

## **19th SGS annual meeting**

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Scientific reviewer

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## Neck pain prevalence, associated factors and short-term response to surgery in patients with degenerative cervical myelopathy: a cohort study of 664 patients from 26 global sites

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### Abstract Content:

**Introduction** Neck pain is a common complaint in patients with degenerative cervical myelopathy (DCM); yet, there is a paucity of high-quality, prospective studies summarizing the prevalence and associated factors of neck pain in this patient population as well as the response of neck pain to surgical intervention.

**Patient sample** Seven hundred fifty-seven patients with DCM were enrolled in either the AOSpine CSM-North America or CSM-International study at 26 global sites from 2005 to 2011. Participating centers were located in North America (n = 12), Latin America (n = 3), Asia Pacific (n = 6) and Europe (n = 5). All patients were extensively assessed preoperatively and at a six-month follow-up. A total of 664 patients had complete neck pain scores preoperatively and were eligible for inclusion in the analysis of this ambispective cohort study.

**Outcome measures** Pain intensity subscore of the Neck Disability Index (NDI)

**Methods** As part of the NDI, a measurement specific to neck conditions, patients were categorized by neck pain as i) none, ii) very mild, iii) moderate, iv) fairly severe, v) very severe or vi) the worst imaginable pain. Frequencies and percentages were used to summarize the prevalence and severity of neck pain preoperatively and at the 6-months follow-up. Patient characteristics and functional assessments (modified Japanese Orthopedic Association score, mJOA) of individuals with and without pain were compared using independent samples t-tests. The association of preoperative neck pain and associated factors such as comorbidities, previous nonoperative treatment, gender, smoking status, and body mass index (BMI) was evaluated by univariable logistic regression to derive odds ratios and 95% confidence intervals.

**Results** Preoperatively, 526 patients (79.2%) reported neck pain, whereas 138 (20.8%) had no neck pain. Of individuals with neck pain, 134 patients (20.2%) rated their pain as very mild, 185 (27.9%) as moderate, 130 (19.6%) as fairly severe, 64 (9.6%) as very severe and 13 (1.9%) as the worst imaginable. Functional status (mJOA,  $p = 0.593$ ), number of stenotic levels ( $p = 0.925$ ), age ( $p = 0.376$ ), and duration of symptoms ( $p = 0.31$ ) did not significantly differ in patients with and without pain. Factors associated with the presence of neck pain were female gender (OR 2.12, CI 1.38-3.26,  $p = 0.0006$ ), BMI  $\geq 27$  kg/m<sup>2</sup> (OR 1.6, CI 1.08-2.33,  $p = 0.017$ ), rheumatologic comorbidities (OR 4.84, CI 1.15-20.4,  $p = 0.031$ ), gastrointestinal (OR 1.93, 1.04-3.57,  $p = 0.036$ ) comorbidities, and age  $< 57$  years (OR 1.75, CI 1.2-2.56,  $p = 0.0038$ ). Non-smoker status (OR 1.09, CI 7.1-1.68,  $p = 0.675$ ), and preoperative immobilization in a soft collar (OR 1.08, CI 0.59-1.97,  $p = 0.788$ ), physiotherapy treatment (OR

1.22, 0.76-1.95,  $p = 0.405$ ) and bed rest (OR 1.25, CI 0.76-2.05,  $p = 0.375$ ) were not associated with absence of pain. Neck pain improved significantly from preoperatively ( $1.83 \pm 1.3$ ) to the 6-months follow-up ( $1.16 \pm 1.0$ ;  $p < 0.0001$ ).

### Conclusion

Here, we demonstrate a high prevalence of neck pain in patients with DCM, a link between gender, body weight, comorbidity and age and highlight a significant response of neck pain six months after surgery. Further studies are needed to assess the mid-term effect of surgery on pain, and the impact of neck pain on quality of life in this patient population.

## Midterm outcome of neck pain after operative intervention in patients with degenerative cervical myelopathy: results from an international multicenter ambispective study of 664 patients

### Presenting Author

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### Abstract Content:

**Introduction** Operative intervention in patients with degenerative cervical myelopathy (DCM) is increasingly recommended as it effectively halts neurological progression and improves functional impairment, disability, and quality of life. Despite the high incidence of neck pain in patients with DCM, there is a paucity of high-quality, prospective studies evaluating the impact of surgery, the role of the surgical approach and the effect of the functional impairment on neck pain outcomes.

**Methods** Data was obtained from merging of the AOSpine Cervical Spondylotic Myelopathy North America and CSM International studies. Both prospective studies enrolled 757 patients at 26 global sites from 2005-2011. Participating centers were located in North America, Latin America, Asia Pacific and Europe. All patients underwent a surgical intervention of the cervical spine and were assessed at 6, 12 and 24 months postoperatively. A total of 664 patients had complete preoperative neck disability index (NDI) scores and were therefore eligible for this analysis. Four hundred and ninety-seven patients had neck pain outcomes at the 24-months follow-up. The surgical approach was defined as anterior only (AP), consisting of anterior discectomy, corpectomy, fusion, fixation and/or graft implantation; posterior only (PA), including posterior laminectomy or laminoplasty; posterior instrumentation and laminectomy (PI) and a combined anterior-posterior approach (AP).

**Results** Preoperatively, 79.2% of patients indicated neck pain, whereas 20.2% rated their pain as very mild, 27.9% as moderate, 19.6% as fairly severe, 9.6% as very severe, and 1.9% as worst imaginable. The overall NDI improved significantly between preoperatively and the 6-, 12- and 24-months follow-up's ( $p < 0.0001$ ) and reached the minimum clinically important difference (MCID) of 7.5 points at every follow-up. The NDI subscore neck pain also improved significantly from preoperatively to all follow-up's ( $p < 0.0001$ ). Out

of 566 patients with a complete NDI assessment at 6 months, 58.6% had an anterior approach only (AP), 11.1% a posterior approach only (PA), 27.3% a posterior laminectomy and instrumentation (PI), and 3% a combined anterior-posterior approach (AP). Patients reported no neck pain in 33% after an AA, in 35% after a PA, in 32% after a PI, and in 29% after an AP approach 6 months after surgery. The neck pain incidence at 24 months postoperatively did not differ in patients with mild (52.9%), moderate (51.7%), or severe DCM (48.1%).

**Conclusion** To our knowledge, this is the first multi-center, international study demonstrating significant improvements in neck pain up to 24 months after operative intervention for DCM. The functional impairment or the surgical approach was independent to the pain response. Further studies are needed that evaluate important predictors of improvement in neck pain and to assess the effect of neck pain on the quality-of-life.

## Severity of degenerative lumbar spinal stenosis affects pelvic rigidity during walking

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### Abstract Content:

#### Introduction

Degenerative lumbar spinal stenosis (DLSS) is one of the most common diseases of the spine that can be treated surgically. Little is known about pelvic rigidity and its role in the development, diagnostics and rehabilitation of the disease.

**Purpose** To determine the association among duration of symptoms, lumbar muscle atrophy, disease severity, pelvic rigidity during walking and surgical outcome in patients with DLSS scheduled for decompression surgery.

**Materials and methods** 29 patients with DLSS who were scheduled for decompression surgery and 23 healthy persons participated in this study. Duration of symptoms were categorized as: < 2 years, < 5 years, and > 5 years. Muscle atrophy at the stenosis level was categorized according to Goutallier. Bilateral cross-sectional areas (CSA) of the erector spinae and psoas muscles were quantified from MRIs. Stenosis grade was assessed using the Schizas classification. Pelvic tilt was measured in standing radiographs. Pelvic rigidity during walking was assessed as root mean square of the pelvic acceleration in antero-posterior, medio-lateral and vertical direction normalized to walking speed measured using an inertial sensor attached to the skin between the posterior superior iliac spines.

**Results** BMI but not duration of symptoms, lumbar muscle atrophy, pelvic rigidity and stenosis grade explained changes in ODI from before to after surgery. Patients with greater stenosis grade had greater pelvic rigidity during walking. Lumbar muscle atrophy did not correlate with pelvic rigidity during walking. Patients with lower stenosis grade had greater muscle atrophy and patients with smaller erector spinae and psoas muscle CSA had a greater pelvis tilt.

**Conclusion** Greater pelvic rigidity during walking may represent a compensatory mechanism of adopting a protective body position to keep the spinal canal more open during walking and hence reduce pain. If this gait pattern persists postoperatively, it could be specifically addressed with physiotherapy and improved in the long term.

## Exploring the pathophysiology of lumbar spinal stenosis: why do patients claudicate?

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### Abstract Content:

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**Introduction** The pathophysiology of neurogenic claudication due to lumbar spinal stenosis (LSS) is poorly understood. Several hypotheses such as impaired blood flow and nerve conduction or lower limb vascular impairment secondary to autonomic nerve fibre dysfunction have been advanced. We hypothesised that lower limb pain could be due to mechanical cyclical traction on the lumbar roots during walking while conduction or blood flow abnormalities could be mere secondary accompanying observations. Should this be the case, passive mobilisation of the legs simulating gait in an erect position should therefore reproduce lower leg symptoms.

**Materials and methods** Patients suffering from neurogenic claudication symptoms with a myelographic bloc on MRI were included. Patients performed an active walking test using a treadmill as well as a separate passive walking test involving an external robotic rehabilitation device (Lokomat) whereby the lower limbs were being passively moved simulating walking while being suspended by the pelvis in a harness, thus replicating weight-bearing erect position. Strain gauges monitored the absence of voluntary muscle activity. Subjects were randomised to start either from the passive (n = 6) or the active part of the experiment (n = 9). Tests lasted for 20 mn and patients were instructed to report on their symptoms as soon as they appear. Primary outcome measure was pain reported by patients on a VAS scale while secondary outcomes included pain free distance walked, sensory symptoms reporting related to distance walked as well as Oswestry disability index (ODI) score and pre-test estimation of walking distance. Statistical analysis was performed using Fisher's exact test.

**Results** Fifteen patients were enrolled in this pilot study with a male/female ratio of 1.6. and an average age of 70 years. They had an average of 1.6 stenotic levels on MRI. Average ODI score was of 33 with an average pre-test reported walking distance of under 545 m. During the experiment, an average walking speed of 2.3 km/h in both passive and active walking tests was recorded. Lower limb pain of an average of VAS 4/10 was reported by all patients on active walking after an average of 116 meters. By contrast passive walking reproduced no pain in 14 out of the 15 patients enrolled, while only a single patient experienced leg symptoms (p < 0.001). Sensory symptoms developed in 11 subjects on active walking after an average of 191 m and in 3 patients during passive walking after an average of 167 m (p = 0.009).

**Discussion** This study suggests that neurogenic claudication is most likely unrelated to a mechanical cause such as traction of the severely compressed nerve roots during walking. A vascular origin is more likely although the exact mechanism is poorly understood. Further research is warranted in order to better understand the pathophysiology of claudication in LSS.

## Evaluation of postoperative weakness of the hip flexion in patients underwent XLIF - an observational study

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### Abstract Content:

**Introduction** Various techniques have been described to perform a lumbar spinal fusion. The extreme lateral interbody fusion (XLIF) is a relatively recent minimal invasive technique but with the disadvantage of splitting the psoas muscle laterally at the target level. The possibility of a temporary or permanent weakness of the hip flexion due to this dissection on the corresponding side is discussed as a disadvantage of this technique.

**Purpose** Our Hypothesis is that with a careful dissection technique under direct sight this complication can be avoided in almost all patients. Primary endpoint of this study was therefore the measurement of hip flexion strength at various time points up to three months postoperatively.

**Materials and methods** Up to now 6 patients were included. All Patients had an XLIF of one or two segments and had no prior spondylolysis of their back. Force evaluations of hip flexion were performed bilaterally 2 days preoperatively, 2 days-, 6 weeks -and 3 months postoperatively. The data were evaluated descriptively and checked for significance using the two-sample *t* test for dependent samples.

**Results** The average force measurement of hip flexion in Newton on the operated side was 29.44 N 2 days pre-op, 22.29 N 2 days post-op, 30.43 N 6 weeks post-op, 24.43 N 3 months post-op. Overall, there was no statistical significant difference pre-op to post-op or side to side.

**Conclusion** Patients who underwent an XLIF procedure had postoperatively no significant weakness of the hip flexion. The hip flexion force was immediate postoperatively less than preoperatively, but a return of the force can be observed throughout postoperatively. All patients returned to pre op hip force within the first 3 months. We therefore postulate that this difference is due to the unavoidable muscle trauma but not to a nerve injury.

## Surgical management of multiple myeloma with symptomatic involvement of the spine

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**Introduction** Multiple myeloma (MM) is the most frequent primary malignancy of the spine, resulting in osteolytic lesions which may lead to spinal instability, pathologic fractures, and spinal cord compression(SCC).

**Aim** To investigate the clinical presentation, surgical indications and outcomes, complications, survival and its influencing factors in surgically treated MM patients with symptomatic involvement of the spine(SIS).

**Methods** Out of 350 MM patients treated at our institution from 2006-2018, we identified 24 patients surgically treated for SIS. A retrospective analysis of prospectively-collected data was done on demographics, clinical presentation, comorbidities, surgical indications and outcomes as well as factors predisposing to postoperative complications and survival.

### Results

The median follow-up duration was 85 months; median overall survival(OS) was 50 months. Clinical presentation at admission included pain(88%), sensory and/or motor deficit(67%) and bowel/bladder dysfunction(25%). Symptomatic pathological fractures occurred in 33%. Predominant surgical indication was rapid neurological deterioration ± SCC, followed by mechanical instability. There were 21% patients with surgical-related complications(< 3 months). Surgical-site infections occurred in 17%, without any obvious predisposing factors. Neurological deterioration, especially in the presence of motor deficit and/or bowel/bladder dysfunction, significantly reduced OS.

**Conclusions** In MM patients, rapid neurological deterioration was identified to be the predominant surgical indication. We have achieved good short- and long-term pain reduction. Surgery is a valuable option for MM patients with SIS who present with rapid neurological deterioration ± SCC and/or mechanical instability.

## Fusion of the L5-S1 segment in degenerative lumbar spine disease using the extreme lateral interbody fusion technique: a case report study

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### Abstract Content:

There are several standard surgical techniques for the treatment of degenerative lumbar spine diseases that failed conservative treatment. Interbody fusion can restore the proper alignment of the spine and can decompress the nerve roots. The XLIF procedure is a relatively recent retroperitoneal and transpsoas major muscle approach allowing the insertion of interbody implants. This approach has very good results but limitations to this procedure exist and it is normally addressed to the L1-L5 segments.

**Purpose** The purpose of this case report study is to demonstrate the possibility of treating degenerative lumbar spine diseases at the level L5-S1 using the XLIF procedure.

**Study design** This study is a single center case report study with 3 cases of degenerative lumbar spine disease treated with a XLIF procedure at the level L5-S1.

**Conclusion** This case report suggests that the XLIF procedure is a safe, feasible and timesaving procedure to treat the segment L5-S1 in selected patients with severe degenerative lumbar spine disease and failed conservative treatment. Preoperative anatomical evaluation of the correlation of the iliac crest to L5 has to be made. The procedure should be performed with the aid of neuromonitoring and direct visualization during dissection of the psoas muscle should be achieved.

## Augmented reality-assisted rod bending in spinal surgery

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**Introduction** In complex deformity cases, surgeons may be confronted with difficulties in shaping and reducing rods into pedicle screw heads, which may result in forceful reduction maneuvers, potential screw loosening or pull-out, and longer surgery time.

**Purpose/aim** This study sought to evaluate the benefit of holographic rods as assistive equipment for manual rod bending.

**Methods** A custom-written application for an augmented reality (AR) system (HoloLens, Microsoft) was designed with the aim of assisting spine surgeons with rod bending. A custom-made pointing is employed to capture the 3D positions of the screw heads. Once all screws have been captured, a spline is generated. The resulting hologram can be moved and rotated freely, and employed as a template for bending the implant. The application indicates the precise length of the required rod.

As a test fixture, we made use of a pelvic-/lumbar spine model with pedicle screws inserted bilaterally L2-5, S1, iliacal. Rod bending (4-mm alloy rod) was performed manually with and without the AR-technology, six times in a randomized fashion on both sides of the spine model by three spine surgeons. An observer recorded the time for bending and inserting the rod, the number of rod-rebending maneuvers, and the accuracy of the rod length.

**Results** The total time spent on bending and inserting the rod was significantly shorter with AR compared to without ( $374 \pm 79$  vs.  $465 \pm 121$  s,  $p = 0.01$ ). The rod length was significantly more often correct with AR (15/18 vs. 4/18,  $p < 0.001$ ). In addition, fewer rebending maneuvers were needed with AR (7/18 vs. 10/18  $p > 0.05$ ).

**Conclusion** AR-assisted rod bending has the potential to reduce surgery time and increase the accuracy of manual rod bending.

## Prediction of pedicle screw fixation strength with individualized finite element models

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**Introduction** The surgical treatment of many spinal pathologies involves pedicle screw insertion into vertebral bone for spinal fusion. Screw loosening is a major complication of these procedures, with a particularly high incidence among patients with low bone quality. Resistance to pull-out from bone is an indicator of the risk of screw loosening. The aim of this study was to develop a computational framework for automated patient-specific pedicle screw pull-out simulations and to validate predicted fixation strength to experimental measurements.

**Methods** Biomechanical pull-out tests along the longitudinal screw axis were performed on 20 lumbar vertebrae of bovine and porcine origin. Specimen-specific finite element models with bone material properties based on CT scans were created using the automatic modelling framework. Computationally predicted pull out strengths were compared to experimental test results.

**Results** Numerical and experimental pull-out strengths were significantly correlated ( $\rho = 0.82$ ,  $p < 0.0001$ ). The simulation results predicted the results from biomechanical tests with a 20% mean error. Our results suggest that maximal pull-out forces are strongly associated with mean vertebral density ( $\rho_{Exp} = 0.86$ ,  $\rho_{Exp} = 1.00 \cdot 10^{-6}$ ;  $\rho_{Sim} = 0.81$ ,  $p_{Sim} < 0.0001$ ) and screw dimensions ( $\rho_{Exp} = 0.66$ ,  $p_{Exp} < 0.01$ ;  $\rho_{Sim} = 0.74$ ,  $p_{Sim} < 0.01$ ).

**Conclusion** Experimental pull-out strength can be predicted with the analysis of automatically created finite element models by considering specimen-specific, heterogeneous bone mechanical properties determined from CT scans with clinical resolution. Once fully validated, this model might be used as a surgery-planning tool to reduce the occurrence of spinal fusion failure.

## Biomechanical comparison of screw-rod constructs using cortical bone trajectory (CBT) and traditional trajectory (TT) pedicle screws with and without one horizontal crosslink

### Presenting Author

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**Introduction** Pedicle screws following the cortical bone trajectory (CBT) proved to be a valid alternative to the traditional trajectory (TT) regarding axial pullout strength and resistance in craniocaudal toggling tests in cadaver experiments. In finite element simulations (FES), CBT screw-rod constructs showed superior rigidity in flexion-extension (FE), while less rigidity was computed in lateral bending (LB) and axial rotation (AR). It was hypothesized, that the addition of a horizontal crosslink (CL) could compensate for this inferiority, since it was observed to increase rigidity of a screw-rod construct in AR and LB.

**Purpose/Aim** The aim of this study was to record the range of motion (ROM) of TT and CBT single level screw-rod constructs in all six major loading directions and to measure the effect of a CL on these constructs.

**Materials and Methods** Spines of four human cadavers (T9 – S1) were cropped into 16 functional spine units (FSU). Eight FSUs were instrumented with pedicle screws following the TT and eight FSU were instrumented with CBT pedicle screws. The instrumented segments were loaded in all six degrees of freedom in three configurations: unfused, fused with two vertical rods and fused with two vertical rods and one CL. The ROM between the cranial and caudal vertebral body was recorded with a 3D motion capture system.

**Results** The ROM of the two groups did not differ significantly in either configuration ( $p > 0.05$ ). The addition of one CL to the fusion did reduce ROM significantly in AR (16.3%,  $p < 0.05$ ), LB (2.9%,  $p < 0.05$ ) and FE (2.3%,  $p < 0.05$ ) for the TT group and in AR (21.6%,  $p < 0.01$ ) for the CBT-group.

**Conclusion** In our study, the primary rigidity of TT and CBT single level screw-rod constructs was equivalent. Inferior rigidity of the CBT constructs in LB and AR as computed in the FES was not observed. However, the addition of a CL to both groups lead to a significant increase in stiffness in AR and significant, but minor increase in stiffness in LB and FE in the TT group.

### Sagittal alignment optimization using a statistical shape model and musculoskeletal simulations

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#### Abstract Content:

**Introduction** The use of Statistical shape models (SSMs) to describe 3D structures such as bones and organs has proved to be useful. The potential of this modelling method to analyze global musculoskeletal properties, however, has not yet been investigated. Therefore, we aimed to develop a SSM for the prediction of healthy spinal sagittal alignments based on the relative positions of sacral endplate and femoral heads. We furthermore hypothesize that the predicted alignment is functionally superior and could support planning of lumbar fusion surgery.

**Methods** Annotated sagittal alignments on 59 lateral EOS images were used for training of the 2D SSM. Annotations comprised femoral heads (FHs), sacral endplate, and both vertebral endplates from C1 to L5. The SSM was employed to predict a healthy alignment for a lumbar fusion patient, based on positions of FHs and sacrum. Personalized musculoskeletal models for the original and the predicted alignment were created in OpenSim and simulated inter-vertebral loads were compared.

**Results** The analysis of global balance by means of sagittal vertical axis showed that balance is reestablished in the predicted healthy alignments. Lumbar lordosis and thoracic kyphosis were more pronounced. Musculoskeletal simulations showed lower lumbar compression forces for the SSM predicted alignment. Shear forces were partially reduced at upper levels and slightly higher at L5/S1 during flexion, otherwise similar.

**Conclusion** The predicted healthy sagittal alignment for given positions of FHs and sacrum in a lumbar fusion patient was balanced. Furthermore, the predicted alignment resulted in lower simulated compressive loads as compared to the original alignment. Including alignment optimization into preoperative planning of spinal surgery could help re-establishing more physiological spinal loading conditions and prevent accelerated degenerative changes.

### Deep learning-based patient specific modeling pipeline for clinical finite element analysis

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#### Abstract Content:

**Introduction** Finite element (FE) models and analyses proof increasingly useful in supporting clinical decision-making in spinal surgery. However, creation of patient specific models still requires time-consuming manual labelling and segmentation of imaging data. Deep learning (DL) and neural network algorithms on the other hand are successfully used for semantic segmentation and computer aided diagnosis. As a novelty we present an automated pipeline combining DL and FE modeling for the creation of patient-specific models of lumbar functional spinal units (FSU).

**Methods** A validated DL network is used as baseline and retrained using a labeled clinical CT dataset containing 52 acquisitions of the lumbar region. Each lumbar vertebral level is segmented and labeled. In parallel, a large dataset of 3D segmented single lumbar vertebrae is used to train level-specific deformable models. After the DL network provides a CT segmentation mask for each level, the deformable model is fitted by non-rigid registration. The resulting surface model is converted into a simulation-ready FE model using a custom-built FE model generator.

**Results** The DL network provides high-accuracy segmentations of lumbar spinal vertebrae (Dice coefficient  $DC = 0.93$ ). Automatic fitting of the deformable model yields surface models which differ from the manually segmented vertebra with RMS errors between 0.5 and 2.6 mm (leave-one-out experiment). RMS errors in the upper range are almost exclusively observed at the pedicles and spinous process.

**Conclusions** The presented pipeline automatically creates FE models of lumbar FSUs directly from clinical imaging data. The functional models are ready for patient-specific intervention planning and suit-

able for simulation of flexion, extension, lateral bending, and axial rotation under combined loading.

### Nasal chondrocytes for intervertebral disc regeneration: an in vitro model for cell-tissue interaction

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#### Abstract Content:

**Introduction** Human nasal chondrocytes (NCs) have been identified as a possible cell source for the treatment of intervertebral disc (IVD) degeneration due to their superior ability to survive and produce extracellular matrix in an IVD environment.

**Purpose/Aims** Assess whether IVD injected NCs could counterbalance further IVD degeneration or possibly even induce regeneration. Therefore, the effects of cell-to-cell interaction between NCs and nucleus pulposus cells (NPs) was investigated in respect to the extracellular matrix (ECM) production and whether NCs integration into NP tissue is modulated by the modality of grafting (cell suspension vs micro-aggregate).

**Materials and methods** To study direct interaction, NPs were co-cultured with NCs in 1:1 ratio as pellets for two weeks in vitro. To study if NC could integrate into an IVD like matrix/tissue, NP micro-tissue was fabricated by pooling eight NPs micro-aggregates (25'000 cells per micro-aggregate, cultured for two weeks) together. GFP-labelled NCs were then added to the NP micro-tissue either as single cell suspension (200'000 cells per micro-tissue) or as 16 micro-aggregates (12'500 cells per micro-aggregate, cultured for two days). Both co-cultures were cultivated for two weeks after being put together. Histological and biochemical analysis were performed to assess the outcome.

**Results** Direct contact of NPs with NCs resulted in an increase of ECM as compared to control monoculture of the single cell types. NCs successfully integrated into the simulated NP micro-tissue either as micro-aggregates or in cell suspension.

**Conclusions** The preliminary results displayed a positive effect of cell-to-cell interaction. These findings validate experimental approach to investigate molecular mechanisms of NCs interaction with NPs and integration into NP accumulated tissue. In the future, the impact of NC cells on the viability, proliferation and ECM production of NPs and vis-versa will be determined with immunohistochemical analyses and a gene profiling of sorted cells after digestion of the construct will be performed.

### Surgery-induced spreading of tumor cells into the circulatory system during vertebral cement augmentation in metastatic spinal disease - a pilot study

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#### Abstract Content:

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**Introduction** Vertebral cement augmentation procedures (VCPs) is a well-established treatment option in cancer patients suffering from metastatic spinal disease (MSD). However, surgery-induced spreading of tumor cells remains a major concern of VCPs in MSD.

**Aim** To evaluate iatrogenic dissemination of tumour cells during VCPs and to investigate the dynamic patterns of circulating tumour cells (CTCs) during the procedure in order to define the best time point for blood sampling.

**Materials and methods** We prospectively recruited 11 consecutive MSD patients suffering from either breast (n = 7), prostate (n = 3) or colon (n = 1) cancer undergoing VCPs at our institution from 2017-2018. One patient was excluded from the study due to clotted blood samples. We obtained Intra-operative biopsies for histopathological confirmation of the primary tumour. Mean age was 66.1 (SD: ± 10.6) years with male:female = 3:8. We collected blood samples at 1, 5, 10 and 20 min after cement application. The samples were analysed by an immunomagnetic-cell-selection-system (AdnaTest, Qiagen), which includes a highly sensitive RT-PCR to detect respective tumour-specific mRNA markers.

**Results** Histopathologically, 9/10 tumours were confirmed. In all of these patients (9/9), mRNA-markers were detected in the circulation at 5 and 10 min. In 5/9 patients, mRNA-markers were detected at all 4 time points. Accordingly, in the histopathologically negative case, mRNA-markers were not detectable.

**Conclusion** We observed surgery-induced spreading of tumour cells into the circulatory system during VCPs in all patients. To best detect CTCs, we suggest to sample patients' blood between 5 and 10 min after cement application. Hence, we have paved the path to investigate prophylactic strategies more efficiently.

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