

SPINEFEST2018

Monday June 11th, 7am-4pm @ MaRS

SCIENTIFIC ABSTRACTS

For Oral and e-poster Presentation



Surgery

UNIVERSITY OF TORONTO

Spine Program

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ABSTRACT # 1

TITLE: ENDOGENOUS INTERLEUKIN-10 DEFICIENCY EXACERBATES VASCULAR PATHOLOGY IN CERVICAL TRAUMATIC SPINAL CORD INJURY

Authors and Affiliations: Anna Badner^{1,2}, Pia M. Vidal¹, James Hong^{1,2}, Justin Hacker¹, Michael G. Fehlings^{1,2}

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Purpose: Although the majority of traumatic SCIs take place at the cervical level, preclinical studies have been disproportionately focused on thoracic insult. With differences in anatomy, physiology and immune response between spinal cord levels, there is evidence that injury pathophysiology may vary, requiring tailored treatment paradigms. Further, as only a few therapies have been successfully translated to the clinic, cervical models are increasingly recognized as essential for the characterization of trauma and therapy.

Methods & Results: Using a novel and clinically relevant cervical contusion-compression mouse model of bilateral incomplete injury, this study aimed to assess the role of Interleukin-10 (IL-10), a potent cytokine with broad anti-inflammatory effects, in SCI vascular pathology. While the effects of IL-10 loss have been previously evaluated, the vascular changes are poorly characterized and limited to the thoracic level. Here, we demonstrate, using *in vivo* high-resolution ultrasound imaging, that IL-10 deficiency is associated with increased acute vascular damage. These effects also fostered modest impairments in long-term functional recovery, assessed by the Basso Mouse Scale (BMS), as well as histological outcomes. Importantly, the loss of endogenous IL-10 led to significant differences in the acute systemic response to SCI, specifically the circulating levels of IL-12 (p70), LIX (CXCL5), IL-1 β , TNF α and IL-6 relative to genotype controls, that may account for the limited longstanding effects on function.

Conclusions: Taken together, this these data demonstrate the role of IL-10 in secondary vascular

injury, highlighting the relationship between vascular and immune function in SCI pathophysiology.

ABSTRACT # 2

TITLE: SMART HUMAN NEURAL STEM CELLS TO DEGRADE SCAR AND OPTIMIZE REGENERATION OF THE CHRONICALLY INJURED SPINAL CORD

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Purpose: Human induced pluripotent stem cell-derived neural stem cells (hiPS-NSCs) are an exciting approach to replace neural circuits, remyelinate axons and provide trophic support after SCI. Unfortunately, after chronic SCI, dense perilesional chondroitin sulfate proteoglycan (CSPG) scarring significantly impairs neurite outgrowth and regenerative cell migration. Scar-modifying enzymes can enhance NSC-mediated recovery; however, nonspecific administration via intrathecal catheters causes off-target effects. We aimed to bioengineer hiPS-NSCs into Spinal Microenvironment Modifying and Regenerative Therapeutic (SMaRT) cells, capable of locally expressing a scar-degrading enzyme to enhance regeneration.

Method: A proprietary scar-modifying enzyme was non-virally integrated into the hiPS-NSC genome. The resultant monoclonal line was extensively characterized in vitro. Immunodeficient rats (N=60) with translationally-relevant chronic C6-7 clip-contusion injuries were randomized to: (1) vehicle treatment, (2) hiPS-NSCs, (3) SMaRT cells, (4) sham surgery.

Results: Human SMaRT cells retain key characteristics. The enzyme expressed by SMaRT cells rapidly degrades CSPGs on biochemical assays and allows neurons to extend into CSPG-rich regions in vitro. Furthermore, unlike wild-type hiPS-NSC media, conditioned SMaRT cell media can degrade post-injury rodent CSPGs in ex vivo injured cord cryosections. While blinded analyses of behavioural and IHC data are ongoing, interim analysis found grafted human cells to be extending remarkably long axons from the brainstem to the low thoracic cord at 32 weeks post-transplant. These axons demonstrate growth cone (GAP43), synapse (synaptophysin), and human cytoplasm (STEM121) markers.

Conclusions: This work provides exciting proof-of-concept data that engineered SMaRT cells can degrade CSPGs in vitro and that human hiPS-NSC transplants can generate long axons in chronic cervical SCI to potentially bridge sensorimotor signal transmission.

ABSTRACT # 3

TITLE: SELF-ASSEMBLING KKQL6KK PEPTIDE BIOMATERIAL OPTIMIZES HUMAN NEURAL STEM CELL TREATMENT FOR TRAUMATIC SPINAL CORD INJURY

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Purpose: Neural stem cells (NSCs) have emerged as a promising therapeutic strategy for regeneration after traumatic spinal cord injury (SCI). Unfortunately, the hostile post-injury microenvironment is a significant hindrance to regeneration. QL6 (K2QL6K2; Medtronic Inc.) is a unique self-assembling peptide biomaterial that reduces inflammation and astroglial scarring in animal models leading to functional recovery. QL6 also reduces cavity volume and supports the survival of mouse NSCs after SCI when used as a co-transplant. However, QL6's ability to

support translationally-relevant human induced pluripotent stem cell-derived NSCs (hiPS-NSCs) is not known.

Method: hiPS-NSCs were passaged into a pseudo-monolayer on QL6. The mechanism of adhesion was assessed by EDTA assay and qPCR. NSC survival, proliferation, and neurosphere formation was extensively characterized in vitro against a geltrex control. T-cell deficient RNU rats (N=65) with C6-7 clip-contusion injuries were randomized to: (1) vehicle treatment, (2) hiPS-NSCs, (3) QL6, (4) QL6+hiPS-NSCs, or (5) sham surgery (laminectomy alone).

Results: hiPS-NSC binding to QL6 is mediated by calcium-dependent cell adhesion molecules. QL6 increases NSC proliferation (cell count and Ki67) compared to a geltrex control and reduces qPCR markers of apoptosis over 7 days. Importantly, QL6 promotes the formation of adherent neurospheres, the native conformation of NSCs, even when applied in a thin 50µm layer, similar in size to microcystic cavitations within the cord. Blinded neurobehavioural assessments of transplanted rats are ongoing.

Conclusions: This work provides proof-of-concept data that a co-administration approach utilizing the QL6 biomaterial to support grafted human NSCs is a viable strategy with implications for translation.

ABSTRACT # 4

TITLE: BLOOD-SPINAL CORD BARRIER STABILIZATION VIA INHIBITION OF PROTEIN KINASE C CAN IMPROVE SPINAL CORD INJURY RECOVERY

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Purpose: Traumatic spinal cord injury (SCI) is a leading cause of paralysis that affects millions of patients worldwide. The disruption of blood-spinal cord barrier (BSCB) by the mechanical trauma is a major challenge that limits most SCI treatments, as it results in infiltration of reactive immune cells into the spinal cord. Therapeutic enhancement of BSCB will attenuate the migration of immune cells, and results in improved recovery after SCI. The aim of this study is to examine the effects of protein kinase C (PKC) inhibition using enzastaurin on BSCB integrity and to determine its efficacy as a treatment for SCI.

Method: Enzastaurin was administered intraperitoneally (25 mg/kg) into 6 rats with clip-compression injury at C6-7. In addition, 6 uninjured rats and 6 vehicle-treated injured rats were included as control cohorts. All animals were sacrificed at 24-hours post-operation. PKC enzymatic activity assay was used to assess the effect of enzastaurin. Western blotting and qRT-PCR was used to analyze the expressional changes. In addition, Evans Blue and ultrasound imaging were used to examine the vasculature permeability and integrity.

Results: Administration enzastaurin results in the inhibition PKC in the spinal cord. This leads to the upregulation of junctional proteins (claudin-5 and occludin) at 24-hours post-injury. Furthermore, enzastaurin reduced the permeability of BSCB and conserved the vasculature network at 24-hours post-injury.

Conclusions: PKC inhibition leads to upregulation junctional proteins and results in reduced permeability of BSCB. This can have a significant impact on the enhancement of neuroprotective regime applied upon traumatic SCI.

ABSTRACT # 5

TITLE: HETEROGENEOUS SECONDARY INJURY RESPONSE FOLLOWING TRAUMATIC INJURY AT DIFFERENT LEVELS OF THE SPINE.

Authors and Affiliations: James Hong, Dario Righelli, Mahmood Chamankhah, Anna Badner, Jian Wang, Yang Liu, Alex Chang, Mohammad Zavvarian, Stefania Forner, Michael Fehlings

Purpose: Traumatic spinal cord injuries (SCI) at the cervical level encompass more than 60% of SCIs globally. However, most cervical clinical trials were founded on preclinical data from thoracic SCI models. We hypothesized that based on the distinct anatomical phenotype between the cervical and thoracic cord, including grey-white matter ratio and vascular supply, that the timeline of SCI-induced pathology would be vastly different between the two levels.

Method: Female Wistar rats were subjected to moderate-severe clip-compression SCI to the C6-7 and T6-7 spinal cord with level and time-matched laminectomized shams serving as controls. The rats were then sacrificed at 3, 7, 14, and 56 days post-surgery. Ultrasound and Power Doppler imaging was used to assess the gross pathology of the injured cord. RNA sequencing was used to evaluate the genome-wide changes over time. Protein analyses were performed using Western blotting and ELISA, while tissue level work was done using immunohistochemistry.

Results: Ultrasound revealed an early onset of syringomyelia and scar deposition at 3 days post-SCI in the cervical cord which coincided with peaks in genome-wide transcriptomic and protein differences, with most of the differences mapping to pericytes and astrocytes—key players in the regulation of the integrity of the blood-spinal-cord-barrier.

Conclusions: For the first time, we have shown a strong rationale for level-specific treatment paradigms at the molecular level, which highlight the narrow time window for intervention in cervical SCI.

ABSTRACT # 6

TITLE: DIRECT NERVE ROOT STIMULATION: A NOVEL APPROACH TO NEUROMONITORING FOR REDUCTION OF HIGH GRADE SPONDYLOLISTHESIS

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Purpose: Traditional methods of neuromonitoring for spinal deformity lack accuracy and reproducibility in monitoring for high grade spondylolisthesis. This project introduces direct nerve stimulation (DNS) as a novel alternative to nerve root monitoring during reduction of high grade spondylolisthesis.

Methods: Prospectively collected intra-operative neuromonitoring data including MEP, SSEP, EMG and DNS was collected on pediatric patients undergoing posterior reductions for high grade L5/S1 spondylolisthesis. All modalities were recorded prior to, during reduction and prior to closure.

Results: 5 patients with high grade spondylolisthesis were analyzed. All patients had positive bilateral straight leg raises. 4 of 5 patients had intact pre-operative motor examinations; 1 patient had unilateral EHL weakness. 3 patients did not have any neuromonitoring alerts during their surgical procedure. Their average change in threshold value from baseline to final stimulation for the L5 nerve root was 1.3 mA. 2 patients had intraoperative alerts of MEPs, SSEPs and EMGs which resulted in greater nerve root stimulation threshold values at closing compared to baseline. In both cases, further nerve root exploration and decompression was performed. Both patients had post-operative neurologic deficits in ankle dorsiflexion.

Conclusion: After establishing pre-reduction thresholds for DNS, increases in DNS threshold were associated with post-operative neurologic deficits in cases of reduction of high grade spondylolisthesis. DNS provided an accurate measure of nerve function in this series. Recognizing increases in DNS thresholds intraoperatively can alert the surgeon to potential real time nerve injuries.

ABSTRACT # 7

TITLE: LONG-TERM FUNCTIONAL OUTCOMES FOLLOWING THORACIC SPINAL CORD INJURY: ANALYSIS IN THE MULTICENTER NORTH AMERICAN CLINICAL TRIALS NETWORK (NACTN) DATABASE

Authors and Affiliations: Blessing N.R. Jaja, MD, PhD; Jetan Badhiwala, MD; Michael G. Fehlings, MD, PhD, FRCS, FACS; Jefferson R. Wilson, MD, PhD, FRCS; on behalf of the NACTN Collaboration

Purpose: To investigate long term functional outcome following thoracic SCI, and the effect of clinical and treatment characteristics.

Method: The study analyzed a cohort with thoracic neurological-level SCI from the North American Clinical Trials Network (NACTN) SCI database. Functional outcomes were assessed according to the Spinal Cord Independence Measure (SCIM) sub-scores for ambulation, bladder, and bowel management at one-year follow-up. Descriptive statistics and regression analysis were applied to examine the association of clinical and treatment variables with the outcomes.

Results: Among the patients with AIS grade A injury, only 5% were independently ambulant or had normal bladder function one year post injury. Among those with SCI from a penetrating injury, none had normal bladder function at one year follow-up. Patients with AIS grade A injury were more likely to have normal bowel (18%) than bladder function or be independently ambulant (1%). In contrast, the group with incomplete injuries were more likely to have normal bladder function (77%) than bowel function (67%) or be independently ambulant (37%) at one year. There was no differences in the outcomes with respect to age, sex, neurological level, education, time to surgical decompression, or with steroid use.

Conclusions: The long term functional outcome following a thoracic SCI is poor, and strongly dependent on the initial injury severity. Injury severity has differential impact on the domains of

bladder, bowel and ambulation outcomes one year after a thoracic SCI. The study underscores the need for intensified efforts to mitigate the primary injury and to reduce evolving secondary damage to preserve the inherent recovery potential of the cord.

ABSTRACT # 8

TITLE: CIRCULATING MICRORNA EXPRESSION PREDICTS SURGICAL OUTCOMES IN DEGENERATIVE CERVICAL MYELOPATHY PATIENTS AFTER ONE YEAR

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Purpose: Degenerative Cervical Myelopathy (DCM) patients with significant spinal cord compression on MRI but mild clinical symptoms represent a significant management dilemma. Early decompression can arrest disease progression, but approximately 5-10% of patients with DCM sustain neurological decline following decompression, representing a substantial risk for an otherwise stable patient. Previous work from our laboratory has identified a set of microRNAs related to DCM diagnosis and baseline severity. We report the results of a prospective longitudinal clinical series designed to evaluate whether these microRNA biomarkers can predict surgical outcome in DCM.

Method: Thirty-five DCM patients undergoing surgical decompression were enrolled at the Toronto Western Hospital. Blood plasma was collected from all subjects prior to surgery, and 8 DCM-associated microRNAs were screened using the Exiqon miRCURY Serum/Plasma PCR platform. Neurological impairment was assessed before surgery and at the 1-year follow-up appointment using the modified Japanese Orthopedic Association (mJOA) scale.

Results: Of the 8 DCM-associated microRNAs, miR132 and miR34a significantly predicted a good outcome (mJOA>15) after surgical decompression (logistic regression, miR132,

OR=3.987, $p=0.033$, AUC= 0.755; miR34a, OR=3.370, $p=0.025$, AUC=0.748), outperforming baseline DCM severity (baseline mJOA, OR=1.463, $p=0.027$, AUC=0.726). Multivariate logistic regression model using miR132, miR34a, and miR154 demonstrated good predictive power in determining surgical outcome (AUC=0.867).

Conclusions: The results reported herein suggest that plasma expression of miR132, miR34a, and miR154 can predict the surgical outcome of DCM. Future studies will be required to confirm their role in DCM pathobiology, and to study the utility of these biomarkers in identifying good surgical candidates.

ABSTRACT # 9

TITLE: VERTEBRAL BODY SEGMENTATION IN CT IMAGES USING DEEP LEARNING

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Purpose: Accurate and fast vertebral body (VB) segmentation has many applications in diagnostics, interventional planning and surgical navigation. Existing algorithms for VB segmentation often do not perform well with pathology (fracture or tumour involvement). Recent successes in applying deep learning, specifically convolutional neural networks (CNNs), for biomedical image segmentation suggests that this approach is helpful in challenging segmenting scenarios. We hypothesize that a trained CNN can quickly, automatically and robustly generate 3D segmentations of healthy and metastatic involved VBs.

Method: Computed Tomography (CT) scans of the vertebral region (T4-L5) of 100 patients with healthy or metastatic vertebrae (osteolytic, osteoblastic, mixed involvement) were acquired.

Ground truth training masks were created using a semi-automated approach with manual correction. CNNs with U-Net architecture were implemented and trained ($N_{\text{training}}=1336$, $N_{\text{validation}}=352$) for 200 epochs in Keras by minimizing the Tversky index.

Results: The network achieved good performance, with 89+6% concurrency for both training and validation data. Prediction time for each volume was less than 0.2s. Segmentation performance was improved with a deeper network (5 layer network, (89%) compared to the 3 layer network (83%)).

Conclusions: This work demonstrates how U-Nets can be used as a rapid method for segmenting 3D CT images of healthy and metastatic VB through feature based learning, without manual identification of hand-crafted features. This work has potential applications in computer-assisted interventions, diagnosis and disease monitoring.

ABSTRACT # 10

TITLE: PROTOCOL FOR A VALIDATION STUDY OF A PATIENT-REPORTED MEASURE TO DIAGNOSE DEGENERATIVE LUMBAR SPINAL STENOSIS AND HIP AND KNEE OSTEOARTHRITIS

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Purpose: Clinical tools have been developed to differentiate degenerative lumbar spinal stenosis (DLSS) and lumbar disc herniation. It is unknown if any of these measures are able to differentiate lower extremity symptoms from DLSS and hip and knee osteoarthritis (OA). The

purpose of this study is to evaluate the validity of a self-report questionnaire (currently in development) to aid in the classification of lower extremity symptoms due to DLSS and hip and knee OA.

Method: A series of patients with DLSS or hip and knee OA will be recruited from primary care settings in Denmark. Diagnoses will be confirmed based on a comprehensive evaluation of clinical symptoms and physical and radiological examinations. Eligible patients will complete a self-report questionnaire and total scores will be calculated. The scores for each group of patients identified by comprehensive evaluation will be statistically compared to determine the cut-off points for each disease.

Results: The sensitivity, specificity and likelihood ratios for the questionnaire will be calculated. A receiver operating characteristic curve will be constructed and the area under the curve estimated. A final cut-off score on the questionnaire for the presence of DLSS and hip and knee OA will be determined.

Conclusions: A self-report questionnaire able to discriminate lower extremity symptoms due to DLSS and hip and knee OA has the potential to be used for more accurate estimates of disease prevalences. This questionnaire may also be implemented in clinical research and practice, allowing for more efficient and optimal management of patients with degenerative conditions.

ABSTRACT # 11

TITLE: GOOD LIFE WITH OSTEOARTHRITIS IN DENMARK®: PREVALENCE AND OUTCOMES OF PATIENTS WITH CONCOMITANT DEGENERATIVE LUMBAR SPINAL STENOSIS AND HIP AND KNEE OSTEOARTHRITIS: A PROTOCOL

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Purpose: The prevalence of concomitant degenerative lumbar spinal stenosis (DLSS) and hip and knee osteoarthritis (OA) is unknown. Additionally, education and exercise interventions for OA may benefit individuals with DLSS. The primary objective (phase I) is to estimate the prevalence of DLSS symptoms among patients enrolled in the Good Life with osteoArthritis in Denmark (GLA:D®) program and explore associations with age, sex, and index location of OA. The secondary objective (phase II) is to evaluate the effectiveness of the GLA:D® program for these individuals.

Method: Phase I is a cross-sectional design where the presence of DLSS symptoms will be assessed using a self-reported questionnaire. Participant demographics, such as age, sex, and presence of OA will also be collected. Phase II is a cohort design where individuals identified in phase I will be enrolled in the GLA:D® program. Outcomes including pain, quality of life, and functional measures will be collected at 3 and 12 months.

Results: Prevalence estimates will be expressed as the proportion of individuals with DLSS symptoms. Regression analyses will be used to calculate association and adjusted rates for variables such as age, sex, and index location of OA. Phase II analysis will report mean differences from baseline to 3 and 12-month follow-up.

Conclusions: This study will provide estimates of concomitant DLSS and hip and knee OA, as well as provide preliminary evidence on the effectiveness of the GLA:D® program for DLSS. These findings have the potential to better inform the non-surgical management of patients with DLSS and OA.

ABSTRACT # 12

TITLE: DRUG REPURPOSING: HIGH DOSE HUMAN IMMUNOGLOBULIN G FOR TREATMENT OF TRAUMATIC CERVICAL SPINAL CORD INJURY

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Purpose: After spinal cord injury (SCI), neuroinflammation exacerbates damage from initial trauma. The severity of neuroinflammation depends on integrity of the blood-spinal cord-barrier (BSCB), which consists of astrocytes, pericytes and endothelial cells. After SCI, a compromised BSCB enhances neuroinflammation by facilitating immune cell migration. Through targeting neuroinflammation, immunosuppressants are used to treat SCI patients. However, as selective components of neuroinflammation are beneficial after SCI, immunomodulation is more effective than general immunosuppression. Human intravenous Immunoglobulin G (hIgG) is used in clinic for treating neuroinflammation. Although we have shown that administration of hIgG (0.4g/kg) is beneficial after SCI, the optimal dose and mechanism of hIgG are unknown.

Method: We use a clinically-relevant rat model of C7/T1 SCI. At 15 minutes post-SCI, hIgG (0.02, 0.2, 0.4, 1, 2g/kg), methylprednisolone or vehicle was administered intravenously. Spinal cord and blood were collected to determine hIgG's immunomodulatory effects.

Results: At 24 hours post-SCI, hIgG co-localized with pericytes, astrocytes and endothelial cells. Relative to hIgG (0.4g/kg), hIgG (2g/kg) achieved superior protective effects on spinal cord vasculature and reduced spinal cord inflammation. Intriguingly, hIgG (2g/kg) increased serum levels of inflammatory cytokines and co-localized (without decreasing protein expression) of vascular cell adhesion molecule-1 – an adhesion molecule used by immune cells to extravasate

into inflamed tissue. These early effects translated into enhanced tissue preservation, bloodflow and functional recovery at 6 weeks post-SCI.

Conclusions: Altogether, this work demonstrates an exciting therapeutic approach where administration of a clinically-relevant biomolecule with a minimally invasive technique mitigates SCI pathology through antagonizing immune cell infiltration.

ABSTRACT # 13

TITLE: THE ROLE FOR BIOPSY PRIOR TO SURGERY IN SUSPECTED CHORDOMA OF THE MOBILE SPINE

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Purpose: 1) To review the management of mobile spine chordomas and 2) to identify two cases of unexpected mobile spine chordomas where a preoperative tissue diagnosis was decided against, despite being recommended in the literature, and may have changed extent of surgical resection.

Method: Two cases of lumbar spine lesions are included that were presumed to be a primary bone and a metastatic tumour. Chordoma was considered in the differential and was the final pathology but preoperative biopsy was decided against.

Results: Intraoperative pathology results suggested chordoma in one case and an unclear pathology in the other and tumour morphology was non-characteristic of the presumed lesions. Based on these factors the operative plan was modified intraoperatively to involve maximal approaches since en bloc resections of chordomas have been shown to reduce local recurrence risk.

Conclusions: Chordomas rarely occur in the mobile spine and have disease free survival benefit with en bloc resection. Since lesions typical for this region infrequently are treated with en bloc resection, a preoperative biopsy for tissue diagnosis has been recommended when chordoma is in the differential as it may change the surgical plan. Here we present two cases of chordomas where preoperative biopsy was discussed with interventional neuroradiologists but not obtained after their review of the cases and if it were done it would have likely significantly altered the surgical approach.

ABSTRACT # 14

TITLE: STEREOTACTIC BODY RADIOTHERAPY (SBRT) FOR SPINAL METASTASES AT THE EXTREMES OF THE SPINE: IMAGING-BASED OUTCOMES FOR CERVICAL AND SACRAL METASTASES

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Purpose: The unique anatomy and biomechanical features of the cervical spine and sacrum may impact treatment outcomes following stereotactic body radiotherapy (SBRT). Our objective was to report imaging-based outcomes following SBRT to cervical and sacral metastases.

Method: We retrospectively reviewed cervical and sacral metastases after SBRT. Outcomes of interest were imaging-based local control (LC), overall survival (OS), vertebral compression fracture (VCF) and other serious adverse effects.

Results: 52 patients were included consisting of 56 cervical spine and 37 sacral segments. Median follow-up was 14.4 months and 19.5 months, respectively, median dose fractionation was 24 Gy in 2. Cumulative LC rates at 1- and 2-years were lower for the sacrum (86.5% and 78.7%) compared to the cervical spine cohort (94.5% and 92.7%). Lack of posterior spinal element involvement was predictive of LC in the cervical spine ($p < 0.0001$), and absence of epidural disease ($p = 0.048$) predicted LC in the sacrum. Median OS was 16.3 months and 28.5 months in the cervical spine and sacrum cohorts. In the cervical spine group, presence of liver and/or lung metastases conferred worse prognosis ($p = 0.0494$). In the sacral cohort, patients with oligometastatic disease ($p = 0.0094$) and breast primary ($p = 0.0168$) had longer OS. Two cases of VCF in the sacrum, one brachial plexopathy and one lumbar-sacral plexopathy were observed.

Conclusions: Although high rates of LC were observed following SBRT to the cervical spine and sacrum, strategies specific to the sacrum may require further investigation to optimize results. Serious sequelae after SBRT to cervical spine and sacrum were rare.

ABSTRACT # 15

TITLE: DEVELOPMENT OF CLINICAL PREDICTION MODELS FOR POSTOPERATIVE SURVIVAL AND QUALITY OF LIFE IN PATIENTS WITH METASTATIC EPIDURAL SPINAL CORD COMPRESSION WHO UNDERWENT SURGICAL TREATMENT

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Purpose: We aimed to develop the first CPMs of survival and quality of life (QoL) based on a large sample of prospective data from surgical patients with metastatic epidural spinal cord compression (MESCC) conducted in accordance to the TRIPOD guidelines.

Methods: We used 10 imputation iterations of 258 surgical patients with MESCC. Using Cox model, we developed a 1-year CPM of survival with the site of the primary tumor, presence of organ metastasis and SF-36 physical component score as predictors. Using logistic regression, we developed CPMs for QoL at 6 weeks, 3, 6 and 12 months; the difference in pre- and postoperative EQ-5D scores ≥ 0.06 as the outcome measure for QoL. Collinearity, interactions and assumptions were assessed. Internal validation was performed using 200 bootstrap iterations. Calibration and discrimination were evaluated.

Results: Although the predicting performance of our 1-year CPM of survival was unsatisfactory, predicting the improvement in QoL at 3 and 12 months postoperatively showed adequate calibration and optimism-corrected discrimination was 0.79 (95% CI: 0.74-0.84) and 0.73 (95% CI: 0.67-0.80), respectively. Preoperative EQ-5D score was the only predictor for both CPMs of quality of life at 3 and 12 months.

Conclusions: We have created and internally validated the first CPMs of QoL at 3 and 12 months after surgery in patients with MESCC. The predictive performance of all current CPMs of survival as well as our CPMs for QoL should undergo full externally validation using data from an independent, related but different patient sample to assess their relative generalizability.

ABSTRACT # 16

TITLE: PREDICTIVE FACTORS FOR SURVIVAL IN SURGICAL SERIES OF SYMPTOMATIC METASTATIC EPIDURAL SPINAL CORD COMPRESSION: A PROSPECTIVE NORTH AMERICAN MULTI-CENTRE STUDY IN 142 PATIENTS

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Purpose: We identified preoperative predictors of survival in Metastatic Epidural Spinal Cord Compression (MESCC) patients surgically treated, examined how these predictors relate to eight prognostic models, and performed the first full external validation of these models in accordance with the TRIPOD guidelines.

Methods: 142 surgically treated MESCC patients were enrolled in a prospective, multicenter, North American study and followed for 12 months or until death. Cox models were used. Non-collinear predictors with <10% missing data, ≥ 10 events per stratum and $p < 0.05$ in univariable analysis were tested through a backward selection. For the original and revised Tokuhashi, Tomita, modified Bauer, van der Linden, Bartels, OSRI and Bollen, we examined calibration graphically, discrimination with Harrell c-statistics and survival by stratifying risk groups with Kaplan-Meier and log-rank test.

Results: Type of primary tumor, sex, organ metastasis, body mass index, preoperative radiotherapy to MESCC, and SF-36v2 Physical Component (PC) and EQ-5D were significant in the univariable analysis. Primary tumor, organ metastasis and SF-36v2 PC were associated with. Calibration was relatively poor overall. Bartels had the best discrimination (0.68; 95% CI: 0.65 – 0.71).

Conclusions: Breast, prostate and thyroid cancers, absence of organ metastasis, and a lower degree of physical disability are preoperative predictors of longer survival in surgical MESCC patients. These results are in keeping with current models. This full external validation of eight prognostic models of survival in surgical MESCC patient revealed that calibration was poor and discrimination was possibly helpful.

ABSTRACT # 17

TITLE: DEVELOPMENT AND VALIDATION OF CLINICAL PREDICTION MODELS OF SURVIVAL AND CLINICAL OUTCOMES FOR PATIENTS WITH METASTATIC EPIDURAL SPINAL DISEASE: A SYSTEMATIC REVIEW

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Purpose: The development and validation are the first phases involved towards the establishment of clinical prediction models (CPMs) in practice. We aimed to identify and assess CPMs created to predict clinical outcomes in patients with metastatic spinal disease (MSD) and subsequent validation studies.

Methods: Three electronic databases were searched (January 1, 1990 to June 20, 2017), without language restriction, to identify studies that developed or evaluated CPMs predicting clinical outcomes in adult patients with MSD (PROSPERO: CRD42017072908). Selected studies were then assessed based on their accordance with the Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD) guidelines.

Results: Among 7,275 unique full-text articles, 107 were included. Among the 43 articles describing the development of a CPM, 25 did not include any assessment related to internal validity, 13 reported the number of outcome events, 6 how missing data were handled and 3 reported outcome-predicted probabilities. Among the 80 studies that evaluated CPMs, 27 articles used a term related to “validation” in their title or abstract, and missing data for predictors or outcome, number of outcome events, both calibration and discrimination were reported in 8, 16 and 3 studies, respectively.

Conclusions: Since 1990, over 40 CPMs predicting clinical outcomes in patients with MESD were developed and 80 studies performing some sort of evaluation of these CPMs were published. Based on the items included in the TRIPOD checklist, the majority of these studies did not report on key methodological and data analysis elements.

ABSTRACT # 18

TITLE: AUTOMATED PIPELINE FOR ANALYSIS AND VISUALIZATION OF SPINAL CORD TRACTS FROM DIFFUSION TENSOR IMAGING

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Purpose: Magnetic resonance diffusion tensor imaging (MR-DTI) tractography is useful for neurosurgery by visualizing white-matter tracts. Commonly applied in the brain, the goal of this work is to extend this technique into the spine, allowing planning of complex spinal surgeries with geometric distorting pathology (tumour, spinal cord injury, degeneration, etc.). This work creates an automated pipeline of the onerous steps of DTI processing, enabling surgical planning and spine research. Specifically, this work would allow following spinal tracts with DTI-tractography into geometrically distorted regions, where anatomical identification could be erroneous.

Method: The pipeline automates processing (segmentation, registration, tensor fitting, tensor warping, and tractography streamline calculation) of MR-DTI, using Spinal Cord Toolbox, 3D Slicer, and custom code, generating streamlines. Pipeline generated streamlines were evaluated in the spine (C2-C6) of ten healthy subjects; spatial correspondence (Dice Coefficient(DSC), Hausdorff distance(HD)) was evaluated in a region(1-2 vertebral levels), where streamlines were not seeded, instead streamlines were followed into the evaluation region from the adjacent regions and compared against atlas-based anatomical labels.

Results: The pipeline executed successfully (~18 minutes/patient, Intel Xeon 3.3GHz) on all subjects without manual intervention. Lateral cortical spinal tract streamline spatial correspondence was good (DSC=0.76±0.1, HD=1.4±0.4mm) in a 1 vertebral level sized region and fair (DSC=0.66, HD=2.1±0.6) for 2 vertebral level sized region.

Conclusions: This work developed an integrated automated pipeline for the processing of spine MR-DTI, allowing for quick consistent and efficient 3D visualization of spinal white-matter tracts. The performance of the pipeline was consistent with being useful for neuro-navigation of the spine following rigorous validation.

ABSTRACT # 19

TITLE: DEVELOPMENT AND EVALUATION OF A NAVIGATION WORKFLOW FOR RADIOFREQUENCY ABLATION OF SPINAL METASTASES

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Purpose: Spinal metastases occur in up to 1/3 of all cancer patients. Improvements in radiofrequency ablation (RFA) have yielded an optimized technology for local control of spinal metastases, but current application utilizes manual treatment planning and execution. The

objective of this study was to develop a navigation workflow to enable implementation of pre-operative plans for RFA of vertebral metastases.

Method: A vertebral RFA navigation workflow was developed within the 3D Slicer platform integrating treatment plans based on pre-procedural CT imaging data with intra-procedural 3D Cone Beam CT (CBCT) images. A PlusServer platform connected to a StealthStation navigation system enables real-time navigation based on patient imaging. Image registration between pre-procedural and intra-procedural CT scans is performed by initial manual landmark registration, followed by automatic 3D-to-3D intensity based rigid registration algorithms. SureTrack optical trackers placed on the RF probes are spatially calibrated to accurately track probe tip poses. To evaluate the system accuracy and reproducibility, the pre-procedural scans and RFA treatment plans are transformed to intra-procedural coordinates containing the probe final treatment pose.

Results: This work successfully integrated data from multiple technologies (CBCT scanner, StealthStation navigation system, SureTrak optical trackers, Osteocool RFA system) within the developed RFA navigation software. RFA probes were successfully tracked on 3D triangulated surface vertebral models and the desired tool pose was achieved in real-time within the intraprocedural reference frame.

Conclusions: Navigated deployment of RFA treatment planning is feasible, and may improve RFA safety and efficacy, to ultimately enhance quality of life for patients with spinal metastases.

ABSTRACT # 20

TITLE: CONFOCAL FOCUSED ULTRASOUND STRATEGIES FOR CONTROLLED BLOOD-SPINAL CORD BARRIER DISRUPTION

Authors and Affiliations: Stecia-Marie Fletcher, Meaghan O'Reilly

Purpose: The Blood-Spinal Cord Barrier (BSCB) poses a major challenge to drug delivery to the spinal cord. Focused Ultrasound (FUS), in conjunction with intravenously injected

microbubbles, has been shown to produce targeted, transient BSCB disruption (BSCBD). A challenge to clinical application is achieving ultrasound delivery through the human spine. Sub-megahertz frequencies required for ultrasound propagation through bone, correspond to long focal zones compared to the size of the spinal canal, and may result in the formation of standing waves, which can compromise treatment safety. Research indicates that multifrequency ultrasound and modulated pulses can reduce focal depth of field (DoF) and suppress standing waves.

Method: The effects of confocal, dual-frequency ultrasound on DoF were investigated both numerically in MATLAB, and experimentally. The effects of standing waves were investigated in ex vivo human thoracic vertebrae. Linear chirp pulses, quadrature phase shift keying (QPSK), and short burst excitations were investigated for suppression of standing waves.

Results: At 500kHz, confocal transducers with frequency difference, $\Delta f=60\text{kHz}$, and angular separation, $\theta=90^\circ$, reduced the DoF by ~85%, compared to a single transducer. Short burst excitations showed greater reduction in standing wave content compared to continuous wave methods – ~60% vs. ~35%. Under confocal exposures, closely timed short pulses, accompanied by QPSK, suppressed standing waves in ex vivo vertebrae, while maintaining a uniform focal spot.

Conclusions: The feasibility of using confocal FUS to create a controlled focus within the thoracic spine was demonstrated in ex vivo vertebrae. These techniques can be adapted for safe FUS-induced BSCBD for drug delivery to the spinal cord.

ABSTRACT # 21

TITLE: DETERMINING THE EXTENT OF CLINICAL PRACTICE VARIATION ACROSS CANADA FOR SINGLE-LEVEL POSTERIOR SURGERY FOR LUMBAR DEGENERATIVE SPONDYLOLISTHESIS

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Purpose: There is considerable practice debate as well as discordant literature on the optimal surgical treatment for degenerative lumbar spondylolisthesis. This study aims to determine the clinical practice variation in surgical treatment that exists across Canada for this patient population.

Method: A review of prospectively collected data from the Canadian Spine Outcomes and Research Network registry was performed (enrolled patients Oct. 2008 – Aug. 2017). Inclusion criteria were patients with a primary diagnosis of degenerative lumbar spondylolisthesis, a chief complaint of radiculopathy or claudication, treated with a single-level posterior lumbar spinal decompression with or without fusion. Statistical analysis was performed evaluating surgical practice, provincial and inter-specialty variations.

Results: 244 patients were included, of which 48% patients received decompression alone and 52% received decompression with fusion. Mean patient age at surgery was 67 years, and 62% were female. Neuro-monitoring was used in 9% and navigation in 30%. In fusion procedures graft choice was allograft (35%) and synthetic graft (10%). There was no statistical difference in fusion rates comparing background surgeon specialty training. Orthopaedic surgeons were six times more likely to perform a transforaminal lumbar-interbody-fusion (TLIF; OR 6.3, $p < 0.001$). There was significant practice variability between Canadian provinces when considering the use of surgical fusion, TLIF and bone allograft ($p < 0.05$).

Conclusions: There is considerable clinical practice variation across Canada in surgery performed for single-level degenerative lumbar spondylolisthesis. This variability is important as both care providers and health system funders consider value-based surgery. Our research motivates ongoing comparative study that should also consider patient reported outcome measures following surgery.

ABSTRACT # 22

TITLE: AMPA RECEPTOR MODULATION AS A THERAPEUTIC STRATEGY TO ENHANCE SURVIVAL OF SPINAL CORD NEURAL STEM CELLS

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Purpose: Transplantation of neural stem/progenitor cells (NSPCs) following spinal cord injury (SCI) is a promising strategy to enhance regeneration but is limited by poor survival of grafted cells. Recently, we demonstrated for the first time that the excitatory neurotransmitter glutamate, which is released after SCI, promotes survival and proliferation of adult spinal cord NSPCs via the AMPA subtype of glutamate receptors. In this study, we examined the therapeutic potential of selective AMPA receptor modulation on NSPC survival using a class of allosteric AMPA receptor modulators known as ampakines.

Method: NSPCs isolated from the periventricular region of the adult rat spinal cord were exposed to ampakines CX546 or CX614 (72h) either alone or in the presence of low dose (50uM) glutamate (in order to mimic glutamate concentrations in the injured cord during the subacute period). To examine the effects of ampakine/glutamate treatment in the setting of oxidative stress, NSPCs were concurrently exposed to high dose hydrogen peroxide.

Results: Treatment with CX546 or CX614 in the presence of glutamate led to a significant increase in live cell numbers compared to controls. This effect was due to both a reduction in cell death and increase in cellular proliferation. Moreover, ampakine/glutamate treatment led to a significant increase in cell survival compared to controls in the setting of oxidative stress.

Conclusions: We present the first examination of the effect of allosteric AMPA receptor modulators on adult spinal cord NSPCs. Positive modulation of AMPA receptors may be a

promising therapeutic strategy in the subacute/chronic phases after SCI to increase survival of endogenous or transplanted NSPCs.

ABSTRACT # 23

TITLE: ESTABLISHING AND IMAGED BASED EVALUATION OF A NEW PRECLINICAL RAT MODEL OF OSTEOBLASTIC VERTEBRAL METASTASIS

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Purpose: The metastasis of cancer to the spine impacts the bone remodeling cycle via increasing bone resorption (osteolytic), bone formation (osteoblastic) or a combination of the two. This study presents a preclinical rat model of osteoblastic vertebral metastasis and characterizes progression through image-based evaluation.

Method: Intracardiac injection of human ZR-75-1 breast cancer cells into a preclinical athymic rat model (n=10) was used. The ZR-75-1 cells were transfected with luciferase to enable monitoring of the progression of tumour involvement through bioluminescence imaging (n=6, IVIS Spectrum, Perkin Elmer). Vertebral metastatic development was also tracked via μ CT imaging, every 3-weeks for 4-months (n=4, Locus Ultra μ CT, GE, 154 μ m). Before euthanasia, 4-months post injection, in-vivo μ CT images were acquired (n=10, Locus Ultra μ CT, GE, 154 μ m). Ex-vivo images were acquired of the excised spine, L1-L3 (n=10, μ CT100, Scanco, 7 μ m). High resolution imaging of L1-L3 allows for quantification of changes in tissue-level stereological features to be evaluated using an in-house developed algorithm. Histology was used to confirm osteoblastic involvement.

Results: All rats exhibited osteoblastic involvement in the vertebrae 4-months post inoculation, with the highest frequency of metastases in Th13-L6. Bioluminescent signals from the

osteoblastic metastases however were variable; signals were not seen or initial signals at early timepoints disappeared over time, in areas of well-established osteoblastic lesions confirmed by μ CT. Histological evaluation confirmed μ CT findings of osteoblastic bone formation.

Conclusions: Intracardiac injection of ZR-75-1 breast cancer cells in rats induces purely osteoblastic vertebral metastases evident on μ CT imaging that can be used for future preclinical studies.

ABSTRACT # 24

TITLE: TRANSPLANTATION OF HUMAN SPINAL OLIGODENDROGENIC NEURAL PROGENITOR CELLS ENHANCES REMYELINATION AND FUNCTIONAL RECOVERY AFTER TRAUMATIC SPINAL CORD INJURY

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The harsh microenvironment generated after traumatic spinal cord injury (SCI) results in significant early necrotic and apoptotic cell death. Oligodendrocytes are particularly susceptible to the death after injury and are one of the first cell types which die resulting in widespread demyelination of both injured and spared axons. Cell replacement therapy with neural progenitor cells (NPCs) represents a promising therapeutic potential for SCI, however, the proportion of NPCs differentiated to oligodendrocytes after transplantation is very low. This is more dramatic for human cells. We have developed a unique method to bias the differentiation potential of tripotent human NPCs towards more oligodendrogenic fate (oligodendrogenic NPCs; oNPCs) while preserving their potential to generate neurons and astrocytes. In clinically-relevant models

of rodent cervical and thoracic clip-contusion SCI, we studied the effects of these novel cells on lesional area, graft-host integration, and functional recovery. Transplanted oNPCs migrated rostrocaudally along spinal cord and differentiated into NeuN+/Tuj1+ neurons and GFAP+ astrocytes as well as Olig2+ immature and GST-pi+ mature oligodendrocytes. Mature human oligodendrocytes also expressed MBP and integrated with rodent NF 200+ neuronal axons, indicating the potential of transplanted oNPCs to remyelinate host axons in both the cervical and thoracic spinal cord. Furthermore, oNPC transplanted rats demonstrated significantly reduced lesion volumes and enhanced tissue preservation, white matter sparing and motor functional recovery. This work provides evidence that partially biasing NPCs towards an oligodendrogenic fate can improve recovery via remyelination and highlights oNPCs as a promising cell-based approach for CNS-repair.

ABSTRACT # 25

TITLE: A PHASE I TRIAL ON THE USE OF PHOTODYNAMIC THERAPY IN VERTEBRAL METASTASES

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Purpose: The spine is a common site of cancer spread. Complications include pathologic fracture and spinal cord compression. Vertebroplasty(VP) and Balloon Kyphoplasty(KP) are minimally-invasive stabilization procedures. Photodynamic therapy(PDT) is a tumor-ablative modality that may complement mechanical stability afforded by VP/KP. This first-in-human study evaluates PDT safety when applied in conjunction with VP/KP.

Methods: This dose escalation trial involved one control group of light only with no systemic drug and four light doses(50J,100J,150J,200J;n=6). Patients eligible for VP/KP in treating pathologic fracture or at-risk lesions were recruited. Exclusion criteria included spinal canal compromise or neurologic impairment. PDT is a 2-step binary therapy of systemic drug followed by intravertebral light activation. Light was applied via bone trochar prior to cementation. Drug/light safety, neurologic safety, generic(SF-36) and disease-specific outcomes(VAS,EORTC-QLQ-BM22,EORTC-QLQ-C15-PAL) were recorded through 6 weeks.

Results: 30(10 male, 20 female) patients were treated; 13 with KP, 17 with VP. Average age was 61 and significantly different between genders(Male 70yrs vs. Female 57yrs,p<0.0005). The primary cancer sites were breast(36.7%), lung(23.3%), prostate(10%) and kidney(10%). All patients completed the study.

No group showed significant increases in pain as defined by the EORTC-QLQ questionnaires. PDT groups for 50J/100J showed significant reductions in pain compared to the control. The 50J group had the best response, comprised mostly of lytic tumors, had an average measured power of 12.1 mW/cm², and had the 5/6 lesions located at L2-L5.

Conclusions: Vertebral PDT appears safe from a pharmaceutical and neurologic perspective. Ongoing study determining safe dose range and subsequent efficacy studies will be required.

ABSTRACT # 26

TITLE: CT-ULTRASOUND FUSION FOR SPINAL SURGERY

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Purpose: CT based navigation is useful for visualization and tracking of bony elements in spinal surgery but provides limited soft tissue contrast and does not accommodate possible tissue displacement caused by surgery. Ultrasound (US) images provide soft tissue information during surgery but can be difficult to interpret and relate to features seen in CT. Therefore, a workflow has been developed so the US imaging plane from most scanners can be shown in the context of 3D CT to enhance the use of US imaging.

Method: The US probe is instrumented with a tracker so that position data is continuously determined by a surgical navigation workstation (StealthStation S7). Video data from a US scanner is continuously digitized using a frame grabber providing a flexible solution workable with most scanners. These data are converted and streamed to 3D Slicer, an open source software platform for medical imaging. Pre- or intra-operative CT data are also loaded in Slicer. Software modules were developed and added to Slicer to perform spatial calibration of the US probe and subsequent image visualization.

Results: The workflow results in a fused 3D display that continually updates as the tracked US probe moves. The fusion is also displayed in the two-dimensional slice as the x-ray volume is traversed. Preliminary experiments in US plane registration result in a root mean square (RMS) error of approximately 1 mm in plane position.

Conclusions: We demonstrated a spine specific workflow allowing the fusion of live US images and 3D CT including a flexible calibration procedure compatible with most US scanners.

ABSTRACT # 27

TITLE: A CT-BASED SIMULATION FOR PREDICTING TRANS-VERTEBRAL ULTRASOUND PROPAGATION: SIMULATION ACCURACY

Authors and Affiliations: Rui Xu (1,2) and Meaghan O'Reilly (1,2)

Purpose: The blood-spinal cord barrier prevents the passage of >98% of therapeutic agents from the bloodstream to the spinal cord parenchyma. Focused ultrasound has been demonstrated to

temporarily increase blood-spinal cord barrier permeability in small animal models. The human vertebral column is irregularly shaped and has drastically different acoustic properties than the surrounding soft tissues, causing focal aberration. We envision the clinical translation of focused ultrasound to the spinal cord using a method in which treatment planning is performed using a numerical model based on patient-specific preoperative CT scans to calculate required phasing of an array to deliver controlled therapeutic exposures to the spinal cord.

Methods: A spherically focused transducer was geometrically focused to the centre of individual thoracic vertebral foramen. Sonication paths through both lamina and posterior arch were tested. Simulation pressures were compared to experiment pressures. Model accuracy was evaluated for maximum transmitted pressure, by voxel pressure, and by focal distortion.

Results: Simulation predicts maximum pressure more accurately than a vertebra-specific insertion loss. Simulation error in voxel pressure was evaluated using root-mean-square error, and was similar to error in a water-only case. Average simulation error across all measurements and simulations in maximum pressure location and weighted >50% focal volume location were 2.3mm and 1.5mm, respectively.

Conclusions: Simulation error is small relative to the dimensions of the transducer focus (4.9mm full width half maximum), the spinal cord (8-10mm diameter), and vertebral canal diameter (15-20mm diameter), suggesting that the developed simulation may be sufficiently accurate for calculating phased array aberration corrections.

ABSTRACT # 28

TITLE: SLIP PROGRESSION IN LOW-GRADE DEGENERATIVE LUMBAR SPONDYLOLISTHESIS AND SYMPTOMATIC DETERIORATION AFTER MINIMALLY INVASIVE DECOMPRESSION

Authors and Affiliations: Robert A. Ravinsky MDCM MPH FRCSC, Eric J. Crawford MD, Y. Raja Rampersaud MD FRCSC

Objective: To determine if there is a relationship between slip progression and symptomatic worsening after decompression without fusion for low-grade degenerative lumbar spondylolistheses (DLS).

Methods: Retrospective review (January 2008 to December 2016) of 1-2 level minimally invasive surgical (MIS) decompression for grade I-II DLS. Included subjects had a minimum of one year follow-up with prospectively collected baseline and follow-up Oswestry Disability Index (ODI) scores. Slip percentage was measured on baseline and follow-up radiographs using Surgimap® software.

Results: Sixty patients (35 females, 58.3%), mean age 65.7 years (standard deviations [SD]:9.83; Range: 46 - 85) met inclusion criteria. Mean length of follow-up was 1.7 years (SD: 0.4; Range: 1 - 2.4). Spondylolisthesis slip percentage increased in 56.7% (34/60) of patients. Slip percentage increased significantly ($p=0.001$) from baseline (Mean: 16.9; SD:1.02) to follow-up (Mean:19.7; SD1.2). A logistic regression model comparing stable with progressive slip percentages, identified that females were more likely to have progressive slips compared to males (Odd-ratio: 7.08, 95% CI: 2.0 – 24.8; $p=0.002$). Seventy-four percent of females (26/35) had progressive slips compared with 32% of males (8/25).

ODI scores improved in 90% (54/60) of patients. ODI scores decreased ($p<0.0001$) from baseline to follow-up, with an average decrease of 21.4 (SD: 2.4). ODI scores and spondylolisthesis slip percentage did not correlate at baseline ($p=0.45$) or follow-up ($p=0.42$), nor did change in ODI scores and change in slip percentage ($p=0.47$). Additionally, change in ODI scores were not different between those with stable slips compared to those with progressive slips at follow-up ($p=0.6$). Furthermore, of the 34 patients with slip progression, there was no difference in ODI score changes ($p=0.5$) for those with 1-5% progression (15/34) compared to those with >5% slip progression (19/34).

Conclusions: Slip progression was more likely to occur in women. Despite a small degree of slip progression in the majority of patients, there was no correlation with symptomatic worsening as measured by the ODI.

ABSTRACT # 29

TITLE: DOES UIV AFFECT RATE OF PJK IN ADULT SPINAL DEFORMITY SURGERY FUSED TO THE PELVIS?

Authors and Affiliations: Robert A. Ravinsky, Jay Toor, Sam Keshen, Colleen Magee, Stephen J. Lewis

Study Design: Retrospective cohort study

Background: The rate of proximal junctional kyphosis (PJK) is high in surgery for adult spinal deformity (ASD), especially when the fusions extend to the sacrum and pelvis. Determining the appropriate upper instrumented vertebra (UIV) can sometimes be difficult. Establishing whether rates of PJK are higher in patients with high thoracic vs lower thoracic UIV, may influence the choice of UIV in ASD.

Objectives: To assess the prevalence of PJK in ASD comparing high thoracic and low thoracic UIV in patients fused distally to the pelvis. A secondary question was to determine if rates of neurologic injury secondary to PJK vary according to high vs low thoracic spine UIV.

Methods: 143 consecutive patients who underwent surgical correction for ASD between 2007 and 2016 with thoracic to pelvis fusions were assessed. Twenty-eight patients were excluded as their imaging was unavailable due to institutional reasons. A further 8 were excluded due to the EMR containing only partial data. 106 cases were examined (average age 61.0, 80% female). Patients were grouped into high thoracic (HT) UIV (T1 to T6) or low thoracic (LT) UIV (T9 to T12). PJK was defined as UIV or UIV+1 fracture, kyphosis $>10^\circ$, or presence of a junctional disc herniation requiring surgery. Presence of PJK was determined by examining 3-foot radiographs at 1 year post-operatively.

Results: There were 61(57.5%) patients in the HT group and 45(42.4%) in the LT group. PJK occurred in 38 patients (62.5%) in the HT group compared to 12 patients (26.7%) in the LT

group (P=0.0004). PJK associated with acute neurologic injury of ASIA A,B or C occurred in two patients in the HT group and 1 patient in the LT group.

Conclusion: One-year postoperative PJK prevalence in adult spinal deformity following thoracic to pelvis fusions was higher when the UIV was in the high thoracic spine compared to the lower thoracic region. PJK with associated major neurological deficits was similar in both groups.

ABSTRACT # 30

TITLE: INTERBODY IMPACTION GRAFTING IN ADULT SPINAL DEFORMITY: 2-YEAR FUSION OUTCOMES

Authors and Affiliations: Robert A. Ravinsky, Colby Oitment, Stephen J. Lewis

Purpose: Interbody fusion is typically performed with a cage, providing a stable conduit for bone to form between adjacent vertebral endplates. In addition to being expensive, cages depend on normal endplate and disc space geometry, and host bone stock. Impaction grafting is an inexpensive alternative for achieving interbody fusion which does not rely on these factors. This paper reviews the outcomes of impaction grafting from a single institution with respect to achieving radiographic union.

Methods: The demographic, surgical and radiographic data from patients undergoing Posterior Lumbar Interbody Fusion (PLIF) were retrieved from a prospective database of surgical procedures, having taken place between January 1st, 2012 and December 31st, 2014. Disc heights were measured using lateral lumbar radiographs pre-and postoperatively and compared to measurements made with Computed Tomography (CT) scans. CT scans were used to assess resorption in the first 6 post-operative months. Both resorption and fusion were assessed between 6-18 and greater than 18 months postoperatively.

Results: 103 PLIFs were analyzed among 75 patients with a mean age of 60 (± 14.8) years. The population was predominantly female (2:1). Disc height was stable over time in all groups and

there were no differences in disc height between those that fused ($N = 42$, $\bar{x} = 10.8 \pm 2.9\text{mm}$) and those that did not ($N = 26$, $\bar{x} = 10.6 \pm 3.9\text{mm}$) ($p > 0.05$), which questions whether disc height measurement is a reliable indicator of whether fusion has occurred. CT scans showed an immediate total resorption of impaction graft bone in 10% of patients, and sub-total resorption in another 10% within the first six postoperative months. This rate of resorption increased over time to a final rate of 56% of discs showing some degree of resorption. Despite this solid interbody fusion occurred in 72% of patients and posterior inter-facet fusion occurred in 89% of patients at final follow up. Qualitatively the graft initially appears as a solid mass on XR and CT and over time follows a pattern of resorption, re-organization and remodeling to take on a spongy appearance.

Conclusions: While our total fusion rates are comparable to the literature, overall interbody fusion rates are lower than what is reported in the literature. This is partly due to subjectivity in reporting radiographic union as the fusion mass formed by impaction grafting is patchy and cancellous and different in quality and appearance from the fusion mass produced by caged constructs. This is the first study to observe the resorption period of impaction grafts which appears to increase over the first postoperative year.

ABSTRACT # 31

TITLE: VALIDATION OF A NOVEL FREEHAND TECHNIQUE FOR TRANSCORTICAL SCREWS IN THE LUMBAR SPINE

Authors and Affiliations: Zachary Tan, Joel Finkelstein

Objectives: Pedicle screw instrumentation has been the widespread standard surgical practice to achieve immediate 3-column stability of the spine. Emerging techniques of posterior spinal instrumentation have been proposed. An example of which is the cortical trajectory screw, which requires a more medialized start point and follows an “up and out” orientation. Previous

cadaveric and virtual modelling studies demonstrate improved biomechanical properties compared to the traditional pedicle screw placement (Perez-Orribo et al, 2013). A potential limitation of the cortical trajectory technique is the potential reliance on image guidance by fluoroscopy or navigation. This study validates an intuitive freehand technique for insertion of cortical trajectory screws in the lumbar and thoracic spine.

Methods: The open source 3D-Slicer software (Version 4.5.0-2016-07-06) with the PedicleScrewSimulatorV4 module and volume rendering of 10 non-pathologic and 10 degenerative lumbar spine CTs were used. The startpoint and trajectory determination was modified as required from those previously published. (Santonin et al, 2009). Identifiable and reproducible anatomic landmarks of the posterior spine were selected and used to place the screws in the safe corridor and idealized trajectory. The surface landmarks catalogued and are proposed to facilitate freehand startpoints and trajectories.

Results: The proposed startpoints and trajectories have been assessed for 10 different thoracolumbar CTs without evidence of medial, inferior or lateral (unless intended for bicortical fixation) breaches. The screw length ranges between 20-25mm. Medial-lateral and cranial-caudal start point and trajectories were variable dependant on the spinal level a) L1-L4; b) L5.

Conclusions: The use of cortical trajectory screw fixation in the lumbar spine has the benefit of a less dissection required allowing for a more minimally invasive approach. There are biomechanical benefits in the osteoporotic spine. A better understanding of the prescribed starting points and trajectories may facilitate this approach and allow wider use.

ABSTRACT # 32

TITLE: OPTICAL TOPOGRAPHIC IMAGING FOR INTRA-OPERATIVE THREE-DIMENSIONAL NAVIGATION IN MINI-OPEN APPROACHES: INITIAL PRE-CLINICAL AND CLINICAL FEASIBILITY

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Purpose: Computer-assisted three-dimensional navigation may guide spinal instrumentation. A novel optical topographic imaging (OTI) system, developed in our laboratory, offers comparable accuracy and significantly faster registration relative to current navigation systems, in open posterior thoracolumbar exposures. Here, we explore the utility of OTI in minimally-invasive (MIS) spinal approaches.

Method: Mini-open midline posterior exposures were performed in four human cadavers. Square exposures of size 25, 30, 35, and 40mm were registered to a preoperative CT scan. Screw tracts were fashioned using a tracked awl and probe, and instrumentation placed. Navigation data were compared to screw positions on postoperative CT imaging, and absolute translational and angular deviations computed.

In-vivo validation was performed in eight patients, with mini-open thoracolumbar exposures and percutaneous placement of navigated instrumentation.

Results: For 37 cadaveric screws, absolute translational errors were (1.79±1.43mm) and (1.81±1.51mm) in the axial and sagittal planes, respectively; absolute angular deviations were (3.81±2.91°) and (3.45±2.82°), respectively (mean±SD). Errors were similar across levels and screw types. The number of surface points registered by the navigation system, but not exposure size, correlated positively with the likelihood of successful registration (OR=1.02, 95%-CI 1.009-1.024, p<0.0001).

55 in-vivo thoracolumbar pedicle screws were analyzed. Overall (mean±SD) axial and sagittal translational errors were (1.79±1.41 mm) and (2.68±2.26 mm), while axial and sagittal angular

errors were ($3.63 \pm 2.92^\circ$) and ($4.65 \pm 3.36^\circ$), respectively. There were no critical radiographic breaches, nor any neurovascular complications from any placed screws.

Conclusions: OTI is a novel navigation technique previously validated for open posterior exposures, which has comparable accuracy for mini-open MIS exposures. The likelihood of successful registration is affected more by the geometry of the exposure than its size.

ABSTRACT # 33

TITLE: QUANTIFICATION OF COMPUTATIONAL GEOMETRIC CONGRUENCE IN SURFACE-BASED REGISTRATION FOR SPINAL INTRA-OPERATIVE THREE-DIMENSIONAL NAVIGATION

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Purpose: Computer-assisted navigation (CAN) may guide spinal instrumentation, and requires alignment of patient anatomy to imaging. Iterative-Closest-Point algorithms register anatomical and imaging datasets, which may fail in the presence of significant geometric symmetry (congruence), leading to failed registration or inaccurate navigation. We computationally quantify geometric congruence in posterior spinal exposures, and identify predictors of potential navigation inaccuracy.

Method: Midline posterior exposures were performed from C1-S1 in four human cadavers. An optically-based CAN generated surface maps of the posterior elements at each level. Maps were reconstructed to include bilateral hemilamina, or unilateral hemilamina with/without the base of the spinous process. Maps were fitted to symmetrical geometries (cylindrical/spherical/planar)

using computational modelling, and the degree of model fit quantified based on the ratio of model inliers to total points.

Geometric congruence in a clinical setting was assessed similarly, in 11 patients undergoing midline exposures in the cervical/thoracic/lumbar spine for posterior instrumented fusion.

Results: In cadaveric testing, increased cylindrical/spherical/planar symmetry was seen in the subaxial cervical spine relative to the high-cervical and thoracolumbar spine ($p < 0.001$). Inclusion of the base of the spinous process decreased symmetry independent of spinal level ($p < 0.001$). Registration with bilateral vs. unilateral hemilamina did not significantly reduce geometric symmetry.

In clinical testing, increased cylindrical/spherical/planar symmetry was again seen in the subaxial cervical spine relative to the thoracolumbar spine ($p < 0.001$), and in the thoracic spine relative to the lumbar spine ($p < 0.001$). Symmetry in all geometries was decreased by 20% with inclusion of the base of the spinous process vs. without.

Conclusions: Geometric congruence is most evident at C1 and the subaxial cervical spine, warranting greater vigilance in navigation accuracy verification. At all levels, inclusion of the base of the spinous process in unilateral registration decreases the likelihood of geometric symmetry and navigation error, important for minimally-invasive unilateral approaches.

ABSTRACT # 34

TITLE: QUANTITATIVE MRI OF THE CERVICAL SPINAL CORD TO MEASURE MICROSTRUCTURE AND TISSUE INTEGRITY

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Purpose: Conventional MRI imaging only provides limited information about the structure and integrity of the spinal cord. We describe a multi-parametric quantitative MRI (qMRI) protocol for microstructure analysis of the spinal cord to determine the precise degree of injury to the spine in the setting of degenerative cervical myelopathy (DCM) as well as traumatic spinal cord injury. Our goal is to identify better techniques for diagnoses and quantification of neurological injury and accurately predict outcomes.

Method: 40 healthy controls and 58 DCM patients have so far been studied. Each patient underwent a battery of clinical assessments including mJOA, ISNCSCI, QuickDASH, GRASSP-M and GaitRITE followed by MRI acquisitions using our protocol in a 3T GE clinical scanner. The multi-parametric protocol combines MRI techniques including conventional MRI, Diffusion tensor imaging (DTI), fractional anisotropy (FA), Magnetization transfer (MTR), T2*WI. Image analysis is done using the Spinal Cord Toolbox (SCT) v.3.0.

Results: Study of healthy subjects identifies an alarming rate of asymptomatic spinal cord compression. 10 measures of tissue injury were identified to create a model, providing good diagnostic accuracy (AUC=95.4%) and correlation with disability measures such as mJOA (R2=0.59). Longitudinal study of DCM patients correlates qMRI findings with clinical assessment and suggest mJOA underestimates progression.

Conclusions: We have established a reliable, clinically feasible qMRI protocol that can be used for diagnosis, detection of subclinical tissue injury and can be potentially be use for prediction of outcomes in DCM.

ABSTRACT # 35

TITLE: Clinical Prediction Model for Determining Patient Discharge Destination Post Posterior Thoracolumbar Spinal Fusion Procedures. A Study of the Canadian Spine Outcomes and Research Network (CSORN)

Authors and Affiliations: Fan Jiang, Greg McIntosh, Mayilee Canizares, Michael H Weber, Raja Rampersaud

Purpose: Post-operative difficulty with patient's discharge after spinal procedures may lead to prolonged hospitalization and reduce the capacity within the healthcare system. Preoperative prediction of discharge destination could have significant impact allowing discharge planning by perioperative interprofessional surgical teams. The objective of this study was to create a prediction model to determine the probability of being discharged home after thoracolumbar posterior spinal fusion.

Method: A retrospective analysis of patients who underwent posterior thoracolumbar fusion between 2008 and 2017 using the multicentre prospectively collected data from the CSORN database (n=1,988). Multivariable logistic regression was used to identify predictors of patient discharge destinations: home versus other facilities using a backward selection procedure. A data-splitting technique was utilized to develop and test the multivariable models.

Results: Regression analyses identified nine significant pre-operative predictors of discharge home: age <66 years (odds ratio [OR]=1.886); not living alone (OR=2.339); ODI score <40 (OR=3.595); diagnosis spondylolisthesis (OR=2.071); MIS procedure (OR=4.677); and levels of fusion >1 (OR=3.86). The final model was internally validated and confirmed the same predictors. ROC curve analysis revealed area under the curve of 0.813. A final clinical prediction rule is represented by the following equation: $\text{Log}(\text{odds of success}) = 0.427 + 1.543(\text{MIS}) + 1.351(\text{Level}=1) + 0.85(\text{Living not alone}) + 0.634(\text{Age}<66) + 1.279(\text{ODI score } <40) + 0.728(\text{Diagnosis of spondylolisthesis})$.

Conclusions: Using the CSORN registry, we constructed a highly sensitive preoperative prediction rule to determine post operative discharge destination following posterior thoracolumbar instrumented fusion.

ABSTRACT # 36

TITLE: The Characteristics of Acute Complications after Traumatic Spinal Cord Injury and the Relation to Long-term Neurological and Functional Outcome

Authors and Affiliations: Fan Jiang, Blessing N.R. Jaja, Michael G. Fehlings, Jefferson Wilson.

Purpose: Traumatic spinal cord injury (SCI) can cause devastating neurological consequences to patients and poses as a burden to healthcare system. Although previous studies have identified complications related to SCI, there is a paucity of prospective multicenter series on the spectrum of complications and their impact on long term neurological and functional recoveries. The objective of this study is to assess the incidence of acute complications after traumatic SCI in the NACTN cohort, and to describe the relation to long-term neurological and functional outcomes.

Method: Total of 801 patients were included from the NACTN database. Negative binomial regression and penalized maximum logistic regression models were fitted to study factors associated with higher incidence of complications and to estimate the likelihood of neurological (AIS improvement >1 point) and functional outcomes according to the Spinal Cord Independence Measure (SCIM) sub-scores for respiration, indoor mobility, bladder and bowel sphincter management 6-months after the injury.

Results: The most frequent complications found in this study were: pneumonia (218 occurrences), respiratory failure (207), anemia (197), and UTI (139). The development of at least one complication was significantly associated with requirement for assistance with breathing (OR=6.29), aid for ambulation (OR=3.43), and support with bladder (OR=4.71) or bowel (OR=3.35) sphincter management at 6-month follow up. However, no difference was noted in the rates of AIS grade improvement of 1 or more points at 6-month.

Conclusions: Complications after SCI are very common, this study contributed to the increasing evidence that acute complications can impact long term functional outcomes.