone union were evaluated. The patients were divided into two subgroups: RF and non-RF. Stepwise procedure in multivariable logistic regression analysis was performed to determine which factors were predictive of the occurrence of the RF. Odds ratios (OR) were calculated to evaluate the association between risk factors and RF. Significance levels were set at a P-value less than 0.05.

**RESULTS:** We recognized 12 RF cases during follow-up. Risk factors for RF were the numbers of instrumented segments (OR=1.29) and pre-operative PI-LL (OR=1.04). Receiver operating characteristic (ROC) curves were made for the number of instrumented segments, pre-operative PI-LL, and LL. The optimal cut-off value was estimated to be 10 segments. Preoperative PI-LL was associated with the difference in LL between pre- and postop. The cut-off value of the preoperative PI-LL and the difference in LL between pre- and postop was 34 and 28 degrees, respectively.

**DISCUSSION:** The literature says that an ideal sagittal alignment after the corrective surgery for ASD can reduce the instrument failure rate. However, the current study demonstrated that the higher correction of the deformity was obtained, the more frequent RF occurred. We used the double cobalt-chromium rods (5.5mm in diameter) without any braces after surgery. The surgical and postoperative rehabilitation strategy, especially on the implant size and braces, should be considered into account to reduce the RF in the surgical treatment for the patients with ASD.

## CLINICAL OUTCOME OF THE CORRECTIVE POSTERIOR LONG FUSION SURGERY FOR PATIENTS WITH MULTIPLE VERTEBRAL-BODY FRACTURES IN VERY SEVERE OSTEOPOROSIS: A MINIMUM TWO-YEAR FOLLOWUP STUDY

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**Introduction:** Multiple vertebral-body fractures due to very severe osteoporosis could be a cause for sagittal imbalance due to kyphotic deformity and, furthermore, can be a cause for paralysis of lower extremities. The surgical treatment for this condition is extremely difficult mainly because of significantly poor bone quality and patient's general status. Additionally, there are few reports regarding surgical outcome of this condition.

**Aim:** The aim of this study was to evaluate clinical outcome of long spinal fusion for this condition with minimum two-year follow up, in which we used S2-alar iliac screw (S2AIS) for distal-end anchor.

**Patients and Methods:** 16 patients suffering from multiple vertebral fractures below Th11, due to very severe osteoporosis, who underwent long spinal fusion with S2AIS, and minimum followup period over two years were enrolled. There are 3 males and 13 females and most of them could not stand or walk because of severe back pain or paralysis of lower extremity. The average age was 76.3 years old (64~87) and follow-up periods were 28.1±4.1 months. For these patients, clinical outcome after surgical treatments were evaluated.

**Results:** The average blood loss during surgery was 950.3±558.9g and surgery time 406.9±70.6min. The anchor for distal-end of spinal fusion was S2AIS in all cases, in which 6 cases underwent spinal fusion to upper-thoracic spine and 10 cases middle to lower thoracic spine (average: Th7.4±1.8). For all cases, multi-level TLIF and Ponte osteotomy were applied to correct kyphotic deformity and hybrid fixation of sub-laminar polyester bands and pedicle screws were applied to proximal-end of fixation. Teriparatide was administered to all patients after surgery. All S2AISs were appropriately inserted, and no clinical problem was identified. One infection and 7 proximal junctional failure cases (43.7%) were reported. The instrument failure (breakage of the rod) was observed in 2 cases at 9 and 18 months after surgery. The salvage surgeries were required for 6 cases (37.5%). The average sagittal vertical axis (SVA) at final followup was 59.9±35.6mm. The lumbar lordosis and thoracic kyphosis were difficult to estimate due to deformity of the vertebral bodies. The average Performance Status (PS) before surgery was 3.4±0.5 and 1.4±0.8 at final followup.

**Conclusion:** Our results indicated S2AIS could be a reliable distal anchor for corrective spinal long fusion even in very severe osteoporosis patients. The combination of multilevel TLIF and Ponte osteotomy seems to be an appropriate method to correct sagittal imbalance due to osteoporotic multiple vertebral-body fractures. We obtained acceptable clinical results for this extremely difficult condition in terms of improved PS, however the major surgical invasion for the patients as well as relatively high rate of the proximal functional failure and required salvage surgery still remain unsolved problems.

## AN ATTEMPT OF INTRAOPERATIVE POVIDONE-IODINE IRRIGATION IN SPINAL SURGERIES FOR THE PREVENTION OF SURGICAL SITE INFECTION

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**INTRODUCTION :** Surgical site infection (SSI) is one of the most serious postoperative complications in spinal surgery. We attempted to reduce SSI rates, using the povidone-iodine irrigation protocol. This study aimed to evaluate the efficacy and the safety of this protocol for preventing postoperative SSI.

**METHODS :** All cases of spinal surgery at our institution between October 2011 and September 2016 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 187 and 151 patients, respectively. This study compared the rate of SSI with and without the use of povidone-iodine irrigation protocol.

**RESULTS:** SSI rate was 1.6% of the study group (3 for 187 patients) and 4.0% of the control group (6 for 151 patients). SSI rate was not statistically significant different ( $p=0.19$ ). Deep SSI occurred 0 cases in study group and in 4 cases in the control group. Deep SSI rate was significantly reduced in study group ( $p=0.027$ ). No adverse events of were occurred in study group.

**DISCUSSION:** In this small preliminary study, povidone-iodine irrigation protocol can be used safely and led to reduce of deep SSI rates compared with only saline irrigation group. 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. Secondary, we could not detect the late onset SSI cases. Future prospective randomized controlled series in larger populations with a long term follow-up duration are needed to corroborate these results.



## RELATIONSHIP BETWEEN SPINOPELVIC ALIGNMENT AND HRQOL SCORE AFTER OSTEOPOROTIC THORACOLUMBAR VERTEBRAL FRACTURES

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### Introduction

Osteoporotic vertebral fractures (OVFs) are common in elderly populations. The vast majority of OVF cases can be treated conservatively through bed rest, bracing, treatment for osteoporosis and pain management. Some cases require surgical treatment due to neurological deficits after vertebral nonunion. The goal of osteoporotic thoracolumbar vertebral fractures include bony union, maintain optimal alignment and health-related quality of life (HRQOL). However, there are few reports of relationship between spinopelvic alignment and HRQOL score after thoracolumbar OVFs. The aim of this study were to evaluate the relationship between spinopelvic alignment and HRQOL score after instrumented fusion surgery as well as conservative treatment for thoracolumbar OVFs.

### Methods

A total of 53 patients (conservative treatment 27 cases, surgical treatment 26 cases) with thoracolumbar OVFs between 2013 and 2015 were included in the study. Surgical treatment included vertebroplasty with posterior fusion surgery due to neurological deficits. We excluded acute OVFs, lower lumbar OVFs (L3-L5), non-ambulatory patient and vertebroplasty or kyphoplasty only cases. Radiographic parameters included thoracic kyphosis (TK), thoracolumbar kyphosis (TL), lumbar lordosis (LL; L1-S1), lower lumbar lordosis (LLL; L4-S1), pelvic incidence minus lumbar lordosis (PI-LL), pelvic tilt (PT), sagittal vertical axis (SVA), and T1 pelvic angle (TPA). Clinical outcomes were evaluated at final follow-up with a VAS score and the Oswestry disability index (ODI). Severe disability defined as an ODI  $\geq 40$ . We assessed the relationship between the ODI score and spinopelvic alignment.

### Results

The mean age of 53 cases was 76 years (range, 60-92 years) with 87% of females. There were no significant difference in TK, LL, PI-LL, LLL, PT, SVA, and TPA between the surgical and the conservative treatment groups. There were no significant difference clinical outcomes including the ODI, and VAS score between the surgical and the conservative treatment groups. The TL was significant greater in the conservative group. Occurrence of severe disability was 40% (12/53 cases). The PI-LL, PT, SVA, and TPA were significantly greater in the severe disability group including the conservative and the surgical groups (figure 1). Severe disability group significantly occurred distal subsequent vertebral fracture of lower instrumented vertebra in the surgical group (8% vs. 54%,  $P=0.03$ ). The logistic regression analysis revealed that the TPA was independent risk factor associated with severe disability (Odds ratio =1.12,  $P=0.003$ ). Receiver operating characteristic (ROC) curve analysis showed that the optimal cut-off value of the TPA was  $24^\circ$  (AUC=0.772, sensitivity=72%, specificity=81%).

### Conclusion:

Forty percent of patients had severe disability after treatment of thoracolumbar OVFs. Optimal global sagittal alignment (TPA  $>24^\circ$ ) is important to treatment of conservative as well as surgical management.

### Comparison of variables between the ODI <40 and the ODI $\geq 40$ group

	ODI <40	ODI $\geq 40$	P
Age	76.5 $\pm$ 6.7	75.0 $\pm$ 7.0	0.418
Gender (female)	81%	81%	1.000
Multi fx	47%	52%	0.782
TK	43.5 $\pm$ 17.2	38.3 $\pm$ 20.1	0.320
TL	29.6 $\pm$ 15.8	33.0 $\pm$ 12.6	0.415
LL	37.4 $\pm$ 15.7	32.2 $\pm$ 19.5	0.292
LLL	35.2 $\pm$ 8.7	36.4 $\pm$ 9.5	0.632
PI	48.8 $\pm$ 6.5	54.4 $\pm$ 8.2	0.008*
PI-LL	11.4 $\pm$ 13.6	22.2 $\pm$ 16.4	0.012*
PT	24.8 $\pm$ 8.8	30.4 $\pm$ 8.1	0.022*
SVA	51.4 $\pm$ 37.5	86.8 $\pm$ 49.7	0.005*
TPA	22.9 $\pm$ 8.1	32.0 $\pm$ 10.4	<0.001*
VAS	26.0 $\pm$ 22.3	49.9 $\pm$ 20.5	<0.001*

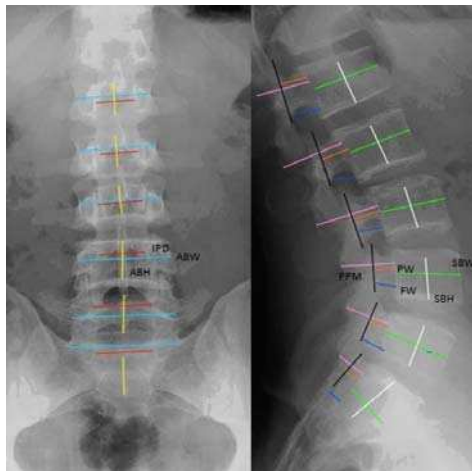
## RADIOGRAPHIC INDICES FOR LUMBAR DEVELOPMENTAL SPINAL STENOSIS

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**Introduction:** Patients with developmental spinal stenosis (DSS) are susceptible to developing symptomatic stenosis due to pre-existing narrowed spinal canals. DSS has been previously defined by MRI via the axial anteroposterior (AP) bony spinal canal diameter. However, MRI is hardly a cost-efficient tool for screening patients. X-rays are superior due to its availability and cost but currently, there is no definition of DSS based on plain radiographs. Thus the aim of this study is to develop radiographic indices for diagnosing DSS.

**Methods:** This was a prospective cohort of 148 subjects consisting of patients undergoing surgery for lumbar spinal stenosis (patient group) and asymptomatic subjects recruited openly from the general population (control group). Ethics approval was obtained from the local institutional review board. All subjects underwent MRI for diagnosing DSS and radiographs for measuring parameters used for creating the indices. All subjects underwent lumbar AP and lateral standing radiographs of the lumbosacral spine (**Figure**).



For MRI, the midline AP bony spinal canal diameter was used to diagnose DSS (L1<20mm, L2<19mm, L3<19mm, L4<17mm, L5<16mm, S1<16mm). All measurements were performed by two independent investigators, blinded to patient details. Intra- and inter-observer reliability analyses were conducted and only parameters with near perfect intraclass correlation underwent receiver operating characteristic (ROC) analysis to determine the cut-off values for diagnosing DSS using radiographs.

**Results:** Imaging parameters from a total of 66 subjects from the patient group and 82 asymptomatic subjects in the control group were used for analysis. ROC analysis suggested sagittal vertebral body width to pedicle width ratio (SBW:PW) as having the strongest sensitivity and specificity for diagnosing DSS. Cut-off indices for SBW:PW were level-specific: L1 (2.0), L2: (2.0), L3: (2.2), L4: (2.2), L5: (2.5), S1 (2.8). The highest sensitivity was 0.92 and highest specificity was 0.99 for all the levels.

**Discussion:** This is the first study to define DSS on plain radiographs based on comparisons between a clinically relevant patient group and a control group. Individuals with DSS can be identified by a simple radiograph using a screening tool allowing for better cost-saving means for clinical diagnosis or research purposes.

**Figure:** On the AP view (left), the interpedicular distance (IPD) and axial vertebral body height (ABH) and width (ABW) were measured. On the lateral view (right), the foraminal width (FW), pedicle width (PW), posterior pedicle margin (PPM), sagittal vertebral body height (SBH) and width (SBW) were measured. The PW was measured from the posterior border of the vertebral body to the line connecting the cranial and caudal facet joints. The vertebral body height and width measurements were taken at the midpoint of the vertebral body in both AP and lateral radiographs from the superior endplate to the inferior endplate.

## RELATION BETWEEN ACHIEVEMENT OF KYPHOSIS CORRECTION AND CLINICAL OUTCOMES IN ELDERLY SPINAL DEFORMITY

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### Introduction:

In the treatment of adult spinal deformity, optimal kyphosis correction should be preoperatively calculated by spinopelvic parameters including pelvic incidence (PI), lumbar lordosis (LL), and thoracic kyphosis (TK). Rose et al introduced the formula:  $PI+LL+TK < 45$  degrees. Schwab et al advocated that  $PI-LL$  should be less than 10 degrees. However, it remains unclear whether these two major formulae could anticipate clinical outcomes in elderly patients. The objective of this study is to verify these two formulae in correction of global sagittal-plane deformity.

### Methods:

We reviewed 22 consecutive patients who had undergone spinal osteotomy for sagittal imbalance. They were one male and 21 females with a mean age of 73 years (58-84 years). Surgical procedures were TLIF with Ponte's osteotomy in five, pedicle subtraction osteotomy (PSO) in 15, and vertebral column resection (VCR) in two patients. Radiographic parameters included PI, LL, TK, kyphosis correction, and anterior deviation of sagittal vertical axis (SVA). Clinical outcomes were evaluated by visual analog scale (VAS) of back pain and Roland-Morris Disability Questionnaire (RDQ). Mean follow-up period was 26 months.

### Results:

Optimal kyphosis correction was averaged 26 degrees in Rose's formula, and 50 degrees in Schwab's formula. Surgically-achieved kyphosis correction was 32 degrees. Achievement of optimal correction (less than 5 degrees between optimal and actual corrections) was 82% in Rose's formula, but 9% in Schwab's formula. Anterior deviation of SVA was 15.7 cm before surgery, 5.5 cm after surgery, and 9.8 cm at the final follow-up. VAS of back pain improves from 74/100 to 31/100. RDQ were 16.4 before surgery, and improved to 8.6 at the final follow-up. Patient's' satisfaction was 66/100.

### Discussion:

Although a majority of patients could not meet the Schwab's formula, they showed favorable clinical outcomes and were satisfied with surgical treatment. Rose's formula was achieved in 82% of patients. The current study suggested that the target based on Schwab's formula is not ne

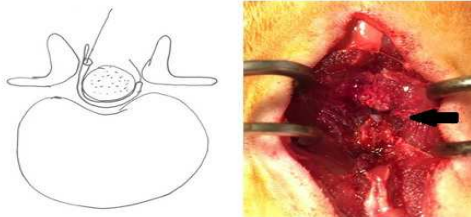
## CREATING A DEVELOPMENTAL SPINAL STENOSIS RAT MODEL AND UTILITY OF SOMATOSENSORY EVOKED POTENTIAL FOR TESTING

Jason Pui Yin Cheung<sup>1</sup>, Prudence Wing Hang Cheung<sup>1</sup>, Yong Hu<sup>1</sup>

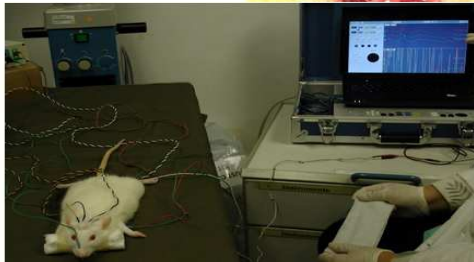
<sup>1</sup>. The University of Hong Kong, /, Hong Kong

**Introduction:** Developmental Spinal Stenosis (DSS) is defined as a pre-existing narrowed spinal column originating from the mal-development of dorsal spinal elements, hence resulting in a reduction of space to accommodate the spinal cord and nerve bundles. It is characterized by a circumferential narrowing of the bony canal. A representative rat circumferential compression model has been created to simulate this pathology for behavioral, neurophysiological and histological testing.

**Methods:** Ten female 13.0 to 14.5 weeks-old Sprague-Dawley rats were randomly divided into the following groups: circumferential compression using stainless-steel wire and silicone sheets, dorsal compression using silicone sheets and control. Laminectomy at L4-L5 was performed. Either 28-gauge stainless steel wire or the silicone sheet (0.51mm thick) were inserted circumferentially around the dura and tied at the dorsal aspect (**Figure**).



For dorsal compression, two overlapping silicone sheets were used to compress only on the dorsal aspect of lumbar spinal cord to simulate the usual pathology of degenerative spinal stenosis. Controls only had exposure of the dura without any compression device. All rats were assessed preoperatively, and at postoperative 1-week, 2-weeks, 3-weeks, 1-month and pre-sacrificing (Sacrifice at 2 months postoperatively). Assessment included behavioral and locomotion tests (rung ladder walking, swimming), electrophysiological tests, and histological analysis of the degree of axonal demyelination of neural tissues.



**Results:** For horizontal rung ladder test, the average Basso, Beattie and Bresnahan (BBB) score at pre-sacrificing was: 8 (circumferential), 14 (dorsal compression) and 16 (control) ( $p < 0.05$ ). The average Louisville Swimming Scale (LSS) for the swimming test at pre-sacrificing was: 1 (circumferential – wire), 2 (circumferential – silicone), 4 (dorsal compression) and 7 (control). Strong correlation between BBB and LSS score was observed. The circumferential group, whether by stainless-steel wire or silicone sheet, caused little or no hindlimb movements not only on walking, but also in swimming with demonstrable high reliance on forelimbs for forward motion in the water. The circumferential compression

group using silicone sheets was the only group with increasing trend of latency at both P1 and N1 for both hind-paws, and consistently higher latency than the dorsal compression group. The axon/myelin areas ratio was the largest for circumferential compression group (0.78) as compared to dorsal compression group (0.68) and controls (0.39).

**Discussion:** This study has successfully demonstrated the use of somatosensory evoked potential to test for increased latency in a novel DSS rat model. The model was sufficient in causing axonal demyelination. Further validation with decompression tests can be tested in subsequent work.

**Figure:** schematic diagram of circumferential compression (top left), intraoperative compression device (top right), somatosensory evoked potential testing (bottom)

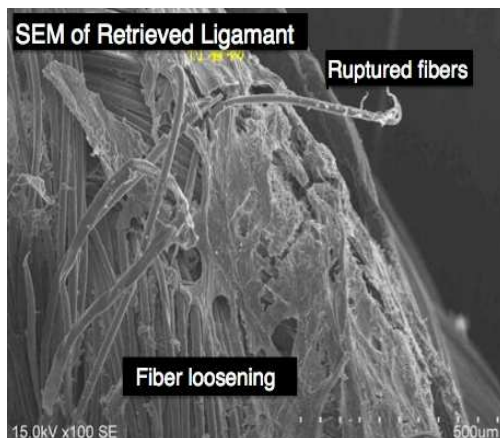
## WHAT HAS OCCURRED IN POSTERIOR DYNAMIC STABILIZATION SYSTEM MORE THAN 10 YEARS AFTER THE SURGERY?: A BIOMECHANICAL AND HISTOLOGICAL STUDY WITH THE RETRIEVED IMPLANTS

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**INTRODUCTION:** Posterior dynamic stabilization can be an alternative to spinal arthrodesis in the treatment of degenerative lumbar instability. One expected advantage of this procedure over spinal arthrodesis is to prevent deterioration of the adjacent motion-segment, because it can stabilize the unstable segment without any rigid bony fusion. Although there are several clinical studies to report its excellent result, it remains to be clarified if the dynamic stabilization *per se* continues to play a role for stabilization in the body. The purpose of the current study was to report what has occurred in the Graf system more than 10 years after the surgery, based on a biomechanical and histological analysis with the retrieved implants.

**METHODS:** Graf implants were retrieved from 2 patients; both males with an age of 65 and 79 years, respectively. Case #1 had undergone resection of the herniated disc at L4/5, followed by Graf flexible stabilization at the same level 13 years ago. He started to complain sciatica and low back pain again 10 years after the surgery. The main pathology was lumbar canal stenosis at the adjacent level of L2/3 and 3/4 to the stabilized segment. He was salvaged by the retrieval of the implants, followed by the decompression and XLIF at L2/3 and 3/4. Case #2 with L4 degenerative spondylolisthesis had undergone the decompression at L4/5, followed by Graf ligamentoplasty at the same level 12 years ago. Bilateral leg pain with severe intermittent claudication recurred 11 years after the surgery. The main pathology was the degeneration at L3/4 segment adjacent to the stabilized one. The Graf implants were retrieved, followed by the decompression and fusion with pedicle screw system at the indexed adjacent segment. A biomechanical test for the retrieved implants was performed using SHIMAZU material testing machine (AGX-100kN). Histopathological study was also performed using H&E stain, immunostaining method, and scanning electron microscopy (SEM).



**RESULTS:** Preoperative X-P and CT showed the solid bony fusion at the segment of flexible stabilization in 2 cases. It was confirmed during the surgery. Macroscopically, no pathological granulomatous tissues and artificial ligament ruptures were observed. A part of the artificial ligament was covered tightly by the fused bony mass. There was no screw loosening. Load-displacement curve under the tensile testing of 500N revealed that elongation of the removed ligaments was smaller than that of the unused new ligaments. H&E staining showed no chronic inflammatory response with any debris. SEM revealed the loosening and microrupture of the ligament fibers.

**DISCUSSION:** The current study demonstrated that Graf ligamentoplasty could not prevent the degenerative change of the adjacent segment more than 10 years after the surgery. The biomechanical and histological deterioration of the ligaments has actually occurred, though the solid bony fusion was obtained. The real effect of the Graf ligamentoplasty might be to obtain so-called "slow bony fusion" at the indexed segment.

## COST ANALYSIS OF SINGLE LEVEL LUMBAR FUSIONS

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### Background and Purpose:

Spine conditions account for a significant proportion of health care spending in the U.S., and the use of health care resources for the diagnosis and treatment of these conditions is increasing more rapidly than other areas of health expenditures. Between 1997 and 2005, there was a 65% increase in health care expenditures for patients with self-reported back and neck problems, yet no evidence of a corresponding improvement in self-assessed health status. The literature demonstrates high variability in spine surgery in regards to both cost and the surgical management of spine pathologies. The purpose of this paper is to promote cost transparency, characterize the determinants of direct costs and report variability in the direct cost of care for single-level lumbar fusions.

### Methods:

Adult patients who underwent primary single-level lumbar fusion between fiscal years 2008-2012 met inclusion criteria. Patients were excluded if they underwent multiple surgeries, had previous surgery in the same location, underwent corpectomy, kyphectomy, disc replacement, surgery for tumor or infection, or had incomplete cost data. Demographic data, surgical data, and direct cost data in the categories of supplies, services, room and care, and pharmacy, were collected for each patient. Surgical strategy was confirmed with CPT coding and administrative implant data. Only circumferential fusions performed in the same day were included in our cohort.

### Results:

The cohort included 532 patients. Direct costs ranged from \$8,286-\$73,727 (median=\$21,781; mean=\$22,890 ± \$6,323). Surgical approach was an important determinant of cost. The mean direct cost was highest for the circumferential approach and lowest for cage-less posterior spinal fusions. The difference in mean direct cost between transforaminal lumbar interbody fusions, anterior lumbar interbody fusions, and lateral transposas fusions was not statistically significant. Surgical supplies accounted for 44% of direct costs. Spinal implants were the primary component of supply costs. Services accounted for 38% of direct costs and were highly dependent on operative time. Comorbidities were an important contributor to variability in the cost of care.

### Conclusion:

The results of this study are useful for promoting cost-transparency and identifying the composition of cost drivers for single-level lumbar fusions as well as the variability within these components. The costs of spinal surgery are highly variable. Important cost-drivers in our analysis included surgical approach, implants, operating room time, and length of hospital stay. Areas of high cost and high variability offer potential targets for cost savings and quality improvements. As the health care economy transitions toward alternative payment systems, it is imperative that sources of variability in spine surgery be addressed such that adequate risk stratification measures are in place and consensus is established amongst providers on the most efficacious manner to deliver care. While it is important to normalize trends of high expenditures in spine surgery, it is hazardous to interpret these findings as avocation for pure cost minimization.

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## DO PEEK MATERIALS CAN BE A RISK FACTOR OF NONUNION? ; FREQUENCY OF OCCURRENCE SURVEY OF VERTEBRAL ENDPLATE CYST AND SUBSIDENCE OF THE CAGE AT THE TIME OF 1 YEAR AFTER PLIF

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### Introduction

The interbody cage of poly-ether-ether-ketone (PEEK) material is widely used for posterior lumbar interbody fusion (PLIF) due to the property that the elastic modulus is closer to bone than titanium (Ti). However, PEEK has not osteoinductive ability and has been reported to be a risk factor for nonunion. In this study, the occurrence of the vertebral endplate cyst formation and the loosening of pedicle screw (PS) after PLIF were compared using Ti and PEEK cage of the same shape.

### Methods

We examined 76 patients treated from April 2013 to April 2014 with PLIF using PEEK (38 patients) or Ti (38 patients) with pedicle screw fixation. Using computed tomography, subsidence of the cage (mm), vertebral endplate cyst formation (cyst sign positive or negative) and loosening of PS were evaluated at preoperative, 1week, 3 months and 1year postoperatively. The Definition of the radiological nonunion is that when either one of the radiolucent line around the cage or pedicle screw loosening was recognized.

### Results

The radiological bone union rate was 71.1% and 81.6% at 1 year for PEEK and Ti groups ( $p=0.26$ ). The subsidence of the cage was 0.64mm and 0.91mm at 1 year for PEEK and Ti groups ( $p=0.41$ ). These values were larger in Ti group, but there was no significant difference between the two groups. One year postoperatively, subsidence of the cage with positive cyst sign was 0.78mm and 0.8mm (PEEK /Ti groups) and with negative cyst sign was 0.6mm and 0.54mm (PEEK /Ti groups) ( $p=0.41$ ). There was no significant difference. Multivariate logistic regression analysis showed that cage materials was not identified as a risk factor for radiological nonunion and vertebral endplate cyst ( $p=0.69$ ). There was no reoperation for clinical nonunion during the follow-up period.

### Discussion

Regardless of the material, the progression of bone cyst was observed in cases of the nonunion in the two groups. Subsidence of the cage was larger in cases with positive cyst sign. Cage material does not affect bone union and vertebral endplate cyst formation.

## ER STRESS AGGRAVATES THE HYPERTROPHY OF THE LIGAMENTUM FLAVUM

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**INTRODUCTION:** The endoplasmic reticulum (ER), a network of membrane-bound tubular and sac-like structures, provides an environment that is conducive for the folding and assembly of proteins into correct conformations that are functional and suitable for transport to their final destination. However, the excess of the load of client proteins in ER capacity lead to ER stress. To restore ER function in stressed cells, the unfolded protein response (UPR) is induced, which activates 3 ER stress sensor proteins including activating transcription factor 6 (ATF6). The ATF6 will move to the nucleus and act as a transcription factor to cause the transcription of ER chaperones, which are proteins that assist the protein folding. The one of the cause of the lumbar spinal stenosis is the hypertrophy of the ligamentum flavum. The thickness of the hypertrophic ligament is several times as much as non-hypertrophic ligament and the pathogenesis of the hypertrophic ligament was the accumulation of the collagen fiber. We speculate that this condition was the over-production of the protein and ER stress was induced. To purpose of this report is to clarify the association of the hypertrophy of ligamentum flavum and ER stress.

**METHODS:** The human ligamentum flavum tissue (n=102, age; 15-86 years) was enrolled and the fibrosis and ER stress marker was analyzed by microarray, qPCR and western blotting. They were divided into four groups based on age and thickness; group 1, young (<39 years) with non-hypertrophic ligament; group 2, middle (40-65 years) with non-hypertrophic ligament; group 3, middle (40-65 years) with hypertrophic ligament; group 4, old (>66 years) with hypertrophic ligament. *In vitro* experiments, ligamentum flavum fibroblasts was isolated from patients. ER stress marker was analyzed using qPCR and western blotting in the treatment of fibroblasts with TGF- $\beta$  to produce collagen. The protein of COL1 was evaluated using western blotting and ELISA in the fibroblasts overexpressed ATF6 or stimulated by ATF6 inhibitor

**RESULTS:** In microarray analysis, the activation of UPR was shown in old group compared to young group. The fibrosis marker (*COI1A-2*, *COI14A-1*, *TGF- $\beta$* ) and ER stress marker (*PERK*, *IRE1*, *ATF6*, *GRP78*, *GRP94*, *ERO1*, *SEL1*) was abundantly expressed in group 3 and group 4 by qPCR. *GRP78* was positively correlated with the expression of *COL1A-2* ( $r=0.66$ ,  $p<0.001$ ) and *GRP94* was positively correlated with the expression of *COL14A-1* ( $r=0.63$ ,  $p<0.001$ ). In western blotting, *GRP78* · 98 was also increased in group 3 and 4. *In vitro* experiments, TGF- $\beta$  treatment increased the mRNA and protein expression of ER stress marker in the fibroblasts. COL1 protein was increased in the fibroblasts over-expressed ATF6 and decreased in the fibroblasts stimulated by ATF6 inhibitor.

**DISCUSSION:** We found that ER stress was induced in the hypertrophic ligament. *In vitro* experiments revealed COL1 protein was increased in ATF6 overexpressed fibroblasts. Thus, ER stress may lead to the aggravation of the hypertrophic ligamentum flavum. Taken together, our results suggest that the regulation of ER stress may shed new light on the treatment of the hypertrophy of the ligamentum flavum.



**RISK FACTORS OF RADIOLOGICAL ADJACENT DISC DEGENERATION WITH LUMBAR INTERBODY FUSION FOR DEGENERATIVE SPONDYLOLISTHESIS.****Takashi Tsuji<sup>1</sup>, Naoyuki Shizu<sup>1</sup>, Daiki Ikeda<sup>1</sup>, Yusuke Oka<sup>1</sup>, Hurumoto Yamada<sup>1</sup>***1. Fujita Health University, Toyoake, AICHI, Japan*

**Introduction.** Although various risk factors have been reported for adjacent segment degeneration (ASD) after lumbar fusion, the exact mechanisms and risk factors related to ASD have not been clear. The present study was conducted to evaluate the risk factors for radiological ASD in patients surgically treated for single-level L4 spondylolisthesis focusing on a single pathology, a specific fusion level, at a set interval.

**Methods.** We assessed preoperative and five-year postoperative radiographs for 72 patients who underwent L4-5 anterior lumbar interbody fusion (ALIF) or posterior lumbar interbody fusion (PLIF) for single-level L4 degenerative spondylolisthesis. Patients with an age at the time of surgery over 70 years, multi-level surgery (e.g. L4-5 fusion in conjunction with L3-4 decompression), spondylolysis, rheumatoid arthritis and trauma were excluded from this study. Postoperative ASD was defined as imaging evidence of one or more of the following conditions at L3-4: 1) a loss of more than 20% of the preoperative disc height, 2) anterolisthesis or retrolisthesis greater than 3 mm, 3) or osteophyte formation greater than 3 mm. We evaluated the following potential risk factors for ASD: 1) age, 2) gender, 3) surgical procedure (ALIF or PLIF), 4) pre-existing disc degeneration, defined as a reduction in disc height of at least 20% compared with other discs, or as listhesis greater than 3 mm, 5) the angle of lordosis at the L4-5 fused segment, and 6) a change in L4-5 disc height (postoperative disc height – preoperative disc height).

**Results.** We found ASD in 18 of 72 patients. Among the potential risk factors evaluated by univariate analysis, female gender ( $p<0.01$ ), PLIF procedure ( $p=0.01$ ) and pre-existing disc degeneration ( $p<0.01$ ) were significantly associated with the development of ASD. Although none of the risk factors was associated with ASD in ALIF group, female gender ( $p<0.01$ ) and pre-existing disc degeneration ( $p=0.02$ ) were significantly associated with the development of ASD in PLIF group. Multiple logistic regression analysis identified the following significant independent risk factors for ASD: female gender (odds ratio 10.80; 95% confidence interval 1.20-96.89), PLIF procedure (odds ratio 7.70; 95% confidence interval 1.82-32.66), and pre-existing disc degeneration (odds ratio 12.29; 95% confidence interval 1.69-89.27).

**Discussion.** To the best of our knowledge, this is the first comparative study of ASD development in patients with L4 degenerative spondylolisthesis treated using conventional ALIF and PLIF procedures. The results of the present study suggested that posterior approach has a relatively high risk for radiological ASD than anterior approach. Therefore, it is important to know that the maintenance of the posterior elements as much as possible during the posterior approach might decrease the incidence of ASD when PLIF procedures are indicated.

## COMPARATIVE STUDY OF THE EFFICACY OF TRANSDERMAL BUPRENORPHINE PATCHES AND PROLONGED-RELEASE TRAMADOL TABLETS FOR POSTOPERATIVE PAIN CONTROL AFTER SPINAL FUSION SURGERY: A PROSPECTIVE, RANDOMIZED CONTROLLED NON-INFERIORITY TRIAL

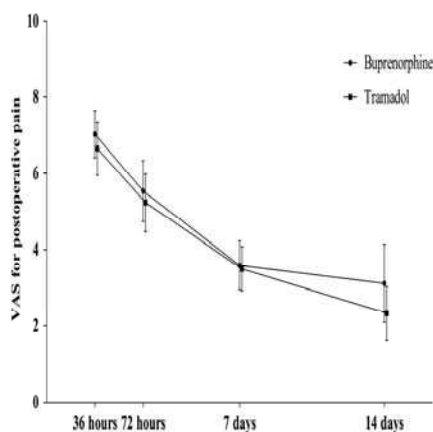
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**Introduction.** There has been little evidence about use of buprenorphine transdermal delivery system (TDS) for postoperative pain management, even though it has been very effective for chronic pain control. Therefore, the purpose of this study was to compare the efficacy of a transdermal buprenorphine patch (5, 10, 15, and 20 µg/h) with that of oral tramadol (150, 200, 250, and 300 mg) for postoperative pain control after single level spinal fusion surgery.

**Methods.** The present study (ClinicalTrials.gov, number NCT02416804) was a prospective, randomized controlled non-inferiority trial designed to determine the efficacy of buprenorphine TDS for alleviating postoperative pain following patient controlled analgesia (PCA) in persons underwent a single level spinal fusion surgery through 1:1 allocation. The primary outcome was the Visual Analog Pain Scale (VAS) score for postoperative back pain at 7 days after surgery. The non-inferior margin of the VAS was set at  $\delta = 1.5$  points. This study was supported by research grants from from Mundipharma Co. The funder had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.



**Results.** The VAS score (primary outcome) for postoperative back pain at 7 days after surgery in the Buprenorphine group was not inferior compared to the Tramadol group. The overall changes in VAS scores for postoperative pain during follow-up assessments over a 2-week period did not differ between both groups. However, the VAS scores for postoperative pain significantly improved with time after surgery in both groups. The patterns of changes in the VAS scores for postoperative pain during the follow-up period were not significantly different between the both groups.

**Discussion.** The efficacy of buprenorphine TDS was not inferior to that of oral tramadol medication for alleviating postoperative pain in the subacute period from 72 hours after surgery, following PCA administration. In addition, adverse events were similar between both groups.

## SURGICAL TREATMENTS FOR 32 PYOGENIC SPONDYLODISCITIS PATIENTS: DELAYED SURGERY, REVISION SURGERY AND 24 MONTHS FOLLOW-UP

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**Introduction:** Pyogenic spondylodiscitis is successfully treated medically in most patients. A minority of patients require surgical treatment for either diagnostic or therapeutic reasons such as neurologic deficit, epidural abscess or uncontrolled sepsis. Pre-operatively, it is sometimes hard to determine which patients will eventually need surgical treatment. The aim of this paper is to identify which patients may require surgical treatment for pyogenic spondylodiscitis and which patients may even require further revision surgery.

**Method:** We included 32 consecutive adult pyogenic spondylodiscitis in a single tertiary medical center from March 1999 to March 2016. The patients who underwent operation after more than 5 weeks conservative treatment were classified into delayed surgery group. Patient demographics, radiographic features, time of surgical treatment were collected. Range of motion of back and leg, VAS, ODI, SF-36, NASS scores and Neurogenic symptoms at preop, postop 1/6/12/24 months follow-up were also recorded. Imaging studies at the time of diagnosis was reviewed for vertebral height loss, disc height loss, kyphotic angle, presence of epidural abscess, and extent and location of spondylodiscitis. WBC, ESR, CRP at the time of diagnosis, blood culture, biopsy culture, and intraoperative culture were also collected.

**Results:** 37.5% (12 in 32) patients failed initial medical treatment and underwent operation at least one month after time of diagnosis, and 15.6% (5 in 32) patients underwent revision operations. In patients who had revision surgery, postoperative SF36 score on General Health, NASS Question 48 and 53 were significantly lower than the scores of other patients, while CRP at the time of diagnosis was significantly higher than control group, as well as thoracic levels were more involved. And for patients who had delay surgery, although preoperative demographics, radiographic features and inflammation markers didn't show any statistically significant difference, postoperative straight leg raise, SF36 score on Social Functioning and Mental Health, NASS Question 48 and VAS scores on Back Pain were significantly worse than the scores of early surgery group.

**Discussion:** Patients who failed medical treatment and subsequently underwent delayed surgery have worse function recovery compared with early surgery group. And Higher CRP at the time of diagnosis was associated with revision surgery, which patients tend to be less satisfied with the operation.

## The influence of the intervertebral disc height and intervertebral disc height index in the single segmental lumbar fusion on the spino-pelvic parameters and clinical outcomes

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**Introduction :** The influence of intervertebral disc height and intervertebral disc height index in the lumbar 4-5 single segment fusion on the spino pelvic parameters and its clinical effect were discussed.

**Methods :** 354 patients conducted with SL4-5 segment standard TLIF operation in our hospital from March 2008 to March 2014 were collected. According to the inclusion and exclusion criteria, a total of 58 patients were enrolled into the research. They were divided into a young age (20-40 years) and middle age (40-60 years) group. Patients were assessed by visual analogue scale (VAS), Oswestry disability index (ODI), lumbar JOA score, measurement of lumbar lordosis (LL), L4-5 (IDH) lumbar intervertebral disc height, L4-5 intervertebral disc height index (IDHI), intervertebral angle of L4-5 (IVA4-5), pelvic incidence (PI), pelvic tilt (PT), sacral slope (SS) and other spino pelvic parameters preoperatively, postoperatively and at final follow-up. The changes of L4-5 intervertebral disc height and L4-5 intervertebral disc height index at different point were statistically analyzed. And the effect on the spino pelvic parameters and clinical efficacy were also analyzed.

**Results :** The average follow-up period was 49.89 months (36-81 months). There are 16 patients in the young age group and 42 patients in middle age group. In the young age group, at different time points(preoperative, postoperative and follow-up), L4-5 IDH was 11.8±1.9 (mm), 15±1.9 (mm) and 13.3±1.8 (mm), and L4-5 IDHI was 0.30±0.04, 0.33±0.04 and 0.29±0.04, respectively. In the middle age group, L4-5 IDH was 11.8±1.9 (mm), 13.9±1.6 (mm) and 12.5±1.8 (mm), and L4-5 IDHI was 0.27±0.04, 0.33±0.03 and 0.29±0.03, respectively. The intervertebral disc height and intervertebral disc height index was significantly increased in postoperative compared to preoperative with statistical difference ( $P<0.05$ ). But the follow-up compared with postoperative, there was a decrease ( $P<0.01$ ). The data shows that L4-5 IDH and IDHI was significantly correlated with IVA4-5 ( $P<0.05$ ), and had no significant correlation with other spino pelvic parameters ( $P>0.05$ ). The post-operation and the last follow-up clinical evaluation shows that VAS, ODI and JOA were significant improved in both of the two groups compared with the preoperative. Among them, the VAS and ODI score in the last follow-up was negatively correlated with postoperative L4-5 IDH ( $P<0.05$ ), and JOA improvement rate was positively correlated with postoperative L4-5 IDH ( $P<0.05$ ). While the final follow-up VAS and ODI score was negatively correlated with postoperative L4-5 IDH ( $P<0.05$ ), and the final follow-up JOA improvement rate was positively correlated with postoperative IDH ( $P<0.05$ ).

**Conclusion :** L4-5 intervertebral disc height and intervertebral disc height index was significantly correlated with IVA4-5. The increase of intervertebral disc height and intervertebral disc height index can improve the clinical efficacy of the single segment fusion.

## CLINICAL OUTCOME OF 69 SYMPTOMATIC THORACIC DISC HERNIATIONS TREATED SURGICALLY THROUGH MINIMALLY INVASIVE LATERAL TRANSTHORACIC TRANS/RETROPLEURAL APPROACH: A 10-YEAR EXPERIENCE

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**Introduction:** Although symptomatic thoracic disc herniation is relatively rare, when symptomatic, surgical treatment can be challenging. Adequate decompression of spinal cord with minimal manipulation are the main principles, as such, the anterior approaches are typically preferred. Complications of standard open anterior approaches lead to evolution of different surgical modifications. Thereby, the rates of complications significantly decreased with utilization of the minimally invasive transthoracic approach. In this study, the authors aimed to present the outcomes and complications of the patients with thoracic disc herniation treated with minimally invasive lateral transthoracic trans/retropleural approach in a single institution by a single surgeon.

**Methods:** Fifty-nine consecutive patients that underwent operative management of TDHs were identified from the authors' database. Sixty-nine symptomatic disc herniations of 59 patients were surgically treated between 2007 and 2016. All patients were treated with a discectomy using the minimally invasive lateral transthoracic trans/retropleural approach and fusion with instrumentation.

**Result:** The distribution of disc herniations according to localization of the disc was as follows: 41 central, 10 paracentral and 18 both central and paracentral. The number of calcified disc herniations was found to be 31. No patient developed neurological deficit. Postoperative neurological improvement occurred in 39 (90.7%) of 43 patients with myelopathy. Mean blood loss, hospitalization period and follow-up period were found to be 391.2 mL, 4.70 days and 18.6 months; respectively. The number of major complications were as follows: pseudoarthrosis in one patient, pulmonary embolism in one patient and pneumonia in one patient and the number of minor complications were as follows: ileus in 2 patients, atelectasis in 1 patient, hydropneumothorax requiring chest tube in 1 patient, small pneumothorax in 1 patient and pleural effusion requiring chest tube in 2 patients. Dural tear occurred in 5 patients. Intercostal neuralgia developed in 3 patients and rib fracture developed in 1 patient. While preoperative visual analog scale pain scores, Oswestry Disability Index scores, SF-36 PCS and mental component summary scores of the patients were 7.7/51.1/ 29.4 and 40.8; postoperative follow-up results were 4.3/39.3/41.1/ and 53.7; respectively.

**Discussion:** Minimally invasive lateral transthoracic trans/retropleural approach is a technique which enables a more efficient decompression of spinal canal without manipulation of the spinal cord compared to posterior methods. As such, decreasing the number of complications due to the approach in standard open anterior technique.

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## PLIF/TLIF FOR NEUROLOGICAL DISTURBANCE WITH LUMBAR VERTEBRAL FRACTURE – PROBLEM WITH THE USE OF IMPLANT FOR THE FRACTURE VERTEBRA

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### Introduction

Osteoporotic vertebral fractures(OVF) in the middle-lower lumbar spine occasionally require surgical interventions due to radiculopathy and/or cauda equina syndrome caused by impacted bony fragment or progressive vertebral slip. Surgeons might concern to use implants for fresh vertebral fracture, because of potential cage subsidence and screw loosening. We perform posterior lumbar interbody fusion(PLIF) or transforaminal lumbar interbody fusion(TLIF) for those who suffered from neurological disturbance caused by OVF in the middle-lower lumbar spine. The aim of this study is to investigate clinical problems related to instrumentation for fractured vertebrae.

### Methods

25 patients who had undergone PLIF/TLIF for neurological disturbance with fresh OVF were reviewed retrospectively for a minimum 6-month follow-up. A mean age was 76.1 years old, and fracture levels were L3 and L4 in nine each, and L5 in seven patients. A mean period to fusion was 2.7 months. Numbers of fusion levels were 1.6. Box cages were used in 17 levels, boomerang were in 16. The pathologies were impaction of bony fragment in 15cases, progression of vertebral slip in ten. Clinical results were assessed by Japanese Orthopedic Association Score (JOA). Occurrence of cage subsidence and/or screw loosening, and revision surgery due to implant failure were also examined. Cage subsidence was defined as more than 3mm craniocaudal cage migration, and screw loosening was defined as presence of circumferential clear zone. Both were assessed in comparison between immediately postoperative and final follow-up radiographs.

### Results

JOA score was improved from 9.8/27 preoperatively and 19.2/27 postoperatively. Mean loss of correction was 2.9 degrees. Cage subsidences were occurred in 10 fusion levels (30.3%), 8 of which were migrated into fractured endplates. There were no association between the shapes of cages and subsidence rate. Screw loosening were occurred in 29 of 130 screws (22.3%); 10 of 48 (20.8%) in fractured vertebrae, and 19 of 82 (23.2%) in unfractured vertebrae. Revision surgeries due to implant failure were required in two cases (8.0%).

### Discussion

Cage subsidences were occurred more frequently in fractured endplate. On the other hands, screw loosening rate were not different between fractured and unfractured vertebrae. Since osteoporosis influences cancellous bone rather than cortical bone, unfractured vertebral body might also have inadequate mechanical strength to hold pedicle screws. Although both cage subsidence and screw loosening were frequently occurred, revision surgery rate was 8.0%. Spinal instrumentation would be safely used for fresh fractured vertebra.

## SURGICAL DECOMPRESSION FOR FORAMINAL AND EXTRAFORAMINAL LUMBAR DISC HERNIATION USING THE FAR-LATERAL APPROACH: PATIENT-RATED OUTCOME DEPENDS ON THE INVOLVED SEGMENT

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### Introduction

Decompression for lumbar foraminal to extraforaminal nerve compression is commonly performed using a far-lateral transmuscular approach (FLA), and is typically associated with good patient outcomes. Results are usually reported as the average for all lumbar levels; however, clinical results may be less predictable for surgery at the lumbosacral level, due to its unique anatomic features. This study compared patient-rated outcomes after far-lateral decompression at L5/S1 compared with higher lumbar levels (L1/2 to L4/5).

### Methods

This was a retrospective study of prospectively collected data from 115 consecutive patients (73 m, 42 f; mean age 62±11 yrs) who had undergone decompression using a paramedian FLA at a single lumbar level (N=89 at L1 to L5, and N=26 at L5/S1) between 1.1.2005 and 1.6.2014. A group of patients (N=1'482) identified from our in-house spine outcomes database (linked to Spine Tango), who had undergone decompression (non-FLA approach) for disc herniation over the same time period, served as controls. Foraminal and extraforaminal nerve root compression were quantified using radiographs and MRI. The multidimensional Core Outcome Measures Index (COMI), which includes separate 0-10 graphic rating scales for leg pain (LP) and back pain (LBP), was completed before surgery, and up to 2 years after surgery.

### Results

Of the 115 FLA patients, 108 (94%) had completed a baseline COMI, and 101 (88%), a 2-year COMI; 96 (83%) had completed a COMI at both timepoints. Follow-up rates were similar for the control group. In the FLA group, at the 2-year follow-up, the reduction in leg pain from baseline was significantly ( $p=0.03$ ) less for those operated at L5/S1 (2.6±2.9 points) than for those operated at L1/2 to L4/5 (4.2±3.4 points); for the control group, no such difference was seen (4.5±3.2 points for L5/S1 and 4.2±3.3 points for L1/2 to L4/5). A 2-point minimal clinically important change score for leg pain was achieved by 77% patients in the control group, both for those operated at L5/S1 and those operated at higher lumbar levels alike; in the FLA group, the corresponding figures were 63% (L5/S1) and 81% (higher lumbar levels) ( $p=0.11$ ). The reduction in COMI score showed a similar pattern to that for leg pain, but the differences failed to reach statistical significance: at L5/S1, FLA 3.5±2.4 points vs control 4.6±3.0 points reduction; at higher lumbar levels, FLA 4.8±3.0 vs control 4.8±2.9 points). There were no significant differences ( $p>0.05$ ) dependent on group or lumbar level for the improvement in LBP.

### Discussion

Decompression of extra- and intraforaminal nerve root compression using FLA results in good patient-rated outcome with significant improvement in the multidimensional COMI at 2 years. However, the improvement in leg pain was inferior for the lumbosacral level compared with the other levels. This may be due to the unique anatomy of the L5/S1 segment, which has a long and narrow nerve channel for the L5 nerve root, especially in the presence of advanced segment degeneration. These results are important in decision-making regarding the appropriate surgical treatment and in the management of expectations during the consent process.

## **SURGERY FOR REFRACTORY COCCYGDYNIA: OPERATIVE VERSUS NON-OPERATIVE TREATMENT**

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**INTRODUCTION:** This is a retrospective study. The purpose of this study is to evaluate the long-term outcomes for patients treated with coccygectomy when compared to a non-surgical regimen of medications and injection. The treatment of coccygodynia remains somewhat controversial. To date, there has only been one small comparative study of operative versus non-operative treatment.

**METHODS:** From 2004-2014, 109 patients presenting with coccygodynia were treated with either surgical total coccygectomy or a non-operative course of physical therapy, injections, anti-inflammatory medications and sitting aides. All had at least two years of symptoms. The treatment decision was made, principally by the patient, with counsel by the attending physician. Prior to surgery, all subjects had received at least two years of NSAIDs, injection therapy, and three-dimensional imaging (CT/MR). Subjects completed visual analogue pain scales (VAS), EuroQol5 dimension, an Oswestry Disability Index (ODI) and a new Coccygodynia Disability Index (CDI) evaluation. Work status, complications and satisfaction were recorded.

**RESULTS:** 61 patients received non-surgical care: 8 declined to participate and 5 could not be located. Patients treated surgically received a total coccygectomy. At an average 4.8 year follow-up (2-9 years), the non-surgical VAS was 5 and the surgical 2 ( $p=0.001$ ); 80% of surgically treated patients were better at two years vs. 55% for non-operative group. EQ-5D ( $p=0.002$ ), CDI (0.01) and PROMIS Pain interference scores (0.02) were also significantly improved. 11 surgical patients (26%) had wound related complications; 7 treated with dressing changes and 4 with surgical debridement, all with successful resolution.

### **DISCUSSION:**

Coccygodynia remains a relatively rare condition that can, however, be quite disabling for those affected. Although numerous forms of non-operative treatment have been proposed, many with notable reported success rates, there has remained a significant portion of this population for whom these measures have failed and surgical treatment has been recommended.

Treatment relief from coccygodynia is also difficult to measure, as there are no functional tests, nor radiographs to follow, and we rely largely on the patient's subjective reports of pain and function. To date, no validated pain or function scales exist to measure outcomes, hence most investigators have relied on visual analogue pain scales and simple responses to satisfaction or not. We have introduced here, a potential scale for measuring coccygeal pain, that appears promising, however, it requires validation.

Despite, these limitations, we believe that total coccygectomy is a valid treatment option for those suffering from chronic coccygodynia, satisfactorily unresponsive to non-operative maneuvers, with long lasting positive results and a relatively low, manageable complication rate. We continue to study methods of reducing wound related complications.

Total coccygectomy is a safe and effective surgical treatment of coccygodynia resistant to non-operative care. Post-operative wound care remains an issue.



## COMPLICATIONS AROUND CORTICAL BONE TRAJECTORY SCREW SYSTEM ASSOCIATED WITH PLIF OPERATION

Tetsuo Dr. Ohwada

### Introduction

Cortical bone trajectory method is newly developed pedicle screw method and spread widely in Japan and Asian countries. This procedure provides small incision with muscle preservation and smaller dead space. Whereas this method has some new complication compared with ordinal pedicle screw method, and few report has been published about complications. Here we report complications around CBT screws associated with PLIF operation.

### Materials and Method

We have selected CBT method as first choice of pedicle screw from 2011, and more than 300 cases of PLIF with CBT screw have been performed. All the complication and unfavorable event were recorded and reviewed.

### Results

Complications have occurred intra-operatively, in post-operative early phase and in late phase.

1. Intra-operative complications: Fracture of pedicle or inferior facet, malposition of the screw: Malposition of the screw is not a rare condition for ordinal method, when medial or inferior pedicle wall penetration occurs, irritation of the nerve root is inevitable. Repositioning of the screw is necessary. Entry point for CBT screw is very solid, so sometimes fracture of the pedicle or articular process occurs, especially in osteoporotic patients. Once fracture occurred stability cannot be expected, so reinsertion of ordinal pedicle screw is recommended.
2. Early phase complications : Loosening at the connector, cage subsidence: Loosening at the connector head was seen in early series of our cases. In 1<sup>st</sup> year, we had seven cases of loosening at the connector out of 104 cases. Small XIA was responsible for this complication, 6cases out of 67cases. Loosening occurred mostly within one month post-operatively, and correlated with subsidence of the cages. In CBT fixation, four head connectors concentrate in central portion, and more stress was concentrated at the connectors. Applied compression force on screws do not affect in lumbar lordosis and might widen the anterior part of the intervertebral spaces. This might be the reason for fragility on sagittal plane. Once a cage subsidence occurs, stability cannot be expected.
3. Late phase complications : Cyst formation around endplate and vertebral body, non-union, screw loosening, and screw breakage: Endplate sclerosis and cyst formation is sometimes seen in PLIF cases. This is thought to be mechanical stress reaction due to less stability. Once cyst formation occurs, possibility of non-union is very high. Long standing non-union leads to screw loosening or breakage.

### Discussion

CBT method is less invasive and soft tissue preserving procedure. Its rigid stability between bone and screws are advantages, but stress should be concentrate on screw/ rod connector. Construct itself is bit weak and possibility of non-union is higher than ordinal pedicle screw fixation. Our two year follow-up result showed 85% of solid fusion, this is bit worse compared with ordinal pedicle screw fixation method. Change of screw insertion point, more lateral and cranial which leads to less lateralization and sagittal angulation with longer screws is a possible solution, connector heads are separated and transverse connector can be applied for better fusion results. If pedicle or articular process fracture occurs during the operation, screws should be inserted from ordinal portion.

**ANTERIOR LUMBAR INTERBODY FUSION FOR DEGENERATIVE LUMBAR SPONDYLOSIS****Kirkham Wood<sup>1</sup>, Todd Alamin<sup>1</sup>, Thomas Cha<sup>2</sup>, Vijay Yanamadala<sup>3</sup>***1. Stanford University, Redwood City, CA, United States**2. Orthopaedic Surgery, Innlandet Hospital Trust, Anders Sandvigsgt 17, 2609, Lillehammer, Norway**3. Orthopaedic Surgery, Massachusetts General Hospital Harvard Medical School, Boston, MA, USA*

**INTRODUCTION:** Low back pain is an extremely common health problem with substantial economic impact throughout the United States. Persistent symptoms secondary to degeneration of the lumbar intervertebral discs remains both a diagnostic and treatment dilemma. Surgery – historically, a fusion procedure – has had mixed results in terms of fusion success and patient reported outcomes. More recent, less invasive techniques, such as anterior discectomy and fusions when limited to one or two segments, may, however, hold promise for less morbidity and more reliable clinical outcomes. We sought to compare two matched groups at more than five year follow-up, one treated with an anterior retroperitoneal fusion of one or two levels of the lower lumbar spine, and a group treated with organized non-operative care consisting of physical therapy, exercise, injections, and anti-inflammatory medications. To date, such a study has not been reported.

**METHODS:** A retrospective review of prospectively collected data on patients who presented to our clinic with complaints of long standing mechanical low back pain, associated with one or two levels of MR documented disc degeneration was conducted. All had failed previous attempts at non-operative care and presented to us for surgical consideration. Patients were then divided into two groups: Operative, which entailed a one or two level anterior approach to the lower lumbar spine and interbody fusion or continued structured non-operative care through physical therapy, medications and activity modifications. All patients filled out patient and disease specific outcome questionnaires and were followed radiographically. Statistical analysis was 2-way ANOVA for intergroup comparisons of ODI and VAS. Preoperative and postoperative data was compared with student's t test. Categorical variables were analyzed with fisher exact test or Chi-squared test.

**RESULTS:** 42 patients were treated with an anterior interbody lumbar fusion and 33 continued with non-operative care. The average follow-up at final analysis was 89 months. (range 30-155). The two groups were evenly matched in terms of age, race, sex, worker's compensation status, litigation status, etiology of pain, smoking history. Of those fused, 17 were at L5-S1, 18 at L4-5 and L5-S1, 5 at L4-5 alone, one at L3-5 and one at L3-4 and L5-S1.

At final follow-up, there were statistical differences in the patient related outcomes regarding pain and function between the two groups. The group treated surgically had lower VAS pain and PROMIS pain intensity scores, better EQ-5D and lower and Oswestry scores as well, all reaching statistical significance. Those treated at one level, L4-5 or L5-S1, also had better outcomes than those treated at two levels. ( $p=0.045$ ). There was, however, no statistical difference in work status or occupation at the time of the survey.

**DISCUSSION:** Anterior lumbar interbody fusion, limited to one or two levels in the low lumbar spine, appears to provide significant and lasting pain relief, with few complications, when compared with non-operative care. ALIF may well be a safe, appropriate and effective surgical treatment for low back pain associated with degenerative lumbar disc pathology.

## POTENTIAL OF POROUS HYDROXYAPATITE/COLLAGEN (HAP/COL) COMPOSITE AS A GRAFT MATERIAL FOR PLIF/TLIF

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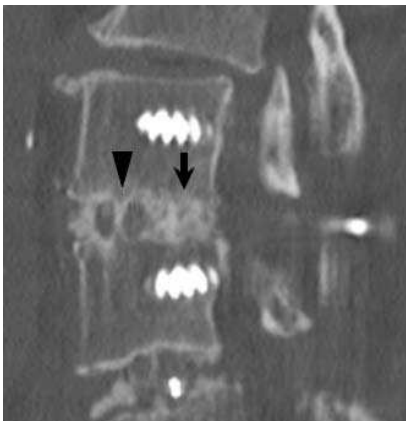
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**OBJECT:** Porous hydroxyapatite/collagen (HAp/Col; RIFIT, HOYA Co Ltd, Tokyo, Japan) is a hydroxyapatite and collagen composite with a bone-like nanostructure (80% HAp and 20% type I collagen) and has bioabsorbability such as  $\beta$ -tricalcium phosphate ( $\beta$ -TCP). This graft material has sponge-like elasticity and is easy to compress and fill into the fusion cage. The graft expands and fits to prepared bony endplate after cage insertion, and thus better bone bridging can be expected compared with conventional bone substitute. In this study, we investigated the utility of porous HAp/Col as a graft material for lumbar interbody fusion.

**METHODS:** Forty-nine patients who underwent posterior or transforaminal lumbar interbody fusion (PLIF or TLIF, 70 levels) using porous HAp/Col were reviewed at three and six months after surgery. Pedicle screw fixation and two box-type cages or one boomerang-type cage were used for all patients. A block of porous HAp/Col was filled into the cage and autogenous local bone was grafted around the cages. Functional radiography and CT scans were used to evaluate fusion status. Radiographic fusion was defined as less than 2 degrees of segmental angular motion and the presence of bridging bone in and around the cage in CT scans.

**RESULTS:** Segmental angular motion was observed less than 2 degrees in 26 of 33 operative levels (78.8%) at 3 months and 33 of 40 (82.5%) at 6 months after surgery. A bridging bone formation through the cage (porous HAp/Col) v.s. around the cage (autogenous local bone) was 21.2% v.s. 23.1% at 3 months after surgery, and 31.4% v.s. 40.0% at 6 months after surgery. Absorption of HAp/Col was observed in 1 of 70 levels (1.4%) at 3 months and 3 of 70 (4.3%) at 6 months postoperatively. At the mid-levels of multi-segmental fusion, HAp/Col graft successfully achieved a bony bridging in 78.0% of levels at 3 months after surgery.

**CONCLUSION:** Porous HAp/Col was likely to require more time for bone formation when compared with autogenous local bone. On the other hand, in the case that porous HAp/Col was grafted to more dynamically stable levels such as mid-levels of multi-segmental fusion, bone formation could be expected at the early phase.



In postoperative CT scan, Hap/Col graft successfully achieved a bony bridging at 3 months after surgery. The arrowhead indicates Hap/Col graft and the arrow indicates autogenous local bone graft.

## MORPHOMETRIC ANALYSIS OF THE RETROPERITONEAL VESSELS WITH RESPECT TO LATERAL ACCESS SURGERY IN ADULT SCOLIOSIS

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### INTRODUCTION:

The minimally invasive lateral approach to the thoracolumbar spine avoids manipulation of abdominal and retroperitoneal structures and decreases risk of injury to paraspinal musculature. In adult patients with scoliosis, the varying anatomical relationship between retroperitoneal vessels and intervertebral disc spaces can increase the risk of vascular injury. In this study, we performed a morphometric analysis on the position of the retroperitoneal vessels with respect to lateral access surgery in adults with scoliosis deformity of the thoracolumbar spine. Specifically, we aimed to determine the variation in anatomic position of retroperitoneal vessels in relationship to curve direction, location, magnitude and axial rotation and the feasibility of approach from the concavity and convexity of the curve.

### METHODS:

The study design was cross sectional reviewing sixty-two MRI or CT scans from consecutive adult patients with scoliotic spinal deformity in the thoracolumbar spine. Axial images were used to measure the anterior-posterior diameter of the inferior vertebral endplate with respect to the disc space perpendicular to the widest length of the disc. The overlap of the retroperitoneal vessels with the endplate were measured at the cephalad end vertebra, apex, and caudad end vertebra of each curve. Overlap and accessible disc space for individual disc spaces were also measured.

### RESULTS:

There was a significant difference in percentage overlap of the apex and cephalad vertebral endplate and inferior vena cava (IVC) in right versus left sided curves ( $p=0.002$ ). Overlap between the inferior vertebral endplate and IVC at the cephalad, apex, and caudad end of the curve was significantly different between thoracolumbar and lumbar curves ( $p<0.05$ ). Axial rotation significantly affected vessel overlap at multiple curve locations while there was no relationship between overlap and curve magnitude. There was a statistically significant difference in accessible disc space and vessel overlap percentage when approaching the curve from the convexity (36.7 mm, 4.9%) versus the concavity (34.0 mm, 12.4%).

### DISCUSSION:

While minimally invasive lateral access surgery offers advantages for surgical management of adult scoliosis when compared to traditional open anterior and posterior approaches, lack of direct visualization can place the retroperitoneal vessels at risk. The overlap between retroperitoneal vessels and inferior vertebral endplates at the disc level in scoliotic spines varies significantly with direction of the curvature, level of the deformity and degrees of axial rotation. When considering vessel anatomy alone, there is a small benefit to approaching curves from the convex side. Surgeons, as usual, will take an individualized case by case approach to avoid approach related vascular complications, but the findings of this study can help guide decision regarding side of approach.

**SURGICAL TREATMENT OF SUPERIOR AND/OR MIDDLE CLUNEAL NERVE ENTRAPMENT****Tomoyuki Konno<sup>1</sup>, Yoichi Aota<sup>2</sup>, Takuya Kawai<sup>2</sup>, Tomoyuki Saito<sup>1</sup>***1. Department of Orthopaedic Surgery, Yokohama City University Graduate School of Medicine, Yokohama, Kanagawa, Japan**2. spine surgery, Yokohama brain and spine center, Yokohama, Kanagawa, Japan***Introduction**

Superior cluneal nerves (SCN) and middle cluneal nerves (MCN) are cutaneous nerves distributed at the gluteal region. It is known that SCN and MCN can become spontaneously entrapped under fascia over iliac crest and under the long posterior sacroiliac ligament (LPSL), respectively (Maigne JY, Doursounian L: Spine 1997 & Aota Y. World J Orthop 2016). In a previous prospective study, 12% of patients of low back pain and leg pain had SCN and/or MCN disorders (Kuniya H, et al: J Orthop Surg Res 2014). Release surgery was indicated only when temporal pain relief was obtained after SCN and/or MCN blocks and repetitive blocks failed to produce sufficient pain relief. In this prospective study, surgical outcome was analyzed.

**Methods**

Diagnostic criteria for suspected SCN and MCN disorder were that the maximally tender point was on the iliac crest or around LPSL and that palpation of the tender point reproduced the chief complaint. When patients met both criteria, a nerve block injection was performed. At the initial evaluation, LBP and leg symptoms were assessed by visual analog scale (VAS) score. Before and 6 months after surgeries, VAS pain levels were recorded. Microscopic surgical release was done in 42 patients (F/M=26/16) with a mean of 70 years. SCN, MCN, and combined SCN and MCN surgeries were done 18, 9 and 15 subjects. During surgeries, at least two branches were released. When obvious nerve degeneration was observed and no voltage was obtained in SNAP, deafferentation was attempted.

**Results**

Before surgeries, the mean VAS score was  $80.0 \pm 19.2$  mm (25–100 mm). At 3 months after SCN surgeries, the mean VAS score significantly decreased to  $32.5 \pm 27.0$  mm (0–100 mm) ( $p < 0.05$ ). After MCN operation, the mean VAS score significantly decreased to  $31.6 \pm 27.0$  mm ( $p < 0.05$ ). Complete and almost complete relief of leg symptoms were obtained in 5 patients. Patients with shorter duration of symptoms (less than 3 years) and with longer duration of the effect of SCN blocks (more than 3 days) had a significantly higher ratio of satisfactory outcome ( $p < 0.05$ ). Ten subjects required additional surgeries because of recurrence of pain; SCN and/or MCN surgeries in 9 and sacroiliac fusion in one.

**Conclusion**

SCN and/or MCN entrapment is underdiagnosed cause of low back pain and leg pain. For a structure to be considered as a potential source of pain, pain must be provoked by palpation of the tender points.

## SURGICAL MANAGEMENT OF THORACIC DISC HERNIATION: ANTERIOR VS POSTERIOR APPROACH

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**Introduction:** Surgical treatment of thoracic disc herniation is principally performed through anterior and posterior approach. However, there is no consensus on the best approach for surgical treatment of thoracic disc herniation. The aim of this study is to compare the outcomes and complications of the patients with thoracic disc herniation undergoing surgery through posterior and anterior approach.

**Methods:** Eighty-seven patients, with total 101 symptomatic herniated thoracic discs, underwent surgery in the same institution between 2007 and 2016 were included in this study. In sixty-nine patients the anterior approach was used and posterior in 18 patients. In the anterior group, the discectomy was performed in 57 patients with minimally invasive lateral transthoracic trans/retropleural technique. In twelve patients this was in conjunction with thoracic surgeons and thoracotomy. In the posterior group, the discectomy was performed with a transfacet pedicle-sparing approach in 9 patients, transpedicular approach in 4 patients, after costotransversectomy in 1 patient and only laminectomy was performed in 4 patients without discectomy. Multilevel thoracic disc surgery was performed in 11 patients. The outcomes and complications were evaluated retrospectively.

**Results:** Anterior and posterior groups were similar in age, gender, body mass index and clinical symptoms. In the anterior group, four patients (5.7%) had major complication (transient neurological deterioration, pseudo arthrosis, postoperative pulmonary embolism and reoperation due to persistent narrowing) and 26 patients (37.7%) had minor complication. In the posterior group, 6 patients (33.3%) had major complication (permanent neurological deterioration, perioperative transient neurological deterioration, pseudoarthrosis and reoperation due to insufficient decompression) and 4 patients (22.2%) had minor complication. VAS score at final follow-up improved in both groups compared to preoperative period ( $p>0.05$ ). In the anterior group, 43 of 50 patients with myelopathy had neurological improvement postoperatively. In posterior group, 8 of 14 patients with myelopathy had neurological improvement postoperatively. Neurological improvement significantly higher in the anterior group than posterior group ( $p<0.05$ ).

**Discussion:** The posterior approach is associated with a higher rate of major complication which includes neurologic deficit as well as incomplete decompression. The anterior approach is a safer and a more efficient method compared to posterior approach.

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## LIFELONG ANTIBIOTIC SUPPRESSION FOR INFECTED INSTRUMENTED SPINES – FACT OR MYTH?

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### **Introduction:**

Surgical Site Infection (SSI) after spine surgery is a morbid and expensive complication, often requiring surgical debridement and long-term suppressive antibiotics. The possible treatment options include removal of hardware after fusion, or retention of hardware with long-term suppression with antibiotics with deleterious side effects. It is unclear whether patients can be taken off suppressive antibiotics with retained hardware. This study aimed to retrospectively analyze the perioperative course and antibiotic regimen that led to the eventual definitive treatment of patients who suffered an SSI after spinal instrumentation.

### **Methods:**

Consecutive adult patients with surgical site infections after spine surgery and instrumentation at a single institution from 2007-2013 were retrospectively analyzed. The patients were grouped into three cohorts based on their definitive treatments: removal of instrumentation, retention of instrumentation with continued antibiotic suppression, and retention of instrumentation with no antibiotic suppression. The patients without suppression discontinued their antibiotics because they were either prescribed short antibiotic courses, had GI side effects, or were advised by the infectious disease consultant. Various domains were compared between the three cohorts: patient characteristics, infection characteristics, debridement characteristics, and antibiotic characteristics. Univariate analysis was conducted between the three cohorts to determine which variables were different.

### **Results:**

Of the 67 patients with SSI after spine surgery and instrumentation, 25 (37%) had their hardware removed, 25 (37%) had their hardware retained and were on antibiotic suppression and 17 (25%) had their hardware retained without any suppression. Those without antibiotic suppression have the longest follow up, averaging approximately 4 years with no recurrence, compared with other cohorts with approximately 3 years (retained with suppression) and 2 years (hardware removed) of follow up. Patient characteristics including the ASA score did not vary significantly between the three groups. Those with hardware removal had later presentation of their infection (85 days post op), as opposed to earlier presentation (19 or 29 days post op) for the suppression and no suppression groups respectively.

### **Discussion:**

Our study demonstrated that none of the patients with retained hardware without suppression had recurrence of infections after long-term follow-up. Therefore, we believe that life-long antibiotic suppression may not be required with acute surgical site infections after early aggressive debridement. Patients with infections detected later are difficult to treat without removal of their original hardware.

## EVALUATION OF THE REVISION SPINE SURGERIES PERFORMED BY ENDOSCOPIC PROCEDURES

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**Introduction:** Success rate continues to fall with each additional surgical undertaking. It is said that the second operation has a 50% chance of success, and after the second operation, patients are more likely to be made worse than better. Furthermore, endoscopic spine surgery requires high-level techniques, especially in the case of revision surgery. Our institution performed 1500 spine surgeries in 2014, including 1296 endoscopic spine surgeries (86.4%). Of the endoscopic surgery cases, 68 cases were revision surgeries.

**Aim:** To evaluate the revision spine surgery performed using endoscopic procedures.

**Materials and Methods:** The study included revision spine surgeries of 51 men and 17 women, having a mean age of 57.0 years (range, 25–87 years). The mean follow up period was 28.5 months (range, 23-34 months). The revision procedure, duration of revision from the primary surgery, cause of the revision surgery, complication, and results of the surgery were examined. The results of the surgeries were calculated by the Hirabayashi recovery rate using preoperative and most recent postoperative JOA scores [(postoperative JOA score–preoperative JOA score) × 100/(23–preoperative JOA score)] (only subjective part is used, and the perfect score is 23 points). The improvement rate for JOA score was categorized as follows: excellent (100%-75%), good (74%-50%), fair (49%-25%), and poor (<25%).

**Results:** Endoscope-assisted posterior fusion re-surgery was performed in 14 cases, and the cause of revision included disc degeneration (9 cases) and spinal instability (5 cases). Endoscopic laminotomy re-surgery was performed in 10 cases, and the cause of revision included re-stenosis (9 cases) and cystic lesion (1 case). Endoscopic discectomy re-surgery was performed in 43 cases, and the cause of revision included recurrent disc herniation (37 cases) and poor cases (6 cases). The mean duration of the revision from the primary surgery was 89.0 (range, 3–600) months. The surgical results obtained are as follows: a) Fusion group - three excellent cases, three good, six fair and two poor cases; b) Endoscopic laminotomy group - two excellent, five good, two fair and one poor case; and c) Endoscopic discectomy group - 24 excellent, 11 good, 6 fair and 2 poor cases. There were six cases of dural tear and one case of surgical site infection but no other serious complication or open conversion cases.

**Conclusion:** All the revision surgeries were performed using endoscopic procedures. Although there were minor complications, the surgical results support the use of endoscopic procedures for revision spine surgery. We also suggest that the revision spine surgery can be performed using an endoscopic procedure.



## SURGICAL OUTCOMES OF FULL-ENDOSCOPIC LUMBAR FORAMINOTOMY FOR DEGENERATIVE LUMBAR SCOLIOSIS

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### **Introduction**

In aged population, degenerative lumbar scoliosis (DLS) is commonly present. It often related with low back pain due to additional degenerative spondylolisthesis and rotatoryolisthesis. Lumbar stenosis is also common problem in combination of ligamentum flavum hypertrophy, facet arthropathy, disc collapse and olisthesis. Patients with DLS frequently presents with foraminal stenosis (FS) on concavity side that causes severe disabling radiculopathy. Decompression and fusion surgery is recommended if pain is refractory to nonoperative treatment. However, fusion surgery is not favorable for patient with the aged osteoporotic bone and medical comorbidities. Full-endoscopic foraminotomy (EF) has advantage for treating radiculopathy in FS in DLS. In this study, we retrospectively reviewed clinical results after EF for treating radiating pain due to FS in DLS.

### **Methods**

Between July 2012 and April 2014, 23 DLS patients who had unilateral severe radiating pain underwent EF by a single surgeon (mean 69.7 (47-87) years old, 11 males and 12 females) with 21.5 months follow-up. Level of surgery were 3 in L3-4, 15 in L4-5, 4 in L5-S1, and 1 in L3-4 and L4-5. EF was performed in patients whose pain was improved on diagnostic selective root block but was refractory to non-operative treatment. Under the direct vision of 8mm full-endoscope, tip of superior facet was resected by 3 mm high speed endoscopic drill. Additional decompression was performed with HO-YAG laser and endoscopic punch and forceps. In case of FS combined with foraminal disc herniation, fragmentectomy was also performed. All procedures were performed under local anesthesia and conscious sedation. Clinical and radiological follow-up was evaluated.

### **Results**

VAS score for leg pain was significantly improved after surgery (8.7 and 2.6, respectively,  $p = 0.002$ ). VAS score for back pain was not significantly changed during follow-up (5.4 and 4.8, respectively,  $p = 0.563$ ). Foraminal dimension measured at mid-pedicular line on MRI showed significant improvement after EF (32.9 mm<sup>2</sup> and 103.2 mm<sup>2</sup>, respectively,  $p = 0.00$ ). Segmental Cobb's angle on AP radiograph remained stable during follow-up period (7.2 and 7.8 degree in preop. and follow-up, respectively,  $p = 0.384$ ). Mean operation time was 45 minutes and bleeding was minimal. Patients discharged within mean 2 days after operation.

### **Discussion**

Full-endoscopic foraminotomy has advantage over conventional open decompression or fusion surgery because all procedure can be performed under local anesthesia for elderly patients with medical problems, thus can avoid fusion related complications such as implant failure or pseudarthrosis. It is an effective and minimally invasive treatment option for treating severe radiculopathy caused by foraminal stenosis in DLS patients.

## FACTOR ANALYSIS OF THE SRS-22 QUESTIONNAIRE IN PATIENTS WITH ADULT SPINAL DEFORMITY

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**Introduction** The Scoliosis Research Society (SRS) questionnaire was designed for patients with adolescent idiopathic scoliosis, but is now also used as the outcome instrument of choice in patients with Adult Spinal Deformity (ASD). No studies have confirmed the four-factor structure (pain, function, self-image, mental health) in ASD or evaluated this in different contexts. Factorial invariance of an instrument over time and in different languages is essential to allow for precise interpretations of treatment success and comparisons across studies. This study evaluated whether Spanish, French, Turkish, and German versions of SRS-22 showed the same four-factor structure as the original instrument and whether this structure was invariant over time.

**Methods** 935 patients with ADS (348 operative, 587 nonoperative), recruited into the European Spine Study Group's (ESSG) prospective observational multicentre study, completed the SRS-22 upon inclusion and at 12 months' followup. Confirmatory factor analysis (CFA) was used to compare a unifactorial solution with the proposed four-factor solution for the 20 non-management items of the SRS-22. The item-loading invariance was tested for baseline versus follow-up data (N=477 patients), and in baseline data from Spanish (N=428), Turkish (N=229), French (N=83), and German (N=195) patients.

**Results** The SRS-22 factor structure did not fit to a unifactorial solution but did fit to the proposed four-factor solution. A constrained model that forced item loadings to be the same across the language versions showed a satisfactory fit to the baseline data (RMSEA = 0.04, CFI = 0.87). However, the loading/contribution of the "function" item #15 ("financial difficulties because of back") was generally low in all language versions (between 0.28 and 0.42), while three questions (#11 "medication use" and #17 "days off in last 3 months" from the "pain" factor; and #14 "back affects personal relationships" from "self-image") showed higher loadings in the Spanish (0.47, 0.49, 0.66) and Turkish (0.59, 0.46, 0.64) versions compared with the French (0.25, 0.28, 0.51) and German (0.36, 0.36, 0.48) versions. A trimmed model that included 16 unproblematic items (to make 4 items for each of the 4 domains, by omitting #15, #14 and #17 (poorly fitting) and #3 (lowest fit in the mental health domain)), and that constrained the structure to be the same in all four languages, showed a good fit to the baseline data (RMSEA = 0.04, CFI = 0.90). Similarly, a good fit was found when this structure was constrained to be the same in the baseline and followup data (N = 477, RMSEA = 0.05, CFI = 0.94)

**Conclusion** The 20 non-management items of the SRS-22 appeared able to characterize the major domains, and a four-factor structure—as proposed by the originators of the instrument—was a reasonable fit to the data. However, we recommend removal of 4 less-well-fitting items, together with adaptation and standardization of item 11 across language versions (to use the SRS-22R formulation for this item), to provide an improved 16-item version of the instrument. The latter showed factorial invariance with respect to language and time of assessment, supporting the validity of such a version in future multicentre outcome studies.

**DISCECTOMY WITH AND WITHOUT BONE-ANCHORED ANULAR CLOSURE FOR HIGH-RISK DISC HERNIATION PATIENTS: COMPLETE EARLY READMISSION AND DELAYED DISCHARGE ANALYSIS FROM A MULTICENTER, PROSPECTIVE, RANDOMIZED STUDY**

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**Introduction:** Readmissions and reoperations within the first few months of surgery are major factors driving negative clinical and financial outcomes. Providers are increasingly being asked to bear the financial burden of hospital admissions that occur within a certain time period after the index surgery, typically 30-90 days. Same-level reherniation and progressive degeneration with disc height loss are the main causes of poor outcome after lumbar discectomy and may necessitate early readmission and reoperation. An anular closure device (ACD) has been developed to address these causes, and a multicenter, prospective, post-market randomized clinical trial (RCT) is ongoing. This report evaluates the early safety of discectomy augmented with a bone-anchored ACD (treatment group) compared with discectomy alone (control group) in terms of delayed discharge and hospital readmission within the first 30, 60 and 90 days after surgery.

**Methods.** The study population for this interim analysis consisted of all enrolled patients (554 total: 278 control, 276 treatment from 21 sites) from an ongoing RCT to demonstrate superiority of discectomy with anular closure relative to discectomy alone. Key inclusion criteria include 6 weeks of failed conservative treatment, posterior disc height of  $\geq 5$ mm, minimum defect width and height, and baseline Oswestry and visual analog scale leg pain scores  $\geq 40/100$ . Key exclusion criteria include prior surgery at the index level. This report, which comports with the study statistical analysis plan, presents safety and early readmission results within the first 30, 60 and 90 days after surgery.

**Results.** Implanted patients in the treatment group had substantially lower incidences of readmissions or delayed discharges and index-level reoperations, compared with the control group.

Treatment	30 days		60 days		90 days	
	Control	Treatment	Control	Treatment	Control	Treatment
Readmission/ delayed discharge AE	All	4.3%	7.2%	7.2%	10.1%	9.1% 12.9%
Related to device/ procedure	2.2%	5.0%	2.9%*	6.5%	3.6%**	7.9%
Index-level reoperations	1.1%	2.9%	1.8%*	5.0%	1.8%*	5.0%

\* Trend for lower incidence Treatment vs. Control (0.05<p<0.10)

\*\* Significantly lower incidence Treatment vs. Control (p<0.05)

**Discussion:** Discectomy augmented with bone-anchored anular closure has a similar safety profile compared with discectomy alone, with similar adverse event rates and minimal device-related complications reported. Furthermore, anular closure was associated with substantially lower rates of reoperations and early readmissions or delayed discharges, compared to discectomy alone. These results suggest that bone-anchored anular closure could play an important role in reducing short-term clinical and financial burdens following lumbar discectomy.

## CLINICAL OUTCOMES OF THE POSTERIOR SPINAL SHORTENING FOR DELAYED PARALYSIS AFTER OSTEOPOROTIC VERTEBRAL FRACTURE

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**INTRODUCTION:** Osteoporotic vertebral compression fracture (OVCF) often causes delayed paralysis because unstable spinal unit compresses the spinal cord. Posterior fusion without anterior reconstruction often results in unacceptable local kyphosis. Crushed upper endplate of the fractured vertebra is not strong enough to maintain normal alignment of the spine. Pedicle subtraction osteotomy (PSO) is a procedure that performed widespread for these cases, however, this procedure has to remain crushed upper endplate and degenerated disc. We applied modified PSO including interbody fusion after removal of crushed upper endplate and degenerated disc to keep normal spinal alignment and improve union rate.

**AIM:** The purpose of this study is to investigate clinical outcomes of the modified PSO for delayed paralysis after OVCF.

**MATERIALS AND METHODS:** Thirty-three patients (22 males and 11 females) who underwent the posterior spinal shortening at our institutions from January 2008 to March 2014 were examined. Mean age was 72.6 (range: 60-85) years, and the fractured vertebrae were found in thoracic region in 14 patients, lumbar region in 19 patients. All patients underwent thoracolumbar spine CT and XP 3, 6, 12 months after the surgery. Clear zone around inserted screws were checked on CT, spine alignment were checked on XP. Basically, pedicle screws were inserted into the vertebrae at 2 above and 2 below of the fracture level, and the reconstructed area was reinforced by claw hooks and/or a tape. Duration of operation, estimated blood loss (EBL), pre- and postoperative local kyphosis, bone union, and complications were examined and compared with respect to Daily teriparatide group and Claw hook group.

**RESULTS:** Mean duration of operation was 346minutes, and mean EBL was 516ml. All patients underwent autotransfusion and additional transfusion was required in 4 patients. The mean angle of local kyphosis was improved from 12.6° to 4.6°, and the loss of correction was 5.6°. In patients with thoracic region, the mean angle of kyphosis was reduced from 14.4° to 10.8° with correction loss equal to 5.6 at the final examination. In patients with lumbar region, the mean angle of kyphosis was reduced from 11.3° to 0° with correction loss equal to 5.4 ° at the final examination. Subsequent vertebral fracture and loosening around pedicle screw was found in 4 patients respectively, but bone union was observed in all patients. There was significantly few that postoperative kyphotic change occurred one case after operation in 15 Claw hook group, and adjacent vertebral fracture occurred one case in 12 daily teriparatide group. Neurological symptoms as gait impairment, pain, and bladder dysfunction were improved in all patients. Frankel grade was also improved in all patients.

**CONCLUSIONS:** The circumferential fusion with the modified PLIF and posterior shortening stabilization provided good clinical outcomes. Even in the osteoporotic spine, appropriate correction and fusion was achieved by pedicle screw system with additional claw hook placement. Moreover daily teriparatide use group significantly had few adjacent vertebral fractures.

## COMBINING TITANIUM SCREWS WITH STAINLESS STEEL RODS FOR ADULT SPINAL DEFORMITY DOES NOT RESULT IN INCREASED IMPLANT RELATED COMPLICATIONS

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### Introduction:

Many surgeons refrain from combining titanium alloy (Ti) implants with stainless steel (SS) screws due to concerns of potential complications from galvanic corrosion. Prior studies have evaluated implant related complications when mixing Ti and SS implants in animal models. However, none have evaluated whether mixed metal implants influence rod fracture rates and other implant-related complications in patients treated with posterior spinal fusion for adult spinal deformity. We hypothesize that there will be similar implant related complications in SS screws with TA rods (SS-Ti), compared to Ti screws with cobalt chrome rods (Ti-CoCr) and all Ti screw-rod constructs (Ti-Ti) in the treatment of adult spinal deformity.

### Methods:

We performed a retrospective review of 67 deformity correction surgeries (SS-Ti n=46, Ti-Ti n=22, Ti-CoCr n=10) that included 5 or more levels of posterior instrumented spinal fusion. Demographic information was reviewed as was the presence of hardware and non-hardware related complications. Differences in baseline demographics, surgical details, and complications were assessed with Kruskal-Wallis tests for continuous variables and Fisher's exact tests for categorical variables. When significant, post-hoc Bonferroni-corrected pairwise tests were used to further assess the nature of the differences. Analyses were conducted in SAS v9.4 with a two-sided level of significance of 0.05.

### Results:

The cohort was 70% female with an average age of 65±12 years and average follow up of 15±10 months [2 weeks – 34 months]. There were 8 (21%) implant related complications in the SS-Ti group, 2 (25%) in the Ti-CoCr, and 6 (33%) in the Ti-Ti group. The SS-Ti group had 12 (30%) non-implant related complications, the Ti-CoCr group had 3 (38%) and the Ti-Ti group had 3 (17%). Neither implant-related nor non-implant related complications significantly differed between groups ( $p = 0.597$  and  $0.436$ , respectively). Procedure length differed among implant types, with SS-Ti procedures being shorter duration ( $6.0 \pm 1.8$  hrs) than Ti-Ti ( $7.8 \pm 1.7$  hrs,  $p=0.026$ ) and Ti-CoCr ( $8.3 \pm 2.1$ ,  $p=0.003$ ) procedures. A greater proportion of patients receiving Ti-CoCr were male (87%) than those receiving and SS-Ti (12%,  $p<0.001$ ) and Ti-Ti (44%,  $p=0.041$ ). Additionally, all Ti-CoCr patients underwent primary surgeries, whereas the SS-Ti and Ti-Ti groups contained a mixture of primary and revision procedures ( $p=0.006$ ). Interbody approach ( $p=0.010$ ), the proportion of staged procedures ( $p=0.004$ ), the proportion having osteotomies ( $p<0.001$ ), and osteotomy type ( $p<0.001$ ) also differed among the implant types.

### Discussion:

In our review, there was no evidence of a difference in the number of implant-related complications among implant types. This parallels the in vitro experience of a 2008 study from the journal *Injury*. Our study was limited by a relatively small sample size, particularly for the CoCr group. Further analysis of retrospective data is being gathered from a second center. This should improve the power for this study and extend the generalizability of the findings. Additionally, planned analyses controlling for differences in baseline patient demographics and surgical details will further strengthen the ability to draw conclusions regarding the use of mixed metal implants in spinal deformity surgery.

## CLINICAL OUTCOME OF TWO-LEVEL LUMBAR TOTAL DISC REPLACEMENT: AN ANALYSIS OF 141 PATIENTS WITH MINIMUM 24-MONTH FOLLOW-UP

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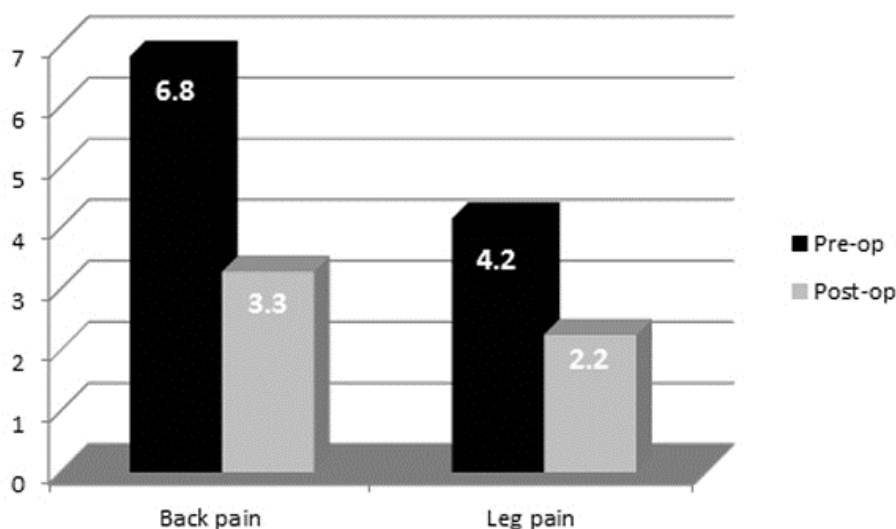
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**Introduction:** There are multiple studies describing the results of single-level lumbar total disc replacement (TDR), but less information is available for 2-level procedures. The purpose of this study was to investigate the clinical outcomes of lumbar TDR at 2-levels.

**Methods:** Records for a spine specialty center were reviewed to identify patients who underwent lumbar TDR and had minimum 24 month follow-up data available. There were 141 patients with a mean follow-up of 54.1 months. All patients had failed at least 6 months of non-operative care. They did not have significant facet joint degeneration. Implants used were either the ProDisc-L or Charite. Data collected included the Oswestry Disability Index (ODI), visual analog scales (VAS) assessing back pain and leg pain, and re-operations. All cases were performed for painful disc degeneration at two adjacent levels.

**Results:** Mean operative blood loss was 96.5 ml. The mean ODI scores improved significantly from 53.0 to 27.7 ( $p < 0.05$ ). VAS back and leg pain scores also improved significantly (Figure 1;  $p < 0.05$ ).



**Figure 1.** Back pain and leg pain both improved significantly ( $p < 0.05$  paired t-test) after 2-level TDR.

Eighteen (12.8%) patients underwent re-operation. Three (2.1%) patients underwent fusion at the TDR levels, 5 (3.5%) were at an adjacent segment, one was for incision and debridement for a superficial wound infection, and 9 patients underwent spinal cord stimulator implantation for pain control.

**Discussion:** The results of this study found that lumbar TDR at two levels produced good results, similar to those reported in the literature for single-level cases. These findings support that 2-level TDR is a viable alternative in the treatment of painful disc degeneration unresponsive to non-operative care in appropriately selected patients.

**CAN MIS-TLIF BE PERFORMED WITH STANDARD IMPLANTS AND INSTRUMENTATION?" - PARASPINAL APPROACH REVISITED.**

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**INTRODUCTION:** With the increasing number of lumbar fusions being performed, many innovations have emerged for which the goal is to minimize invasiveness and improve outcome. Many procedures require specialized retractors, implants or insertion instruments. Availability of such instruments in developing nations with lower economy is a cause for concern. Authors describe their experience with paramedian MIS-TLIF utilizing standard implants and instruments and compare the results with classical TLIF.

**MATERIALS AND METHODS:** A prospective randomized study with 20 individuals undergoing single-level TLIF for spondylolisthesis randomized into "classical"(n=10) or "MIS"(n=10) groups was conducted in rural part of India. Blood loss, postoperative pain (VAS-back & VAS-leg), analgesic requirements and daily life activities during hospital stay and at the 3-month follow-up were evaluated. Pre & post-operative MR images were studied to evaluate invasiveness of procedures.

**RESULTS:** Paramedian approach was successfully performed in all patients with no conversions to classical TLIF. There was no significant difference in either VAS-back or VAS-leg pain. mean length of incision was 3.5cm (2.8-4cm) and 6.3cm (5.3-7.6cm); surgery-time (min) was  $140 \pm 33$  &  $179 \pm 35$ ; C-arm-time(s)  $15 \pm 3$  &  $30 \pm 5$ ; estimated-blood-loss (ml) was  $757 \pm 255$  &  $150 \pm 30$ ; drainages (cc)  $480 \pm 326$  &  $175 \pm 50$  and hospital-stay (day) was  $8 \pm 1.5$  &  $5 \pm 1.5$  respectively for classical and MIS group. axial t1 and t2 weighted images revealed less altered signal in the paraspinal musculature in MIS group.

**DISCUSSION:** The study documents the feasibility of MIS-TLIF through paramedian approach with the clinical results comparable to classical TLIF with added advantages of lower blood loss, reduced hospital stay, lower analgesic requirements and faster recovery of daily life activities. importantly, paramedian MIS-TLIF requires only standard implants, instruments, and retractors with no added cost and can be adopted easily.

## DOES SMOKING IMPACT ON OUTCOMES FOR POST-OPERATIVE BACK PAIN PATIENTS COMPLETING REHABILITATION?

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**Introduction.** The purpose of this study was to compare clinical outcomes based on smoking status of those with a recent history of elective lumbar spine surgery (n=1017) completing post-operative rehabilitation.

**Methods.** This retrospective study of prospectively collected low back pain (LBP) cases was a collaborative effort of spine care rehabilitation clinics in New Zealand and Canada. Patient enrolment occurred between January 2008 and October 2012.

**Results.** There were 395 cases from New Zealand and 622 from Canada. Of the total cohort, 518 (51%) were smokers. At baseline, smokers had significantly higher levels of numeric pain rating, higher rate of general practitioner visits and lower perceived function (assessed by a modified version of the Low Back Outcome Score) ( $p < 0.05$ ) compared to non-smokers. Adjusting for baseline differences, post surgical smokers had significantly less functional improvement after rehabilitation than the non-smokers ( $p < 0.001$ ), but achieved similar levels of improvement in pain and similar return to work rates.

**Discussion.** LBP patients with a history of smoking had pain and return to work outcomes post operatively that were comparable to non-smokers, but failed to reach similar levels of functional improvement.



**ACCURACY OF MODELS FOR PREDICTING PATIENT CENTERED OUTCOMES AFTER SURGICAL AND NON-OPERATIVE TREATMENT FOR LOW BACK PAIN CONDITIONS**

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**Introduction:** Accurate prediction of patient centered outcomes following surgical or non-operative treatment for low back pain conditions is necessary to support clinical decision making for patients and their health care providers. Data from long term longitudinal follow-up in the Spine Patient Outcomes Research Trial (SPORT) have been used to develop models for this purpose, using as key outcomes physical function (SF-36 PF), sciatica or stenosis pain bothersomeness, satisfaction with symptoms, sex life, and sleep. To improve prediction accuracy, important patient-specific baseline prognostic factors were included in the models. The accuracy of predicted outcomes through eight years was evaluated in this study.

**Methods:** One thousand bootstrap datasets of the same size as the original studies were generated by randomly sampling with replacement from the SPORT combined randomized and observational cohorts for intervertebral disc herniation (IDH), spinal stenosis (SPS), and degenerative spondylolisthesis (DS). For each data set, the modeling procedure was repeated. First, variables for adjustment were selected based on best fitting models for outcomes at one year using linear or binary regression models according to penalized variable selection methods using the BIC (Bayesian) information criteria. Two-way interaction terms were included in the selection process. The selected variables were then included in longitudinal models to estimate parameters for predicting outcomes at 6 weeks, 3 months, 6 months and annually for 8 years following the initiation of treatment. Finally, the model estimates from each dataset were used in the original SPORT cohorts to predict actual outcomes. The accuracy for physical function and pain bothersomeness predictions was summarized in terms of the average deviation from the observed score (bias), and the average squared deviation (mean squared error). For the binary outcomes of satisfaction with symptoms, sex life, and sleep, the C-statistic was calculated, giving the proportion of predicted probabilities for positive outcomes exceeding those for negative outcomes. Means and 95% confidence intervals were computed using the accuracy summaries from all bootstrapped data sets.

**Results:** The bootstrapped model predictions were approximately unbiased for the continuous function and pain scores (Table 1). However, the root mean squared prediction errors were substantial, ranging from 17% to 20% of the range for SF-36 PF and 18% to 21% for the range of pain bothersomeness. For satisfaction with symptoms, sex life, and sleep, the prediction percentages were approximately unbiased (Table 2). However, the average C-statistics were only moderate, ranging from 0.63 to 0.75.

**Discussion:** The predictions generated by the SPORT models are generally accurate as assessed by robust methods for internal validation studies. However, prediction uncertainty needs to be included as a factor in clinical decision making.

Table 1. Bootstrap Root Mean Squared Prediction Error and Bias with 95% Confidence Interval (bootstrap n=1000)\*

	Root Mean Squared Prediction Error (95% CI)		Bias (95% CI)	
	SF-36 Physical Function†	Sciatica/stenosis Bothersomeness Index‡	SF-36 Physical Function†	Sciatica/stenosis Bothersomeness Index‡
Intervertebral disc herniation	17.4 (17, 17.9)	4.3 (4.1, 4.4)	0.22 (-0.5, 0.9)	-0.07 (-0.3, 0.1)
Spinal stenosis	19.3 (18.7, 20)	5.1 (4.9, 5.3)	0.31 (-0.8, 1.5)	-0.1 (-0.4, 0.2)
Degenerative spondylolisthesis	19.6 (18.9, 20.3)	5.1 (4.9, 5.2)	0.17 (-1, 1.3)	-0.1 (-0.4, 0.2)

\* Bias = (observed change from baseline - predicted change from baseline);  
 Root Mean Squared Prediction Error = the square root of the sum of the squared bias divided by n.  
 † The SF-36 Physical Function score ranges from 0 to 100, with higher score indicating less severe symptoms.  
 ‡ The Sciatica/stenosis Bothersomeness Index ranges from 0 to 24, with lower scores indicating less severe symptoms.

Table 2. Bootstrap C-statistic, Root Mean Squared Prediction Error and Bias with 95% Confidence Interval (bootstrap n=1000)\*

	C-statistic (95% CI)			Bias (95% CI)		
	Satisfaction with symptoms	Sleep	Sex life	Satisfaction with symptoms	Sleep	Sex life
IDH	0.67 (0.66, 0.68)	0.63 (0.61, 0.65)	0.69 (0.67, 0.72)	0.01 (-0.01, 0.02)	0.01 (-0.01, 0.03)	0.01 (0, 0.03)
SPS	0.66 (0.65, 0.67)	0.69 (0.66, 0.72)	0.77 (0.76, 0.79)	0.01 (-0.01, 0.03)	0.02 (0, 0.04)	0.01 (-0.01, 0.03)
DS	0.68 (0.67, 0.7)	0.69 (0.65, 0.72)	0.75 (0.68, 0.79)	0.01 (-0.01, 0.03)	0.02 (0, 0.04)	0.01 (-0.01, 0.05)

\* Bias = (observed value - predicted probability);  
 Root Mean Squared Prediction Error = the square root of the sum of the squared bias divided by n;  
 IDH indicates intervertebral disc herniation; SPS, spinal stenosis; DS, degenerative spondylolisthesis; CI, confidence interval.

## PATHOMECHANISMS OF SCIATICA INDUCED BY STRAIGHT LEG RAISING (SLR) TEST IN LUMBAR DISC HERNIATION . CHANGES OF INTRARADICULAR OXYGEN SATURATION AND ELECTROPHYSIOLOGICAL VALUES

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**Introduction:** The straight-leg-raising (SLR) test has been one of the most significant of clinical signs when making a clinical diagnosis of lumbar disc herniation.<sup>4</sup> It is interesting to study to what extent oxygen saturation and electrophysiological values are disturbed in the nerve roots when sciatica is experienced in lumbar disc herniation. This study is to investigate the relationships among nerve root movement, intraradicular oxygen saturation and electrophysiological values during an intraoperative SLR test *in vivo*.

**Methods:** The subjects were 11 patients with lumbar disc herniation who underwent micro-discectomy (8 men and 3 women aged 32.0 years on average [range, 25-43]). Regarding operated disc levels, all patients were operated on L4/5 disc. The patients' legs were allowed to hang down to the angle at which sciatica had occurred and the change of nerve root action potentials and intraradicular oxygen saturation were measured. A sensor of the pulse oximeter which adhered to nerve root retractor put on the nerve roots above the herniation. After removal of the hernia, a similar procedure was repeated. The periradicular specimens collected during surgery were examined by light and electron microscope. During the SLR test performed pre-operatively, 5 patients developed sciatica at an angle of 10 degrees and 6 patients at 30 degrees. This test was performed only on those who gave informed consent.

**Results:** The intraoperative SLR test showed that the hernia compressed the nerve roots to increase their flatness, resulting in a clear disturbance by which gliding distance was reduced to only few millimeters. During the SLR test, amplitude of action potential and intraradicular oxygen saturation showed a sharp decrease at the angle that produced sciatica. During the SLR test, the intraradicular oxygen saturation was decreased by 3.0~41.3% (average  $\pm$  SEM.: 22.1 $\pm$ 13.6%) after initiating the test. When the angle of the legs was returned to zero degrees, amplitude and oxygen saturation showed an immediate improvement and the value recovered to that obtained before the SLR test. After removal of the hernia, the nerve roots showed smooth gliding in all patients. The intraoperative SLR test conducted after removal of the hernia showed no significant decrease of amplitude and oxygen saturation in the nerve roots. When the SLR test was performed at 1 week after the operation, all the patients were negative and did not develop sciatica, unlike the results obtained preoperatively.

**Discussion:** When sciatica was experienced during the SLR test, hernia mass caused relatively strong mechanical stretch to develop at the nerve roots, resulting in about 70-80% decrease in intraradicular oxygen saturation. Our data suggest that temporary ischemic changes in the nerve root cause transient conduction disturbances. It was predicted that disturbed blood flow caused by this mechanical stress led to development of edema and anoxemia, constituting an inductive factor of ectopic discharge responsible for pain.<sup>1,2,3</sup>

**Conclusion:** When sciatica was experienced during the SLR test, the amplitude and intraradicular oxygen saturation deteriorated significantly after the SLR test.

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