Intra-arterial Encephalography from Acutely Implanted Aneurysm Embolization (WEB) Device in Awake Humans

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Introduction: Endovascular electroencephalography (evEEG) utilizes the cerebrovascular system as a minimally-invasive conduit to record electrical activity from adjacent neural structures, mitigating the poor spatial resolution and risks of open craniotomy associated with extracranial EEG and electrocorticography, respectively. The safety, feasibility, and efficacy using the Woven Endobridge (WEB) intracranial aneurysm embolization device for evEEG has yet to be investigated in humans.

Methods: Fifteen patients undergoing awake endovascular treatment of unruptured cerebral aneurysms via WEB device were included. The WEB Device, composed of nitinol with a platinum core, served as a single-electrode intravascular contact by connecting its distal deployment wire to an EEG receiver. After deployment into the aneurysm and before detachment during awake surgery, subjects were presented with a value-based decision-making task for 10 minutes while endovascular WEB recordings were captured and referenced with scalp electrodes. All recordings were completed within the standard 10-minute monitoring period to ensure stable WEB positioning, stagnation of contrast inside the aneurysm sac, and adequate flow through the afferent and efferent arteries. Therefore, OR time was not extended for research participation nor was any additional surgical risk introduced to the participants.

Results: All patients underwent successful embolization and evEEG recording with no complications. Event-related potentials (ERP) were detected on scalp EEG in 6/15 (40%) patients. Of these 6 patients, low-gamma (30-70Hz) response on WEB channels was captured in 4/6 (75%) cases. In these 4 patients, the WEB device was deployed into the anterior communicating artery, basilar tip, and two middle cerebral artery aneurysms. EKG artifact on WEB channels was present in 11/15 cases.

Conclusion: Placement of an implantable WEB device within the cerebral aneurysms of awake subjects is capable of capturing task-specific electrical brain activities. Future studies are warranted to further establish safety, efficacy, and support for evEEG as a potential tool for neural recording, deep brain stimulation, and brain-machine-interface.
Neuroprotective Effect of Steroid Receptor Coactivator Stimulator (MCB-613) in a Murine Ischemic Stroke Model

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Introduction: Stroke is the leading cause of disability and death worldwide. Currently, thrombolysis and thrombectomy are the gold standard for acute interventions; however, these strategies have a limited treatment window and effect. Neuroprotection in stroke is a strategy to reduce neurologic injury secondary to ischemia and extend the window of salvageable brain. On potential candidate is MCB-613, a small molecule stimulator of steroid receptor coactivators that is implicated in cellular regeneration, immune cell modulation, and angiogenesis, that is being newly studied in tissue repair after injury.

Methods: We conducted a middle artery occlusion model in 20 rats, randomly assigned to intraperitoneal injection with MCB-613 or vehicle after 30 minutes following reperfusion. After 24 hours, rats were scored for behavior using the Bederson score. Afterwards, they were immediately perfused, and brains were removed and cut. The brain slices were then fixed and stained with 2,3,5-triphenyltetrazolium chloride to visualize infarction volume. Immunohistochemical analysis was also done to look at the extent of neuronal apoptosis and immune cell infiltration.

Results: The MCB-613 group showed a 50% reduction in infarct volume, compared with the vehicle only group (0.5 vs 0.21, p = 0.001). In addition, behavior scores were significantly improved in the treatment group (Bederson score 3.8 versus 1.8, p = 0.01). On close examination of the penumbra, neuronal apoptosis was decreased in the treatment group, as were microglia and neutrophil infiltration.

Conclusion: In the early experiments using a rat MCAO model, MCB-613 has shown to reduce infarct volume by 50% and persevere neurologic function 24 hours after stroke and reperfusion. This process seems to be mediated by a decrease in neuronal apoptosis in the penumbra and decreased immune cell infiltration. Further studies are currently underway to study the treatment effect over a longer period of time and further delineate a molecular mechanism with whole transcriptome analysis.
102: Analysis of Spinal Canal Diameter in the Placement of Thoracic Spinal Cord Stimulator (SCS) Paddle Leads

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Introduction: Neurologic deficit is a rare complication of thoracic spinal cord stimulator (SCS) paddle lead implantation. Interestingly, multiple authors believe the incidence of neurologic complications after SCS paddle lead placement is under-reported. This study looked at imaging characteristics to help predict safe paddle lead placement.

Methods: Patients undergoing thoracic laminectomy for new SCS paddle lead placement were identified from January 2018 to October 2021. Preoperative thoracic canal diameter was measured in the sagittal plane perpendicular to the disc space from T5/6 to T11/12. These thoracic levels were chosen because they span the most common levels targeted for SCS placement. Comparison of patients with and without new neurologic deficit was performed using an unpaired Student’s t-test (Prism 9, GraphPad Software).

Results: One-hundred and seven of 112 patients initially identified had thoracic imaging available for review. Two of 112 (2%) patients complained of transient neurologic deficit after thoracic SCS placement. Both patients had SCS paddle lead placement at T8/9 and single-level laminectomy for placement and average canal diameter <12 mm. The average canal diameter of patients with and without neurologic deficit was 10.1 mm (range 6.1 – 12.3 mm) and 12.3 mm (range 6.9 – 19.0), respectively (P < 0.0001).

Conclusion: Postoperative neurologic deficit is a rare complication after thoracic laminectomy for SCS paddle lead placement. The authors recommend ensuring a thoracic canal diameter of at least 12 mm to accommodate a SCS paddle lead measuring 2 mm thick. If canal diameter is <12 mm, aggressive undercutting of the lamina or a second laminectomy should be considered.
103: Case Series: Postoperative Radiculopathy After Spinal Cord Stimulator Placement

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Introduction: Spinal cord stimulators (SCS) have been used to treat various refractory chronic pain conditions, such as complex regional pain syndrome and failed back surgery syndrome (FBSS). While SCS is effective in the treatment of chronic neuropathic pain, they are not without complications. We investigated the rate of post-operative radiculopathy of any kind following SCS placement in a series of 196 patients.

Methods: We found 196 consecutive patients treated for chronic back pain or FBSS using SCS between 2013 and 2019. All patients underwent laminotomy and placement of paddle type SCS lead over the thoracic or cervical spinal cord. Patients who developed radiculopathy or other postoperative complications were identified with a retrospective chart review based on follow-up clinic notes.

Results: In this case series, 167 patients reported improved chronic pain symptoms (88.8% improvement, eight patients lost to follow-up). The rate of post-op thoracic radiculopathy was 4.3% (8 patients out of 188). Of those patients, three required revision or removal of the SCS, 2 had gradual resolution of symptoms several weeks post-operatively with conservative medical management alone, and two were lost to follow-up.

Conclusion: Postoperative radiculopathy is a rare but distressing complication following SCS implantation for refractory chronic back pain. While some patients require surgical correction to alleviate the radiculopathy, others can be managed medically until the radiculopathy resolves.
104: Whole Exome Sequencing and Integrative Multi-omics Approach Identify Biological Mechanisms and Critical Spatiotemporal Points Related to Neurodevelopmental Symptoms of Craniosynostosis

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Introduction: Craniosynostosis (CS) is the most common cranial birth defect, occurring one in every 2,000 live births. Many children with CS experience neurocognitive deficits despite optimal surgical management. Recent advances in understanding the genetic causes of CS have identified risk genes and pathways, however the etiology of the neurodevelopmental delays seen in those with CS remains unclear.

Methods: We analyzed whole exome sequencing data from 404 trios with non-syndromic craniosynostosis to identify additional novel causes of the condition, while concurrently using whole-brain transcriptomics to construct a spatiotemporal model of gene expression in the developing brain. Single-cell RNA-seq data from embryonic mouse meninges and developmental human whole-brain were used to identify cell populations significantly expressing CS genes.

Results: We identify strong enrichment for genes mutated in craniosynostosis in the ganglionic eminence during mid-fetal development (post-conception weeks 8-21) affecting astrocytes, dura fibroblasts, oligodendrocytes and parvalbumin-positive inhibitory neurons. These genes are implicated in osteoblast differentiation, neural stem cell differentiation and epigenetic regulation, suggesting that the genetic mutations that cause craniosynostosis concurrently impact neurogenesis. Moreover, we find that CS-enriched gene co-expression modules and cell types are also enriched with autism and neurodevelopmental disorder genes. Formal neurodevelopmental assessment of 56 children with craniosynostosis with matched exome sequencing data show that damaging mutations in highly constrained genes correlate with poor neurodevelopmental outcomes, irrespective of the surgery performed to treat the patient.

Conclusion: This data suggests that neurodevelopmental outcomes in CS are largely intrinsic to the underlying mutations causing craniosynostosis, and are likely independent of the specific clinical management chosen.
105: Is Cranial Ultrasound Prognostic Beyond the Papile Grade? A Volumetric Analysis of Germinal Matrix Hemorrhage-intraventricular Hemorrhage

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Introduction: High-grade (grade III/IV) germinal matrix hemorrhage-intraventricular hemorrhage (GMH-IVH) is associated with lifelong complications including hydrocephalus and poor neurodevelopmental outcomes. Early prognostic radiologic markers are unknown. We sought to determine whether volumetric measurements of hemorrhage and ventricular size on early cranial ultrasound (CUS) in high-grade GMH-IVH are associated with hydrocephalus and neurodevelopmental outcome at 2 years.

Methods: This was a retrospective cohort study of prospectively recruited infants with grade III and/or IV GMH-IVH admitted to St. Louis Children’s Hospital Neonatal Intensive Care Unit between 2007 and 2015. All patients underwent formal neurocognitive testing at 2 years corrected age using the Bayley Scales of Infant and Toddler Development, 3rd edition (Bayley-III). Patients with missing/incomplete Bayley-III scores or unviewable CUS images were excluded. A single physician blinded to outcome performed CUS measurements of GMH volume, periventricular hemorrhagic infarction (PVHI) volume, and fronto-temporal horn ratio.

Results: 58 infants with high-grade GMH-IVH were identified on the existing database and 43 infants (14 females, mean 25.0 weeks estimated gestational age) met inclusion criteria. Highest grade GMH-IVH was noted, on average, on day of life 6.9. Larger left-sided GMH volumes were associated with worse Bayley-III composite cognition scores (p=0.0103) and the eventual need for shunt placement (OR 2.25, 95% CI 1.27-5.33, p=0.0171) even after controlling for IVH volume. Larger left and right-sided PVHI volumes were associated with worse Bayley-III composite motor scores (p=0.0422 and p=0.0395, respectively).

Conclusion: Larger left-sided GMH volume was associated with worse cognitive outcomes and need for shunt placement. Larger PVHI volume, regardless of laterality, was associated with poor motor outcomes. Location-specific hemorrhage volumes on postnatal CUS, particularly in progenitor-rich regions of the developing brain, may offer prognostic information in high-grade GMH-IVH with implications for cognitive outcome and hydrocephalus development.
106: Resection of the Fusiform Gyrus Predicts Decline in Object Naming

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Introduction: Temporal lobe resections often result in significant confrontation naming decline. However, the precise substrates responsible for these deficits are not known, and a clear understanding of the most critical constituents might influence surgical strategies to minimize language declines. We used multivariate voxel-based lesion symptom mapping (VLSM) to relate changes in language function, measured using the Boston Naming Test, to dominant temporal lobe resections.

Methods: Data were obtained from 95 patients who underwent surgical resection in the dominant left temporal lobe for epilepsy. Patients underwent neuropsychological testing and MRI prior to and following surgery. Lesion masks were traced on postoperative MRIs and aligned to standard MNI space. The effects of preoperative scores were removed from postoperative scores via linear regression. VLSM was performed using multivariate support vector regression. A surface-based mixed-effects multilevel analysis (SB-MEMA) was used to estimate group-level broadband gamma activity during picture naming across a subset of patients with ECoG recordings, and results were integrated with VLSM.

Results: VLSM analysis revealed that loss of the posterior ventral temporal cortex was significantly associated with a decline on BNT. We also found that the posterior margin of ATL resections was linearly correlated to a decline in BNT performance with a clinically significant decline occurring once the resection extended 6 cm from the anterior tip of the temporal lobe. ECoG analysis showed a significant increase in activity in the middle fusiform gyrus (mFus) preceding articulation. The thresholded SB-MEMA map overlapped with 75% of the significant cluster from VLSM.

Conclusion: The importance of the ventral temporal cortex in lexical access is shown using multivariate VLSM and ECoG. While it was previously assumed that mFus lesions do not cause pervasive impairment, our data support the role of the mFus as a critical semantic access hub. Surgical approaches in temporal lobe epilepsy should strive to preserve the mFus.
107: Epidural Stimulation Restores Muscle Synergies by Modulating Neural Drives in Complete Spinal Cord Injured Patients

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Introduction: Approximately 50,000 people in the United States with spinal cord injury (SCI) are ASIA A. The ESTAND study has demonstrated restoration of volitional control with epidural spinal stimulation over time in this subset of patients. In the initial study, the amplitude of muscle movement improved in the first few weeks, but then decreased. In a nested study, we measured neuromuscular control during these changes from ballistic movements to more refined control, using muscle synergy and complexity analysis over time.

Methods: Results from six motor/sensory complete SCI participants and nine healthy control participants are reported. Surface EMG (sEMG) from 10 muscle groups bilaterally are recorded while subjects perform a set of tasks with and without stimulation. The analysis of complexity (Higuchi Fractal Dimensional analysis) is then performed on the sEMGs. The muscle synergies from sEMG are extracted using non-negative matrix factorization algorithm to measure changes in neuromuscular control. From the sEMG data, motor neuron activity is also estimated in the rostral-caudal plane of the spinal cord.

Results: The resulting analysis shows that complexity of muscle activity is reduced in the SCI participants when SCS is turned on compared to when stimulation is off. Muscle synergy structure improved and the number of synergies decreased, indicating improved muscle coordination over time. By the final stimulation session, SCI participants on average were able to achieve the same number of muscle synergies observed in the control participants.

Conclusion: This study provides support for the origins of synergies being the neural hypothesis instead of the task based, whereby a patient can perform the same task while their neural control is modulated independently with SCS. Overall, this study shows that long term use of epidural stimulation generates neural plasticity in the spinal circuitry that leads to improved motor control as reflected via changes in muscle synergies.
108: Quantifying the Need for Emergency Neurosurgical Intervention Around the World

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Introduction: EVD placement is one of the mainstay therapies for the management of elevated intracranial pressure. Indications include traumatic brain injury, hydrocephalus, meningitis, and various other pathologies. While there is a marked paucity of neurosurgical care globally, the number of patients who require an EVD are frequently found in low-middle income areas. For this reason, we seek to quantify the need for EVD placement globally to determine regions that would benefit from technological advancement in the domain.

Methods: Worldwide distribution of neurosurgeons with the incidence of indication for EVD (TBI, meningitis, and hydrocephalus) were compiled from the World Neurosurgery Workforce in 20161-3. The aggregated values were scaled from 0 to 1 relative to their minimum and maximum. A model was constructed with neurosurgeon distribution comprising 60% of the model, and indications for EVD comprising 40% of the model. Indication scores were computed using this model and visually represented using the rworldmap package in R.

Results: Our global analysis found Montenegro, with an indication score of 0.776, Equatorial Guinea, with an indication score of 0.709, and the Bahamas with an indication score of 0.708 to be the top three targets for improved access to neurosurgical care based on the low numbers of practicing neurosurgeons and high indications for neurosurgical treatment. The generated world map in Figure 1 shows the comparative analysis of neurosurgical need for different countries, with darker regions indicating a higher need for neurosurgical access due to more indications for treatment.

Conclusion: Emergencies require neurosurgical access within hours of the inciting event, resulting in major burden to regions with high incidence of neurosurgical emergencies such as severe TBI. Our analysis shows that targeting select regions for deployment of neurosurgical resources and development of new neurosurgical technology for guided EVD placement may reduce the global burden of emergency neurological conditions.
109: The Impact of a Problem-based Note Template on Neurosurgical Quality Metrics

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Introduction: To date, little work has focused on how note templates can affect quality metrics in neurosurgery. Here, we investigate how switching from an inpatient system-based note template to a problem-based note template affects the mortality index and case mix index of a neurosurgery service line.

Methods: On a neurosurgery service line at an urban, level I trauma, academic teaching hospital, an intervention was made to change the history and physical and progress note templates from system-based to problem-based. Data comparing the monthly case mix index and mortality index was collected for the twelve months preceding intervention and the four months following intervention. The data was statistically analyzed utilizing a t-test, with a significance level of $p \leq 0.05$.

Results: The monthly case mix index average rose from 4.56 in the 12 months preintervention to 4.90 in the four months after intervention, representing a significant change ($p = 0.033$). The monthly mortality index average fell from 1.16 in the 12 months preintervention to 0.72 in the four months following intervention, also representing a statistically significant change ($p = 0.048$).

Conclusion: Switching from a system-based to a problem-based charting system on a neurosurgery service line at an urban, level I trauma, academic teaching hospital led to a statistically significant increase in the case mix index and a statistically significant decrease in the mortality index. Given the implications of these findings in an era of value based care, further research is warranted on the relationship between charting and quality outcomes within neurosurgery.
110: Hounsfield Unit as a Predictor of Adjacent Level Disease in Interbody Fusion Surgery

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Introduction: Standardized “Enhanced Recovery After Surgery” (ERAS) protocols have been implemented across the medical field in an attempt to improve perioperative outcomes. Multimodal analgesic regimens utilizing acetaminophen and gabapentin are critical to ERAS protocols and have been proposed as a method of effectively controlling postoperative pain while simultaneously reducing opioid requirements, however, studies in neurosurgical cohorts are scarce. This study aims to investigate the impact of preoperative analgesic medications on postoperative opioid use and outpatient opioid refill rates following neurosurgical interventions.

Methods: Utilizing a large retrospective dataset of 8704 opioid-naïve adult patients who underwent a neurosurgical intervention at a quaternary care institute, preoperative and perioperative analgesic use was obtained through chart review. Standardized oral morphine equivalents (OMEs) were used to compare inpatient and outpatient opioid requirements and physicians were made aware of individual opioid requirements. The efficacy of the outpatient discharge opioid prescription was assessed with regard to opioid refills. Multivariate analysis was conducted to identify predictors of opioid refills.

Results: Of the 8704 opioid-naïve neurosurgical patients included in this cohort, 2768 (32%) patients used preoperative gabapentinoids or benzodiazepines. Patients who used preoperative gabapentinoids required higher doses of opioids in both the inpatient and outpatient settings (p < 0.001). Preoperative gabapentinoid (OR=2.4; 95% CI 2.1-2.7) and benzodiazepine (OR=1.4; 95% CI 1.2-1.6) use was associated with increased risk of opioid refills in the outpatient setting.

Conclusion: Despite current efforts to incorporate non-opioid analgesic medications into ERAS protocols, this study demonstrates that, even in opioid-naïve patients, consumption of non-opioid analgesics results in higher opioid use in the acute postoperative period. This warrants further study into the impact of preoperative non-opioid analgesic use on postoperative opioid medication requirements in the acute and chronic periods following neurosurgical interventions.
111: Functional Outcomes After Surgery for Grade 1 Lumbar Spondylolisthesis: A 5-year QOD Study

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Introduction: Large, long-term studies of functional outcomes after decompression or fusion for degenerative lumbar spondylolisthesis are lacking.

Methods: The Quality Outcomes Database was queried for patients over age 18 who underwent surgery for single-level grade 1 lumbar spondylolisthesis. The Oswestry Disability Index (ODI) was assessed preoperatively and at 3, 12, 24, 36, and 60 months postoperatively.

Results: The query returned 608 patients. Mean age (95% CI) was 62.2 (61.2-63.1) years, and 42.4% were male. Decompression only was performed in 23% and decompression with fusion in 77%. Mean ODI (95% CI) at baseline, 3 months, 12 months, 24 months, 36 months, and 60 months were 46.7 (45.3-48.1) (n=602), 26.3 (24.7-28) (n=532), 22.1 (20.3-23.9) (n=473), 22.4 (20.6-24.2) (n=453), 21.9 (18.6-25.1) (n=145), and 23.7 (21.8-25.5) (n=433). Significant improvement in mean ODI from baseline was observed at all time points (p<0.0001). In the decompression-only group, mean ODI improvements (95% CI) at 3, 12, 24, 36, and 60 months were 16.4 (13.1-19.7) (n=126), 18.3 (14.3-22.3) (n=106), 15.8 (12-19.6) (n=106), 14 (6-22) (n=21), and 18.8 (14-23.6) (n=88). In the decompression and fusion group, mean ODI improvements (95% CI) at 3, 12, 24, 36, and 60 months were 21.6 (19.7-23.5) (n=406), 26.1 (24.1-28) (n=367), 25.2 (23.1-27.4) (n=346), 27.3 (23.9-30.7) (n=122), and 22.7 (20.5-24.9) (n=341). Utilizing multivariate linear regression, fusion was independently associated with greater ODI improvement at 3, 12, 24, and 36 months (p<0.05) but not 60 months (p=0.07). Three-year reoperation rate was 7.1% overall and similar between decompression-only and decompression plus fusion groups (9.4% vs 6.4%, p>0.05).

Conclusion: In this large study with 60 months or longer follow-up after surgery for single-level grade 1 lumbar spondylolisthesis, patients experienced significant and sustained improvements in function. Addition of fusion to decompression was associated with greater improvements in function through 36 months. Rate of reoperation was low and similar between the two groups.
112: Surgical Management of Spinal Nerve Schwannoma of the Sacrum: A Retrospective Study and Literature Review

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Introduction: Sacral schwannomas are rare and account for a minority of spinal schwannomas. The aim of our study is to present our institution’s experience treating sacral schwannomas surgically between the years 1997 and 2018. In addition, we assess the literature for surgical cases of sacral schwannomas in order to demonstrate tumor characteristics and outcomes following surgical resection.

Methods: Through our retrospective review of patients with sacral schwannoma at our institution, we report our findings on the epidemiology of sacral schwannomas, their presentation, various treatment options, and patient outcomes. These findings were compared to those in the literature.

Results: Data on demographics, symptoms, lesion characteristics, surgical management, and outcomes were collected for 28 patients treated surgically for sacral schwannoma between 1997 and 2018 at Mayo Clinic. Thirty-one studies involving patients with sacral schwannoma treated surgically were found in the literature. Mayo Clinic patients compared to those in the literature experienced similar age at diagnosis and symptoms, with the most common symptom being pain and the least common being sexual dysfunction in both cohorts.

Conclusion: Patients with sacral schwannomas, uncommon tumors of the spine, may experience variable outcomes based on a variety of factors including demographics, tumor characteristics, symptoms, and surgical treatment. Prognosis improves when the surgical approach towards sacral schwannomas is prepared and executed appropriately.
113: The Impact of Nerve Reconstruction on Long-term Shoulder and Elbow Function in Neonatal Brachial Plexus Palsy

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Introduction: Timing and indications for surgical intervention for neonatal brachial plexus palsy (NBPP) remain controversial, likely contributing to underutilization in this population. Employment of nerve reconstruction is approximately 10-fold less than ideal, as evidenced by the 30-40% of unoperated patients who have significant lifelong disablements. Here, we interrogate a large dataset of NBPP patients to illustrate the effectiveness of nerve reconstruction for recovery of shoulder and elbow function as compared to natural history of NBPP patients managed non-surgically.

Methods: All patients seen at a single tertiary referral center for NBPP from 2005-2020 were included in the database. Exclusion criteria included patients initially seen after 2 yo or only seen for only 1 appointment. AROM for shoulder abduction, exorotation, and elbow flexion was collected at each clinic visit by 1 of 2 program occupational therapists. AROM values were normalized between 0 and 1 and plotted against patient age and a logistic regression fit to the data using open-source packages from Python Seaborn.

Results: 325 non-operative and 100 operative children were included in the analysis, and we demonstrate the rate of recovery of shoulder and elbow AROM over 5000 days (mean follow-up of 1777 and 1353 days for non-operative and operative children, respectively). We observed parallel rates of recovery (slope of curves) for shoulder abduction in the operative versus non-operative children, but the absolute recovery was less for the operative patients. In contrast, for elbow flexion and shoulder exorotation, the operative patients demonstrated much higher rates of recovery for the operative group versus the non-operative group, and the absolute recovery at 5000 days was the same for both groups.

Conclusion: Fuller understanding of the long-term rates of functional recovery with and without surgery can guide surgeons and physiatrists / therapists towards the appropriate timing and indications for nerve reconstruction to improve outcomes for children with NBPP.
114: Effects of Hours of Sleep on Immediate Post-concussion Assessment & Cognitive Testing (ImPACT): Comparing Baseline to 1st Concussion Performance

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Introduction: The influence of sleep duration on baseline and post-concussion neurocognitive performance prior to Immediate Post-Concussion Assessment & Cognitive Testing (ImPACT) is poorly understood. Since the ImPACT test is widely used in adolescent athletics for assessing the presence of concussion, it is important to research the multiple factors that affect testing performance. While some research reports correlations between fewer hours of sleep and lower scores on baseline tests, others have not observed any such associations and have not compared baseline scores directly to post-concussion ImPACT tests based on hours of sleep.

Methods: We queried a database of 11564 ImPACT tests taken from 2009-2019 with athletes aged 12-22. There were 11564 baseline concussion tests and 7446 post-1st concussion ImPACT tests. Linear regression was used to model the effect of sleep on baseline and post-concussion ImPACT scores adjusting for sex, age, learning disability, ADD/ADHD, number of prior concussions/loss of consciousness concussions, number of games missed, and strenuous exercise before testing.

Results: In baseline testing, there was no relationship between hours of sleep the night prior to the ImPACT test and scores on any of the composite measures. Post-1st concussion, hours of sleep was significantly associated with changes in composite measures in Verbal Memory (0.51 point increase/hour, 95%CI: 0.26-0.77, p<0.0001), Visual Memory (0.36 point increase/hour, 95%CI: 0.10-0.63, p=0.0078), and Impulse Control (0.25 point decrease/hour, 95%CI: -0.37 to -0.12, p=0.0001). Hours of sleep were not significantly correlated with Reaction time or Visual Motor Scores.

Conclusion: Hours of sleep did not alter neurocognitive metrics at baseline but did have an impact on the 1st post-concussion test. These findings suggest that individuals may compensate for lack of sleep at baseline but not after concussions. Concussions may reduce cognitive reserve or detract from the brain’s resources making sleep even more important for proper neurocognitive functioning post-concussion. Future work will analyze the effects of sleep on test performance after multiple concussions.
115: Presentation, Treatment and Outcome of Traumatic Dural Venous Sinus Thrombosis

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Introduction: Dural venous sinus thrombosis (dVST) is a cause of stroke and raised ICP. Anticoagulation treatment is indicated to prevent propagation of thrombus and promote recanalization. Following traumatic brain injury (TBI), with the widespread use of vascular imaging such as CT venography (CTV), traumatic dVSTs are increasingly diagnosed although the natural history, management and outcomes remain unclear.

Methods: We performed a 5-year, single-center retrospective review of acute TBI patients diagnosed with traumatic dVST at a Level I trauma center. Demographic and clinical features were examined.

Results: From 2016 – 2020, 118 patients were diagnosed with traumatic dVST. The mean age was 38, with 76% male. The commonest mechanisms of injury were fall from height (32%), vehicular accident (20%) and ground level fall (16%). The mean presenting GCS was 11/15 with 28% of patients intubated. Skull fractures were present in 98% with 52% extended to the skullbase. Common sites of traumatic dVST were transverse (48%) and sigmoid (26%) sinuses, and in 96%, skull fracture crossed the injured sinus. In 50 patients with adequate follow-up, 26 received treatment for dVST, including 20/26 receiving aspirin, 4/26 therapeutic anticoagulation and 2/26 aspirin and anticoagulation. The median treatment period was 3 months. Endpoint of treatment was complete or partial resolution of dVST. Regardless of management, patients did not experience significant adverse sequelae from dVST. There was no difference in outcome in patients who received treatment compared to patients who did not, measured by the Glasgow Outcome Scale on follow up (4.3 and 4.5, p = 0.32).

Conclusion: Traumatic dVST is a frequently encountered clinical entity, although the incidence of complications is low. In significant TBI with fracture across the sinus, CTV should be obtained to exclude dVST. A 3-months course of antiplatelet therapy result in complete or partial resolution of the dVST, without adverse complications.
116: Enhanced Immunogenicity via Protein Phosphatase 2A (PP2A) Inhibition in SB28 Mouse Glioma Model

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Introduction: Immune checkpoint blockade (ICB) therapy has drastically improved treatment in many cancer types but falls behind in its use within glioblastoma (GBM), one of the most lethal forms of brain cancer. One of the major barriers is that GBM cells are poorly immunogenic, resulting in a lack of T cell infiltration. Therefore, it is critical to identify underlying mechanisms to enhance GBM tumor immunogenicity. Protein phosphatase 2A (PP2A) is a ubiquitous serine/threonine phosphatase that is implicated in the DNA damage response. While PP2A inhibition has been shown to impair DNA repair and control tumor growth, the impact of PP2A inhibition on tumor immunogenicity has yet to be explored. We hypothesize that PP2A inhibition will trigger the cGAS-cGAMP-STING axis, hyperactivate the IRF3 pathway, in turn increasing downstream Type I Interferon (IFN) signaling and enhancing tumor immunogenicity.

Methods: WT-SB28, a luciferase-expressing murine glioblastoma cell line, was used to generate a CRISPR PP2A KO-SB28. Immunogenic markers MHCI and PDL1 were stained in WT and KO SB28 cells and quantified through flow cytometry. Through qPCR, gene expression of factors downstream of the IRF3 signaling pathway was measured. In vitro, bone marrow-derived dendritic cells (BMDC) were co-cultured with WT and PP2A KO-SB28 OVA at ratios of 1:5 and 1:10. FACs was used to quantify the expression of dendritic cell activation markers. Finally, WT and KO-SB28 cells were injected into the cerebellum of immunocompetent mice to monitor survival.

Results: PP2A KO-SB28 showed a dramatic increase of MHCI and PDL1 cell surface expression and IFNb, CXCL10, and ISG15 gene expression over WT. Expression of dendritic cell activation markers such as CD86 and CD80 was enhanced in BMDC co-cultured with KO cells. In vivo, prolonged survival was seen in mice injected with PP2A KO cells.

Conclusion: PP2A inhibition promotes enhanced tumor immunogenicity via the IRF3 signaling pathway in SB28 glioma models.
117: Convection-delivered Adenoviral Gene Therapy Reprograms the Immunosuppressive Glioblastoma Microenvironment

National Brain Tumor Society (NBTS) Award

Jacob S. Young MD (San Francisco, California) Nam Woo Cho, MD PhD; Tim Casey-Clyde, BS; Raquel Santos, BS; Kyounghee Seo, BS; Joanna Phillips, MD PhD – UCSF; Mitchel Berger, MD – UCSF; Tomoko Ozawa, MD PhD; David Raleigh, MD PhD

Introduction: Immune checkpoint inhibition has not improved outcomes for glioblastoma patients, and single-cell approaches reveal the glioblastoma microenvironment is largely comprised of immunosuppressive cells. We hypothesized intratumor convection enhanced delivery (CED) of adenoviral gene therapy could recruit and activate anti-tumor immune cells in the glioblastoma microenvironment.

Methods: Syngeneic GL261 glioblastoma cells (30x10^5 cells/mouse) were implanted into the frontal lobe of immunocompetent C57BL/6J mice (18 mice/arm). Intracranial bioluminescence (BLI) and body weight measurements were used to assess glioblastoma growth and treatment toxicity, respectively. After tumor engraftment, glioblastomas were treated with conformal ionizing radiation mimicking stereotactic radiosurgery (SRS) in human patients (18Gy/1Fx), or CED of attenuated adeno-associated virus 9 (AAV9) vectors encoding Ccl4, Il1b, or Apoa1 (2x10^11 vg/mouse), cytokines driving recruitment and activation of anti-tumor immune cells in other intracranial tumors. Glioblastomas were collected for histologic, single-cell, and molecular analyses 5 days after treatment (6 mice/arm), and at the time of euthanasia after monitoring for survival (12 mice/arm). Treatment responses were assessed using H&E and IHC staining for macrophages (Iba1) or T cells (CD3). CED targeting was validated using AAV9-GFP and confocal microscopy, and results were compared to untreated glioblastoma controls. Mass cytometry of immune cell types in the glioblastoma microenvironment, cytokine expression in glioblastomas and peripheral blood, and validation using syngeneic SB28 glioblastomas are underway.

Results: Histologic analyses revealed treatment with AAV9-CCL4, AAV9-IL1, or SRS induced glioblastoma macrophage infiltration compared to AAV9-GFP or untreated control glioblastomas. Treatment with AAV9-IL1, AAV9-APOA1, or SRS induced glioblastoma T cell infiltration and tumor fibrosis compared to AAV9-GFP or untreated control glioblastomas. SRS prolonged survival compared to untreated control glioblastomas (23 days versus 14 days, p<0.001). There was no evidence of toxicity.

Conclusion: Convection-delivered adenoviral gene therapy and SRS can reprogram the glioblastoma immune microenvironment, revealing a strategy that may sensitize glioblastomas to immune checkpoint inhibition.

Leica Award

Constantinos G. Hadjipanayis MD, PhD, FAANS (New York, New York) Katherine Ember, PhD; Rajeev Agarwal, PhD; Juliette Selb, PhD; Frederick Dallaire, PhD; Arthur Plante, PhD; Melissa Umphlett, MD; Nadejda Tsankova, MD, PhD; Caroline Riza, BS; Armand Harb, BS; Lily McCarthy, BS; Frederic Leblond, PhD; Kevin Petrecca, MD, PhD

Introduction: Optimal brain tumor surgery maximizes tumor cell removal and minimizes surgery-induced neurological deficits. Raman spectroscopy (RS) is a laser-based, label-free, optics-based approach that can identify molecular features of tissues, enabling discrimination between tissue types. We present the first multi-center study that assessed the effectiveness of a handheld RS probe-based device to classify tumor and brain tissues during surgery.

Methods: In vivo RS data were acquired from 2 centers using a handheld probe from 68 patients with glioblastomas (GBs), brain metastases (BMs), and meningiomas. Measurements and corresponding biopsies were taken from the tumor bulk, tumor margins, and surrounding brain tissue. Biopsy sections were pathologically classified by tumor cell density. Spectral information and associated pathological labels were used to build machine learning classification models.

Results: Classification models identifying tumor and non-tumor tissues were generated using a training (80% of patients) and testing set (20%) from one center for each tumor type. Models achieved accuracies of 82% (training) and 87% (testing) for 25 GBs, 96% (training) and 97% (testing) for 15 BMs, and 95% (training and testing) for 13 meningiomas. These models generated an 81% accuracy when applied to data from 12 patients with meningioma or metastasis for which data was acquired independently at a different center. Performance of models increased from 56% accuracy for a tumor cell burden of 15-50% to 69% for 50-90% invasion.

Conclusion: This RS-based tumor detection device can discriminate between normal and tumor tissue across tumor types with 90% accuracy and 87-97% specificity and can identify invasive tumor cells at the margin. The in vivo and in real time capabilities make this device ideal for maximizing tumor resection and minimizing normal brain resection.
201: A Novel and Targetable Mechanism of Immuno-secretory Function at the Choroid Plexus-cerebrospinal Fluid Interface

Stephanie Robert MD, PhD (New Haven, Connecticut) Benjamin Reeves, BA; Emre Kiziltug, BA; Jason Karimy, BS; Arnaud Marlier, PhD; Phan Duy, PhD; Amrita Singh, BA; Garrett Allington, BA; Jinwei Zhang, PhD; TuKiet Lam, PhD; Rashaun Wilson, PhD; Tyrone DeSpenza, BA; Ana Greenberg,.; Brian Hilton,.; Adam Kundishora, MD; Xue Zeng, PhD; Eric Delpire, PhD; Seth Alper, MD, PhD; Kristopher Kahle, MD, PhD

Introduction: Post-infectious hydrocephalus (PIH) is the most common cause of acquired hydrocephalus worldwide, and management remains neurosurgical cerebrospinal fluid (CSF) shunting. We previously demonstrated post-hemorrhagic hydrocephalus (PHH) is driven by a TLR4-mediated choroid plexus (ChP) inflammatory response resulting in acute hydrocephalus. Using a rat model of PIH, we demonstrate ventriculomegaly and CSF hypersecretion is associated with alterations in a novel SPAK-mediated ion transportome and define a common TLR4-mediated ChP immune response in both IVH and LPS-mediated inflammatory hydrocephalus.

Methods: SPAK and TLR4 knockout (KO) rats were generated using Crispr/CAS9. A catheter was implanted into the lateral ventricles of adult male rats; E. coli (+/-LPS), LPS, or blood was administered over 48-72h. CSF secretion was measured by catheter placement into the ventricle. ChP were harvested for immunohistochemistry (IHC), genomic/proteomic analysis, and single-cell RNA sequencing (scRNAseq). SPAK-associated ChP targets were identified through liquid chromatography/dual mass spectroscopy (LC-MS/MS) analysis of purified SPAK-protein complex; candidates were validated by WB/IHC.

Results: Bumetanide-sensitive, SPAK-dependent CSF hypersecretion and ventriculomegaly was observed after intraventricular LPS or IVH infusion. LPS and IVH triggered robust ChP inflammation, and phospho-activation of SPAK, and the bumetanide-sensitive cation-chloride-cotransporter NKCC1. SPAK LC-MS/MS pull-down assay revealed three important SPAK-bound proteins, Na/K ATPase (alpha-1 subunit), K+ channel KCNJ13/Kir7.1, Cl- channel CLIC6, and AQP1; IHC demonstrated increased apical colocalization of these targets with SPAK. Importantly, ChP inflammation, CSF hypersecretion, and ventriculomegaly were abrogated with knockout of SPAK or TLR4, and in animals treated with systemic immune-modulatory drugs.

Conclusion: Multiomic analysis identifies a novel, common, and targetable mechanism of PIH and PIH, mediated by a SPAK-regulated ChP ion transportome, and initiated by TLR4-dependent inflammatory response. CSF hypersecretion and hydrocephalus are attenuated with inhibition of TLR4, SPAK, and through systemic immune-modulation. Our findings uncover a targetable mechanism for the pharmacological treatment of PIH, PHH, and potentially other forms of inflammatory hydrocephalus.
202: Comparing Posterior Cervical Foraminotomy with Anterior Cervical Discectomy and Fusion in Radiculopathic Patients: An Analysis from the QOD

Stewart Dunsker Award for Best Clinical Spine Abstract

Mohamad Bydon MD, FAANS (Rochester, Minnesota) Praveen Mummaneni, MD, MBA; Erica Bisson, MD, MPH; Giorgos Michalopoulos, MD; William Mualem, BS; Sally El Sammak, MD; Michael Wang, MD; Andrew Chan, MD; Mohammed Ali Alvi, MBBS, MS; Regis Haid, MD; John Knightly, MD; Clinton Devin, MD; Brandon Sherrod, MD; Oren Gottfried, MD; Khoi Than, MD; Jacob Goldberg, MD; Michael Virk, MD, PhD; Nitin Agarwal, MD; Steven Glassman, MD; Paul Park, MD; Kai-Ming Fu, MD, PhD; Brenton Pennicooke, MD, MS; Anthony Asher, MD

Introduction: Posterior cervical foraminotomy (PCF) is often offered as an alternative to anterior cervical discectomy and fusion (ACDF) for the management of cervical radiculopathy. This study's objective was to compare clinical and patient-reported outcomes between PCF and ACDF in patients presenting with radiculopathy.

Methods: The Quality Outcomes Database (QOD) was queried for patients who underwent ACDF or PCF for radiculopathy. Multivariable model-based imputation was utilized for missing data. To create two highly homogeneous groups, optimal matching was performed at a 2:1 ratio between the two groups on 40 baseline variables (including demographics, comorbidities, symptoms, patient-reported scores, indications, and levels treated). Outcomes of interest were estimated blood loss (EBL), length of stay (LOS), readmissions, reoperations, patient-reported satisfaction (based on the North American Spine Surgery index - NASS), increase in Quality-adjusted Life Years (QALY), and decrease in Neck Disability Index (NDI), arm and neck pain scores.

Results: A total of 10,765 eligible patients with annual follow-up were identified, of which 319 underwent PCF. The patients undergoing ACDF had more comorbidities, more complex pathologies, lower QALY scores, and higher NDI and neck pain scores at baseline. After optimal matching, the two groups included 638 and 319 patients. ACDF was associated with slightly higher satisfaction (NASS 1-2) rates at 3 months (91.8% vs. 87.8%, p=0.04). The ACDF group also had lower arm pain scores at 3 months after surgery (1.6 vs. 2.3, p=0.005; MCID: 76.2% vs. 67.7%, p=0.005), which lost significance at 12 months. PCF was associated with a shorter LOS (0.5 vs. 0.9 days, p<0.001). The differences in the rest of the outcomes were not significant.

Conclusion: In this study, ACDF was found to provide slightly higher 3-month satisfaction and arm pain control, but this difference attenuated at the 12-month follow-up. One-year reoperation rates and patient-reported outcomes did not differ between the two groups.
203: Single-cell Transcriptome Analysis Reveals Dynamic Cell Populations and Differential Gene Expression Patterns in a Mouse Cerebral Aneurysm Model

Young Neurosurgeon Abstract Award

Isabella G. McCormack MS (New Orleans, Louisiana) Alejandra Martinez, PhD; Giovane Tortelote, PhD; Crissey Pascale, MA; Kristen Nordham, BA; Natalie Suder, MS; Mitchell Couldwell, MS; Aaron Dumont, MD, MBA

Introduction: The circle of Willis (CoW) is the most common location for cerebral aneurysms to form in humans. Although the major cell types of the intracranial vasculature are well known, the heterogeneity and relative contributions of the different cells in healthy versus aneurysmal vessels have not been well-characterized. Here, we present the first comprehensive analysis of the lineage heterogeneity, altered transcriptomic profiles and functional states of vascular cells from healthy and aneurysmal mouse CoW vessels using single-cell RNA sequencing (scRNAseq).

Methods: Cerebral aneurysms (CA) were induced in adult male mice using an elastase model. ScRNAseq was then performed on CoW samples obtained at 14 days post-aneurysm induction.

Results: Unbiased clustering analysis of the transcriptional profiles from >3900 CoW cells identified 19 clusters representing 10 cell lineages: vascular smooth muscle cells (VSMCs), endothelial cells, fibroblasts, pericytes and immune cells (macrophages, T and B lymphocytes, dendritic cells, mast cells and neutrophils). Seurat clustering analysis identified 5 VSMC subpopulations and 6 monocyte/macrophage subpopulations with distinct transcriptional profiles. VSMC subpopulations were classified as being proliferative, stress-induced senescent, quiescent, inflammatory-like or hyperproliferative. The transcriptional signature of the metabolic pathways of ATP generation was found to be downregulated in 2 major VSMC clusters when CA was induced. Elastase exposure also induced significant expansion of the total macrophage population and this expansion was further increased with CA rupture. Both inflammatory and resolution-phase macrophages were identified, and a massive spike of neutrophils was seen with CA rupture. Additionally, the neutrophil-to-lymphocyte ratio (NLR) which originated from the elastase CA induction mirrored that which has been observed in humans.

Conclusion: Our data identify CA disease-relevant transcriptional signatures of vascular cells in the CoW. Furthermore, we characterize the heterogeneity and cellular responses of VSMCs and monocytes/macrophages during CA progression, which provides insight into their function and their role in CA pathogenesis.
204: Microenvironmental Correlates of Immune Checkpoint Inhibitor Response in Human Melanoma Brain Metastases Revealed by T Cell Receptor and Single-cell RNA Sequencing

American Brain Tumor Association Young Investigator Award

Christopher Alvarez-Breckenridge MD PhD (Houston, Texas) Samuel Markson, PhD; Jackson Stocking, BS; Naema Nayyar, BS; Albert Kim, MD; Magali de Sauvage, BS; Matt Strickland, MD; Joana Mora, BS; Juliana Larson, BS; Ashish Dahal, BS; Maria Martinez-Lage, MD, PhD; Matthew Frosch, MD, PhD; Elizabeth Gerstner, MD, PhD; brian Nahed, BNAHED@MGH.HARVARD.EDU; William Curry, MD; Bob Carter, MD, PhD; Mario Suva, MD, PhD; Daniel Cahill, MD, PhD; Ryan Sullivan, MD; Scott Carter, PhD; Priscilla Brastianos, MD

Introduction: The emergence of immune checkpoint inhibition (ICI) for patients with metastatic melanoma has significantly improved their clinical outcomes. However, the central nervous system (CNS) is frequently a site of disease progression and nearly 50% of patients with metastatic melanoma succumb to CNS disease. Thus, treatment of melanoma brain metastases (MBM) is an unmet clinical need. We hypothesized that response to ICI is reflective of unique features within the tumor microenvironment of the brain.

Methods: To study the nature of the tumor microenvironment in MBM, we collected 27 freshly resected MBM and performed single cell RNA sequencing (Smart-Seq2) and T cell receptor clonotyping from MBM and matched blood to dissect intratumoral immune cell heterogeneity.

Results: Lymphocyte analysis demonstrated unique T cell phenotypes and clonal dynamics that were not explained by intratumoral hemorrhage. Utilizing differential gene expression, brain tumor associated, clonally expanded T cells exhibited significant expression of NKG7, PRF1, HAVCR2, TIGIT, and GZMB. Moreover, we observed significant variation along the exhaustion/memory axis between detectably expanded and non-expanded T cell clones. We similarly observed distinct T cell functional states between unique, clonally expanded intratumoral T cells that diverge from clones shared with both the tumor and blood. Lastly, utilizing the single pre-treatment patient who went on to respond to ICI, we were able to perform a composite T cell histologic, phenotypic and clonal analyses within this patient compared the remainder of the cohort.

Conclusion: We identified T cell clonal expansion in the blood as a biomarker of response to ICI. Additionally, we observed evidence of overlap between clonally expanded T cells in the blood and brain which ultimately evolves into phenotypically distinct, tumor exclusive T cell populations. These findings provide novel insights into T cell clonal dynamics within the CNS and the relationship between the cranial and extracranial compartments in the setting of ICI.
205: Prospective Validation of Machine Learning Technique for Automated Intraoperative Frozen Diagnosis of Brain Tumors

KLS Martin Award

Siri Sahib S. Khalsa MD (Ann Arbor, Michigan) Sandra Camelo-Piragua, MD; Diana Thomas, MD; Jose Otero, MD; Brian Goodwin, PhD; Corey Jaskolski, MS; Peter Ouillette, MT-ASCP; Daniel Orringer, MD; Todd Hollon, MD

Introduction: Neurosurgeons rely on rapid histologic diagnosis during brain tumor surgery for surgical decision-making. Although frozen sectioning is available at most surgical hospitals, nearly half of these hospitals do not have access to intraoperative neuropathology consultation. The authors previously described an artificial intelligence program to automatically diagnose whole frozen slides among the following supratentorial enhancing tumors: metastatic carcinoma, high-grade glioma, lymphoma, and meningioma. We present a validation study of this technique using prospectively collected frozen specimens.

Methods: In our previous work, labeled frozen images were used to train a deep machine learning algorithm called a convolutional neural network. An additional algorithm combined these field-of-view diagnoses into whole-slide diagnoses. The authors tested a new set of prospectively collected intraoperative frozen section specimens, and compared the automated whole-slide diagnosis with board-certified neuropathologist interpretation.

Results: Thirty-six prospectively collected intraoperative frozen section slides were tested from a single academic center. The automated algorithm correctly diagnosed 8/8 carcinomas, 12/12 high-grade gliomas, 4/4 lymphomas, and 12/12 meningiomas, with an overall whole-slide diagnostic accuracy of 100%. Results for additional slides from two academic medical centers will be able to be reported at the time of presentation.

Conclusion: We previously developed a computer program to automatically distinguish between the core differential diagnoses for adult supratentorial enhancing brain tumors, using traditional intraoperative frozen section slides. Here we present validation of this technique with prospectively collected data. This algorithm may be beneficial to centers without access to intraoperative neuropathology consultation during brain tumor surgery. The authors continue with efforts to generalize the algorithm for use in different medical center and types of slide scanners.
206: Evaluating Efficacy of a Novel Hydrogel-CXCL9-mRNA Vaccine in Combination with Temozolomide in a Murine Glioma Model

Stryker CNS Tumor Award

Yusuf Mehkri BS (Gainesville, Florida) Farhad Dastmalchi, DVM; Aida Karachi, DVM PhD; Elias Sayour, MD PhD; Hector Mendez-Gomez, PhD; Thomas Angelini, PhD; Duane Mitchell, MD PhD; Maryam Rahman, MD

Introduction: Glioblastoma has had disappointing preliminary response to immunotherapy. We have created an immunotherapy platform that overcomes treatment resistance with the combination of a chemokine (CXCL9) and a novel mRNA-nanoparticle in a polyethylene glycol (PEG) hydrogel scaffold. This hydrogel-CXCL9-mRNA (HCM) vaccine results in robust recruitment of multiple immune cell subsets with anti-tumor efficacy in aggressive syngeneic murine models. Due to the immunomodulatory effects of temozolomide (TMZ), we sought to evaluate the immune response and survival in tumor bearing mice treated with a combination of TMZ and the HCM vaccine.

Methods: Survival was compared between 5 groups of 8 C57BL/6 mice implanted intracranially with KR158-luciferase (10,000 cells). Vaccine - produced using 25 g total tumor RNA, 500ng CXCL9, nanoparticle and PEG hydrogel - was injected subcutaneously near cervical lymph nodes. Animals in the vaccine alone group and combination groups (pre-TMZ and mid-TMZ) received three doses over 15 days of HCM vaccine. In the pre-TMZ group, animals received the first dose of the HCM vaccine one week before the TMZ cycle. In the mid-TMZ group, animals received the first HCM vaccine dose one week after the first dose of TMZ. Animals were monitored twice daily, and Kaplan Meier curves generated for survival analysis.

Results: Animals treated with HCM vaccine had significantly improved survival compared to control (pre-TMZ: p=0.002, mid-TMZ: p<0.001, hydrogel alone: p<0.001). TMZ alone showed no difference in survival compared to controls. There was no significant difference between pre-TMZ and mid-TMZ, demonstrating no difference in timing of delivery. Hydrogel alone group showed improved survival compared to both pre-TMZ (p=0.0033) and mid-TMZ (p=0.0001). Results demonstrate that TMZ abrogated the survival benefit from the vaccine.

Conclusion: The HCM vaccine demonstrates significant anti-tumor efficacy and improved survival in the KR158 tumor bearing animals. The role of TMZ in combination with immunotherapy is an area that warrants further studies.
207: CNS Drug Screening Identifies Metixene as a Novel Autophagy Modulator in Brain Metastases

Ronald L. Bittner Award on Brain Tumor Research

Jawad Fares MD, MSc (Chicago, Illinois) Deepak Kanojia, PhD – Research Assistant Professor, Neurological Surgery, Northwestern University; Alex Cordero, PhD – Postdoctoral Research Fellow, Neurological Surgery, Northwestern University Feinberg School of Medicine; Edgar Petrosyan, MD – Postdoctoral Research Fellow, Neurological Surgery, Northwestern University Feinberg School of Medicine; Victor Arrieta, MD – Postdoctoral Research Fellow, Neurological Surgery, Northwestern University Feinberg School of Medicine; Peng Zhang, PhD – Research Assistant Professor, Neurological Surgery, Northwestern University Feinberg School of Medicine; Jawad Fares, MD; Deepak Kanojia, PhD – Research Assistant Professor, Neurological Surgery, Northwestern University Feinberg School of Medicine; Alex Cordero, PhD – Postdoctoral Research Fellow, Neurological Surgery, Northwestern University Feinberg School of Medicine; Edgar Petrosyan, MD – Postdoctoral Research Fellow, Neurological Surgery, Northwestern University Feinberg School of Medicine; Victor Arrieta, MD – Postdoctoral Research Fellow, Neurological Surgery, Northwestern University Feinberg School of Medicine; Irina Balyasnikova, PhD – Associate Professor, Neurological Surgery, Northwestern University Feinberg School of Medicine; Atique Ahmed, PhD – Associate Professor, Neurological Surgery, Northwestern University Feinberg School of Medicine; Deepak Kanojia, PhD – Research Assistant Professor, Neurological Surgery, Northwestern University Feinberg School of Medicine; Jason Miska, PhD – Research Assistant Professor, Neurological Surgery, Northwestern University Feinberg School of Medicine; Atique Ahmed, PhD – Associate Professor, Neurological Surgery, Northwestern University Feinberg School of Medicine; Irina Balyasnikova, PhD – Associate Professor, Neurological Surgery, Northwestern University Feinberg School of Medicine; Jason Miska, PhD – Research Assistant Professor, Neurological Surgery, Northwestern University Feinberg School of Medicine; Atique Ahmed, PhD – Associate Professor, Neurological Surgery, Northwestern University Feinberg School of Medicine; Irina Balyasnikova, PhD – Associate Professor, Neurological Surgery, Northwestern University Feinberg School of Medicine; Atique Ahmed, PhD – Associate Professor, Neurological Surgery, Northwestern University Feinberg School of Medicine; Irina Balyasnikova, PhD – Associate Professor, Neurological Surgery, Northwestern University Feinberg School of Medicine; Jason Miska, PhD – Research Assistant Professor, Neurological Surgery, Northwestern University Feinberg School of Medicine

Introduction: Brain metastases are the final frontier in neuro-oncology for which more efficacious therapies are required. Lack of treatments limits patient survival and results in poor outcomes. Using a CNS drug library, we probed cancer susceptibilities to identify novel, effective agents against breast cancer brain metastases (BCBM).

Methods: We conducted a blinded CNS drug screen on two BCBM cell lines using 320 agents that are known to be permeable through the blood-brain barrier (BBB) and approved by the U.S. Food and Drug Administration. Experiments to analyze the anti-cancer efficacy of top agents were conducted. In vivo models of brain metastases, using immunodeficient mice, were used to check for survival benefit. Functional studies to understand the mechanism of action were pursued.

Results: Metixene, an antiparkinsonian drug, was identified as a top therapeutic agent against BCBM. It was capable of inducing caspase-mediated apoptosis in different metastatic breast cancer subtypes. In addition, it was effective against HER2-positive and triple-negative BCBM, as well as trastuzumab-sensitive and resistant cell lines. Orthotopic xenograft assays revealed a significant reduction in mammary tumor weight and volume upon metixene treatment (P<0.0001). Treatment of mice bearing intracranial xenografts with metixene improved survival significantly (P=0.0008). Furthermore, metixene treatment improved survival significantly in a murine, intracarotid model of multiple brain metastases (P=0.03). An exploratory Reverse Phase Protein Array to identify molecular responses that mediate the anti-cancer activity of the chosen therapeutic agent, showed autophagy as a primary biological mechanism regulated by metixene in comparison to controls (P < 0.05). Immunofluorescence staining of LC3 showed a significant increase in the accumulation of puncta in metixene-treated cells (P = 0.015).

Conclusion: Metixene is a promising, BBB-permeable therapeutic agent against BCBM, with minimal reported side effects in humans. Our preclinical findings merit further investigation and potential introduction of metixene onto the clinical scene.
208: Improvement in Resident Performance for Minimally Invasive Lumbar Decompression Using a State-of-the-art Simulator

Ibrahim Hussain MD (New York, New York) Carolin Melcher, MD; Sertac Kimaz, MD; Jacob Goldberg, MD; Fabian Sommer, MD; Rodrigo Navarro-Ramirez, MD; Branden Medary, BS; Roger Hartl, MD

Introduction: The learning curve for spine surgery trainees acquiring techniques with minimally invasive tubular cases requires mastery of skills outside those learned for open decompression. Surgical simulation can complement traditional methods of skill acquisition by providing realistic anatomy, tactile feedback, and complication situations that can be discovered, practiced on, and addressed prior to surgery on a live patient. Our objective was to quantify the educational benefit to surgical trainees of using a state-of-the-art simulator to perform minimally invasive (MIS) unilateral laminotomy for bilateral decompression (ULBD) for lumbar stenosis.

Methods: Twelve orthopedic and neurological surgery residents performed 3 MIS ULBD procedures over 2 weeks on a simulator guided by established AO Spine metrics. Video recording of each surgery was rated by 3 blinded, independent experts using a global rating scale. The learning curve was evaluated with attention to technical skills, skipped steps, occurrence of errors, and timing. A knowledge gap analysis evaluating participants’ current versus desired ability was performed after each trial.

Results: From trial 1 to 3, there was a decrease in average procedural time by 31.7 minutes. The cumulative number of skipped steps and surgical errors decreased from 25 to 6 and 24 to 6, respectively. Overall surgical proficiency improved as indicated by video rating of efficiency and smoothness of surgical maneuvers, most notably with knowledge and handling of instruments. The greatest changes were noted in junior rather than senior residents. Average knowledge gap analysis significantly decreased by 30% from the first to last trial (P=0.001), signifying trainees performed closer to their desired technical goal.

Conclusion: Procedural metrics for minimally invasive ULBD in combination with a realistic surgical simulator can be used to improve the skills and confidence of trainees. Surgical simulation may offer an important educational complement to traditional methods of skill acquisition and should be explored further with other MIS techniques.
209: Outpatient versus Inpatient Lumbar Discectomy: A Matched Study Investigating Patient-reported and Surgical Outcomes

James H. Mooney MD (Birmingham, Alabama) Giorgios Michalopoulos, MD; Daniel Zeitouni, BA; Sally El Sammak, MD; Mohammed Alvi, M.B.B.S.; Michael Wang, MD, FACS; Domacoj Coric, MD; Andrew Chan, MD; Praveen Mummaneni, MD, MBA; Erica Bisson, MD, MPH; Regis Haid, MD; John Knightly, MD; Clinton Devin, MD; Brenton Pennicooke, MD; Anthony Asher, MD; Mohamad Bydon, MD

Introduction: Spine surgery represents an ideal target for cost reduction, with outpatient surgery resulting in significant cost savings. With an increased focus on value-based health care, lumbar discectomy is increasingly performed outpatient when appropriate.

Methods: The Quality Outcomes Database (QOD) was queried for patients undergoing elective one- or two-level lumbar decompression for degenerative spine disease. Patients were grouped as outpatient if they were discharged on the date of surgery and as inpatient if they stayed in the hospital for one or two days. Cases of incidental durotomy were excluded from the cohort as a potential trigger for changing outpatient status. To create two highly homogeneous groups, optimal matching was performed at a 1:1 ratio between the two groups on 33 baseline variables (including demographics, comorbidities, symptoms, patient-reported scores, indications, and operative details). Outcomes of interest were readmissions and reoperations at 30 days and 3 months after surgery, overall satisfaction, and decrease in Oswestry Disability Index (ODI), back and leg pain at 3 months after surgery.

Results: The study cohorts consisted of 4,345 patients in each group. The 30-day readmission rates were 4.9% and 5% for the outpatient and inpatient groups, respectively, while the 30-day reoperation rates were 1.6% and 1.2%. The 3-month readmission rates were 5.3% and 5%, and the 3-month reoperation rates were 2.3% for both groups. Overall satisfaction at 3 months was 87.5% and 88% for the outpatient and inpatient groups, respectively. ODI, VAS leg pain, and VAS back pain scores were all lower in the outpatient group at 3 months, but the difference was clinically insignificant. Non-inferiority of outpatient surgery was documented for all outcomes.

Conclusion: Outpatient lumbar discectomy demonstrated non-inferior clinical outcomes at 30 days and 3 months after surgery compared to inpatient discectomy. Patient-reported satisfaction from surgery, ODI, and pain scores were also similar between the two groups.
210: Sarcopenia as a Predictor of Survival in Oncological Spine Surgery: Validation of CT Morphometric Measurement of Psoas Size

Rafael De la Garza Ramos MD (Bronx, New York) Joshua Benton, MD; Yaroslav Gelfand, MD; Saikiran Murthy, DO; Reza Yassari, MD

Introduction: Sarcopenia is a syndrome characterized by loss of muscle mass and strength. In patients with metastatic spine disease, it was recently proposed as a biomarker associated with postoperative survival. The objective of this study is to validate the use of sarcopenia as a prognostic factor for survival in our population and to validate specific proposed cut-off measurements used to define this condition.

Methods: A total of 104 patients with complete preoperative CT imaging who underwent oncological spine surgery at our institution between 2013 and 2021 were identified. Sarcopenia was defined as a cross-sectional area of the psoas muscle at the L4 pedicle level less than 10.5 cm² for men and less than 7.2 cm² for women based on the work by Zakaria et al. The main dependent variable was overall survival (OS). 30-day survival (30S) and 90-day survival (90S) were also examined. All survival analyses were done following Kaplan-Meier methods.

Results: The average age of all patients was 62 years and 61/104 were male (58.7%). Sarcopenia was diagnosed in 40/104 patients (38.5%); its prevalence was 46.5% in women and 32.8% in men (p=0.157). Median OS was 19.5 months for all patients. However, median OS was 4 months for sarcopenic patients and 26 months for non-sarcopenic patients (log-rank, p=0.005). 30S and 90S were significantly lower for patients with sarcopenia (p=0.009 and p=0.003, respectively). After controlling for age, sex, BMI, functional status, rapid-growing tumor type, and presence of pathologic fracture, sarcopenia remained as an independent significant risk factor for mortality (Hazard Ratio 2.2; 95% CI, 1.06 – 4.56; p=0.035).

Conclusion: Sarcopenia is an important and significant risk factor for survival after oncological spine surgery. The proposed cut-off values were significant in our population and can be used for preoperative risk stratification and improved decision-making. Future research into preoperative optimization and treatment of sarcopenia is needed.
Internal Neurolysis versus Intraoperative Glycerin Rhizotomy for Trigeminal Neuralgia

William H. Sweet Young Investigators Award

Risheng Xu MD PhD (Baltimore, Maryland) Divyaansh Raj, BS – Johns Hopkins University School of Medicine; Joshua Materi, BS – Johns Hopkins University School of Medicine; Safwan Alomari, MD – Johns Hopkins University School of Medicine; Yuanxuan Xia, MD – Johns Hopkins University School of Medicine; Sumil Nair, BA – Johns Hopkins University School of Medicine; Pavan Shah, BS – Johns Hopkins University School of Medicine; Nivedha Kannapadi, BS – Johns Hopkins University School of Medicine; Timothy Kim, BS – Johns Hopkins University School of Medicine; Judy Huang, MD – Johns Hopkins University School of Medicine; Chetan Bettegowda, MD PhD – Johns Hopkins University School of Medicine; Michael Lim, MD – Stanford University School of Medicine

Introduction: Internal neurolysis (IN) and intraoperative glycerin rhizotomy (ioGR) are emerging surgical options for patients with trigeminal neuralgia without neurovascular contact.

Methods: We retrospectively reviewed all patients who underwent IN or ioGR for trigeminal neuralgia at our institution. Patient demographics, immediate postoperative outcomes, as well as long term neurological outcomes were compared.

Results: Out of 1044 patients who underwent open surgical treatment for trigeminal neuralgia, 56 patients underwent IN and 91 underwent ioGR. 138/147 of these patients had no evidence of intraoperative neurovascular conflict. All patients who underwent IN and 96.7% of patients who underwent ioGR had immediate postoperative pain relief. At last follow-up, patients who underwent IN had lower BNI pain intensity scores (p=0.05), better BNI facial numbness scores (p<0.01), and a greater degree of pain improvement (p=0.05) compared to those who underwent ioGR. Patients who underwent IN also had significantly lower rates of symptomatic pain recurrence (p<0.01) at last follow up over an average of 9.5 months.

Conclusion: Internal neurolysis appears to provide patients with a greater degree of pain relief, lower rates of facial numbness, and lower rates of pain recurrence compared to intraoperative glycerin rhizotomy. Future prospective studies will better characterize long-term pain recurrence and outcomes.
212: Twelve-month Outcomes from RCT: 10kHz Spinal Cord Stimulation for Treating Non-surgical Refractory Back Pain

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Introduction: Most evidence for clinical- and cost-effectiveness of spinal cord stimulation (SCS) is for treating chronic refractory back and leg pain following spine-surgery, with limited evidence where the patient has no prior surgery and is a poor surgical candidate. But inconsistent health care payer reimbursement and lower clinical adoption provides an impetus for providing stronger evidence for SCS treating this condition that we have termed “Non-Surgical Refractory Back Pain” (NSRBP). We present the 12-month results comparing 10kHz SCS to conventional medical management (CMM) in this population.

Methods: NSRBP patients as defined above, with spine surgeon consultation required for confirmation, were randomized 1:1, to CMM with and without 10kHz SCS. CMM was provided according to physicians’ best practice and clinical guidelines. Primary and secondary endpoints including responder rate (% with ≥50% pain relief), function, quality of life, and change in daily opioid use, and were analyzed at 3 and 6 months respectively, with follow-up to 12 months.

Results: There were 159 NSRBP patients (age 55.3±11.9 years, time since symptoms onset of 11.4±10.9, multiple etiologies) were randomized to either CMM alone (n=75) or to 10kHz SCS (n=83). All primary and secondary endpoints were met for the 10kHz SCS group, with clear benefit over CMM alone (p<0.001). Serious adverse events were limited to 4 procedure related in 10kHz SCS subjects. At 12 months the 10kHz SCS arm maintained 78.1% (95%CI 66.0–90.2) responder rate, ODI of 24 points (95%CI 19.8-28.2), EQ-5D-5L index of 0.780 (95%CI 0.633-0.927), and a 49.6% (95%CI 32.3-66.9) reduction in daily opioid use.

Conclusion: This study demonstrates that the addition of 10kHz SCS to CMM results in profound improvements in pain relief, function, and quality of life in these NSRBP patients who have been deemed not surgical candidates and exhausted all available appropriate nonoperative medical management.
213: Durability of 10-kHz Spinal Cord Stimulation for Painful Diabetic Neuropathy: 18-month Multicenter Randomized Controlled Trial Results

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Introduction: Approximately 6 million US adults are living with painful diabetic neuropathy (PDN) and many find conventional treatments ineffective. The published 6-month SENZA-PDN data demonstrated 10-kHz spinal cord stimulation (SCS) substantially relieves pain and may improve sensation in patients with refractory symptoms.

Methods: Prospective, multicenter, randomized controlled trial (SENZA-PDN) to document the impact of 10-kHz SCS on PDN. Participants had PDN symptoms ≥12 months, refractory to medications, lower limb pain intensity ≥5cm (0-10cm visual analog scale [VAS]), and hemoglobin A1c ≤10%. Patients (n=216) were allocated 1:1 to 10-kHz SCS (Nevro Corp.) plus conventional medical management (CMM) or CMM alone and followed for 18 months with an option to crossover at 6 months.

Results: Patients assigned 10-kHz SCS experienced substantial, sustained pain relief with 78% improvement over 18 months (baseline VAS=7.6 cm, 18-month VAS=1.7 cm). Additionally, this group reported average 65% reduction in sleep disturbance due to pain and 65% improvement in pain interference with mood and daily activities. No 10-kHz SCS participants elected to crossover. At 6-month follow-up, 93% of eligible CMM patients elected to crossover and results were similar to those seen in the original SCS group: 70% pain relief over 18 months (baseline VAS=7.3 cm, 18-month VAS=2.2 cm). Crossover patients reported average 55% reduction in sleep disturbance due to pain and 61% improvement in pain interference. There were no significant differences between the crossover results and those observed in patients originally assigned 10-kHz SCS.

There were no stimulation-related neurological deficits and no explants due to ineffectiveness. There were 6 total explants (3.9%), 5 due to procedure-related infections and 1 as a precaution for endocarditis.

Conclusion: SENZA-PDN, the largest RCT to-date of SCS management of PDN, will inform the treatment continuum. Observed short-term results are durable over 18 months for patients with symptoms refractory to conservative care.
215: Can Paddle Spinal Cord Stimulators Be Safely Replaced?

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Introduction: Paddle leads for spinal cord stimulation (SCS) offer more streamlined energy delivery and advantages in some patients. However, there is concern for how safely SCS paddles can be replaced once previously implanted due to scar tissue and the relative vulnerability of the thoracic cord. Here we share our experience on redo SCS paddle placement.

Methods: Participants who underwent SCS replacement at Albany Medical Center between 2011-2020 were identified. The medical records were reviewed for demographic data and information regarding initial complications, reason for removal or revision, subsequent complications of redo surgery, timing of redo surgery, and whether the implant was later removed. Percutaneous lead revision cases performed over the same time period were used as a comparison group.

Results: 412 patients were identified to have had a SCS-related procedure based on billing codes. Of these, 41 involved replacement of epidural leads (27 paddles, 14 percutaneous). Most paddles were revised and replaced at the same setting (n = 24; 88.9%). 14 of 27 paddle replacements (51.8%) required an additional laminectomy. Reoperations with initial placement that occurred more than 1 year ago were significantly more likely to require an additional laminectomy (p = 0.0003). Despite the invasive nature of paddle replacement, there was no difference in complications (p = 0.212) or rates of infection when compared to that of percutaneous leads.

Conclusion: The present study is the first to characterize the safety profile of SCS paddle replacement surgeries. Here we demonstrate replacement of paddle leads in the same setting with additional laminectomies if needed due to scar, is associated with low rates of complications. This validates the feasibility and low risk profile of replacing paddle leads when clinically indicated.
216: Surgical Revascularization Decreases Stroke and TIA Risk in Children with Sickle Cell Disease and Moyamoya Syndrome: Results of the Stroke in Sickle Cell Revascularization Study (SiSCRS)

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Introduction: Recent studies have suggested that surgical revascularization may be a safe and effective therapy to reduce risk of cerebrovascular complications in patients with sickle cell disease and moyamoya syndrome (SCD-MMS). These studies have been limited by small sample size and lack of a control group for comparison.

Our goal is to investigate whether revascularization surgery reduces the risk of cerebrovascular events (CVEs) in comparison to conservative management alone in a retrospective cohort of children with SCD-MMS.

Methods: A retrospective review of data from 14 major U.S. pediatric neurosurgery centers of SCD-MMS patients (<18 y.o.) was performed. Detailed information on sickle cell disease, stroke and surgical histories were extracted. The incidence of CVEs (stroke and TIAs) between patients treated with surgical revascularization was compared to those with conservative management alone. Multivariate regression models were generated and logistic regression analyses were performed.

Results: A total of 141 patients with SCD-MMS were studied. 78 (55.3%) were treated with conservative management and revascularization surgery (Surgery group) and 63 (44.7%) were treated with conservative management alone (Conservative group). Patients in the Surgery group had reduced odds of developing a CVE over the duration of their risk period (odds ratio = 0.27, 95% CI: 0.08-0.94, P = .040). Furthermore, when comparing patients in the Surgery group during their pre-surgical periods and post-surgical periods, patients had markedly reduced odds of developing a CVE after surgery (odds ratio = 0.22, 95% CI = 0.08-0.58, P = .002). Postoperatively, 5 patients had CVEs and 5 had non CVE complications.

Conclusion: Our retrospective study provides strong evidence that revascularization surgery can be performed safely and reduce risk of CVEs in patients with SCD-MM. This is the largest study of its kind to date. A prospective study will be needed to validate these findings.
217: Modeling the Effect of Repetitive Mild Traumatic Brain Injury on Long-term Seizure Risk in Children

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Introduction: Mild traumatic brain injury (mTBI) has previously been associated with increased long-term seizure risk. However, the multiplicative impact of repeated mTBIs is not well-established.

Methods: Data were extracted from the Optum Clinformatics DataMart database (2003-2021). Children (age <18 years) diagnosed with ≥1 mTBI event were included. Exclusion criteria included prior seizure events or prior antiepileptic drug (AED) use. The primary outcome-of-interest was new-onset seizure. Comorbidities were included based on a 36-factor index previously associated with epilepsy risk in children. Time-varying multivariable Cox regression was used to ascertain the multiplicative impact of multiple mTBI events on long-term seizure risk. A risk-stratification model integrating comorbidities, mTBI characteristics, and demographics was constructed using this framework and validated on a withheld subset (30% of the data) to identify patients with high seizure risk.

Results: A total of 156,118 children were included (median age: 13 years (IQR 9-15). Most children (69.4%) had only one mTBI event, while 30.6% had ≥2 and 6.7% had ≥3 mTBI events. Median follow-up was 1.9 years (IQR 0.8-3.8). Median time to seizure following initial mTBI event was 306 days. Adjusting for demographics, mTBI characteristics, and comorbidities, each repeat mTBI with no loss of consciousness (LOC) resulted in a moderate increase in seizure risk (HR=1.26, 95%CI 1.16-1.36) while each repeat mTBI with brief LOC (<1 hour) resulted in even higher risk increases (HR=2.05, 95%CI 1.89-2.23). Other contributing features included ICU use (HR=2.43, 95%CI 1.96-3.03), subarachnoid hemorrhage (HR=1.74, 95%CI 1.32-2.28), and emergency department admission (HR=1.63, 95%CI 1.32-2.01). The risk-stratification model, which integrates 3 demographic, 6 mTBI-specific, and 14 comorbidity features, identified a patient subset (7.5%) with significantly elevated 5-year seizure risk (4.7-fold; 7.4% [95%CI 6.2-8.6] vs 1.8% [95%CI 1.6-2.1]).

Conclusion: Our risk-stratification model identified children at markedly increased risk for seizures following repeated mTBI and can be used to prospectively guide surveillance and early intervention.
218: Predicting Changes in Cranial Index Following Spring Mediated Cranial Vault Expansion in Non-syndromic Sagittal Craniosynostosis: Stepwise and Machine Learning Algorithm Approach

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Introduction: Spring-mediated cranial vault expansion (SMC) is an increasingly utilized tool in non-syndromic sagittal craniosynostosis but variables impacting outcomes, including bone thickness, are incompletely understood. The aim of this study was to determine variables that interact to predict SMC outcomes, primarily changes in cranial index (CI).

Methods: Patients with non-syndromic sagittal craniosynostosis undergoing SMC at our institution between 2014 and 2021 were included. Clinical data, including CI over time (immediately postoperative; one, three, six months; and one, three, and five years postoperative), were obtained from patient medical records. Skull thickness was determined from patient preoperative CTs using Materialise Mimics. Stepwise selection, least absolute shrinkage and selection operator (LASSO), and random forest machine learning methods were used to determine variables most predictive of changes in CI.

Results: One hundred and twenty-four patients (94 males) with mean surgery age of 3.59 ± 0.87 months and average skull thickness 1.83 ± 0.38 mm were included in this study. Random forest machine learning identified maximum spring force and mean thickness as highly predictive variables with increased in mean squared error (IncMSE) as 0.0173 and 0.0136, respectively, and more predictive than sex (0.0013) and age at surgery (0.0004). In stepwise analysis, maximum spring force (β = 0.108, CI = 0.056 – 0.161, p < 0.001), anterior spring force (β = 0.052, CI = 0.006 – -0.097, p = 0.027), and duration of spring placement (β = 0.002, CI = 0.000 – 0.003, p = 0.046) best predicted changes in CI, and LASSO analysis identified the same three variables as most predictive (β = 0.027, -0.006, 0.0005, respectively).

Conclusion: This study demonstrates maximum spring force, duration of spring placement, and parietal bone thickness may be good predictors of CI changes in patients undergoing SMC. Age at surgery and other demographic variables were inferior predictors in models using our cohort.
219: Effects of Socioeconomic Status on Glial Tumor Survival in Pediatric Populations: A Population-based Study

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Introduction: Gliomas are relatively common in the pediatric population. While prior studies have examined the differences in glioma survival by various demographics, few have examined the effect of socioeconomic status (SES) on glioma survival in pediatric populations.

Methods: This was a population-based study of pediatric patients (ages 0-14) using data from the National Program of Cancer Registries (NPCR, 2001-2014) and Surveillance, Epidemiology, and End Results (SEER, 2000-2015) programs. SES quartiles were created based on data from the Integrated Public Use Microdata Series and American Community Survey, defined as Q1 (upper) through Q4 (lowest). Analyses were stratified by race/ethnicity into Non-Hispanic Whites (NHWs), Blacks, American Indians/Alaskan Natives and Asian/Pacific Islanders (AIAN/APIs), and Hispanic Whites (HW). Survival analyses were performed, and hazard ratios are reported.

Results: For all glioma diagnoses, Q1 had the highest 1-year (89.2%), 5-year (78.5%), and 10-year (75.9%) relative survival, with a linear trend between survival and SES quartile. For the NPCR, Q4 and Q2 had a 27% (1.27, p=0.0004) and 11% (1.11, p=0.0293) higher risk of death, respectively, than Q1. When controlling for SES, HWs had a 40% increased risk (1.40, p<0.0001), blacks a 55% increased risk (1.55, p<0.0001), and AIAN/APIs had a 34% increased risk of death (1.34, p=0.0017) compared to NHWs. Within the SEER, all quartiles had a higher risk of death from glioma than Q1 (Q2: 1.28, p=0.0067; Q3: 1.25, p=0.0179; Q4: 1.32, p=0.0351). When controlling for SES, HWs had a 52% increased hazard of mortality (1.52, p<0.0001) and blacks had a 70% increased hazard of mortality (1.70, p<0.0001) than their WNH counterparts.

Conclusion: There was a linear trend between SES and survival, with Q1 having better survival. When adjusting for SES, all race/ethnicities had a higher risk of death than their NHW counterparts. These findings suggest that glioma survival is influenced by both SES and race.
220: Impact of Syndromic Conditions on Outcomes after Decompression in Children with Type I Chiari Malformation and Syringomyelia: an Analysis of the Park-Reeves Syringomyelia Research Consortium Registry

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Introduction: Pediatric patients with Chiari I Malformation (CM-I) may present with other developmental syndromes in addition to CM-I, yet our understanding of the impact of such concomitant diagnoses on outcomes after posterior fossa decompression (PFD) is limited.

Methods: A database of clinical information from CM-I patients enrolled in the Park-Reeves Syringomyelia Research Consortium at 36 clinical sites was created. Here only patients receiving PFD were included and were identified as syndromic based on prior diagnoses of Ehlers-Danlos, neurofibromatosis type I, Noonan, Costello, Kabuki, Crouzon, Pierre-Robin, Goldenhar, Beckwith-Wiedemann syndromes, megalencephaly capillary malformation, or cystic fibrosis. Primary outcome-of-interest was six-month postoperative complication rate; secondary included in-hospital outcomes (duration of stay, blood loss, and operating time) and redo PFD risk.

Results: The cohort included 884 patients (median age=10.2, range 0.7-20.6 years; 514 (58.1%) female gender). 959 PFDs were performed, with 70 patients receiving at least one redo PFD (median time to redo=8.3 months). Of all PFDs, 757 (85.6%) were performed with duraplasty. In total, 37 patients were considered syndromic. Age, pre-operative radiological measurements, and general medical comorbidities were comparable between syndromic and non-syndromic patients. Elevated blood loss (≥50ml) was more frequent among syndromic patients (43.8% vs 21.1%, \( p = 0.003 \)). On average, syndromic patients had 20.0% longer hospitalizations durations (19.5% vs 7.7% ≥7 days, Fisher Exact \( p=0.015 \)). Six-month all-cause postoperative complication risk and redo PFD rate were not different in syndromic patients. However, CSF leak was significantly more common in syndromic patients compared to non-syndromic counterparts (15.2% vs 3.9%, \( p = 0.002 \)) and more frequently required external CSF drainage (21.2% vs 4.4%, \( p<0.001 \)). Rate of occipitocervical fusion at initial PFD was higher for syndromic patients (5.4% vs 1.1%, \( p = 0.020 \)).

Conclusion: Syndromic children with CM-I receiving PFD may be at higher risk for prolonged hospitalizations and post-operative CSF complications.
221: Novel 3D Modeling of Brain and Ventricular Compliance in Children with Hydrocephalus Using Deformation-based Morphometry

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Introduction: Hydrocephalus is a challenging condition to treat in children as patients may present with nonspecific symptoms and ventricles may exhibit varying tissue compliance. Typical assessments of ventricular responsiveness are only qualitative and limited to the ventricular space even though stress and shear forces extend across the brain. Here we present a novel visualization of brain compliance following treatment of hydrocephalus by topographically projecting the magnitude of deformation experienced at the voxel-level.

Methods: We identified a series of pediatric patient with acute, initial presentations of obstructive hydrocephalus and with pre- and post-operative spoiled gradient recalled echo T1-weighted MRI imaging. We confirmed ventricular responsiveness by first measuring changes in ventricular volume between imaging pairs. To subsequently visualize deformation (affine and non-linear elements), we aligned image pairs with ANTs-based rigid registration and then overlaid post-operative on pre-operative images. We use the calculated voxel transformations to derive two visualizations of compliance: (1) a 2D-vector map projecting the resulting deformation field on structural brain MRI and (2) a 3D-heat map projecting the volumetric responsiveness of baseline ventricular boundaries.

Results: 10 children with diverse pathologies underwent definitive treatment of their hydrocephalus. There was a significant reduction in ventricular volume (150.3 cm3 to 84.9 cm3, p value = 0.0032, paired t-test) following all interventions. Deformation vectors were with the greatest change along the lateral ventricular spaces, relative to the genu and splenium. There was a trend towards proportionally reduced vector magnitudes within the cortical layer with increasing age (p = 0.069, Pearson).

Conclusion: We present 3D modeling for displaying the measure of centripetal deformation following ventricular intervention for hydrocephalus. Such vector-based changes in brain topography enables visualization of dynamic deformational change in the brain after treatment of the hydrocephalus.
223: Intra-arterial Transplantation of Mitochondria After Ischemic Stroke Reduces Cerebral Infarction

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Introduction: Mitochondria are powerhouses of the cell and are responsible for metabolic homeostasis during normal and pathological conditions. Mitochondrial dysfunction has been associated with secondary injury after cerebral ischemia. We postulated that transplantation of mitochondria into ischemic brain may mitigate injury caused by ischemia.

Methods: We used biochemical methods to purify autologous mitochondria from a single punch biopsy of skeletal muscle. The mitochondria were assayed for biological activity. Using mouse models of cerebral ischemia and reperfusion, we delivered viable mitochondria to ischemic brain parenchyma via an intra-arterial route. Using high-frequency focused ultrasound, we selectively opened the blood brain barrier over ischemic penumbra and assessed change in delivery of intra-arterial mitochondria and incorporation by various cell types. Using magnetic resonance imaging guided high-frequency ultrasound we assessed safety of selective blood brain barrier opening after cerebral ischemia.

Results: Purification of active mitochondria can be performed with minimal biochemical means within 15 minutes of a punch biopsy. The yield of mitochondria isolated is in the order of 10^9. Following delivery, mitochondria distribute through the stroked hemisphere and integrate into neural and glial cells in the brain parenchyma. Consistent with functional integration in the ischemic tissue, the transplanted mitochondria elevate concentration of adenosine triphosphate in the stroked hemisphere, reduce infarct volume and increase cell viability relative to controls.

Conclusion: Mitochondria can be isolated in pure form in a clinically relevant time scale. The purified cellular components are biologically active. They can be readily administered intra-arterially into a stroke bed. The delivery of mitochondria can be enhanced via selective opening of the blood brain barrier using focused ultrasound. The mitochondria incorporate into cellular components of the central nervous system, thereby increasing viability. This represents a novel treatment strategy that can be combined with endovacular thrombectomy to aid in the improvement of outcomes after large vessel occlusion.
224: Non-invasive Vagus Nerve Stimulation to Mitigate Subarachnoid Hemorrhage Induced Inflammation: A Pilot Randomized Controlled Trial

Louise Eisenhardt Travel Scholarship

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Introduction: Inflammation plays an important role in morbidity following subarachnoid hemorrhage (SAH). Transcutaneous auricular vagus nerve stimulation (taVNS) provides a novel, non-pharmacologic, non-invasive approach to immunomodulation with potential to improve outcomes in SAH.

Methods: Patients with SAH were randomized to taVNS or sham stimulation with patient, medical team, and outcomes assessor blinded to treatment arm. Patients underwent twice daily treatments, and plasma and cerebrospinal fluid (CSF) were collected every three days to quantify inflammatory markers. Rates of cerebral vasospasm and chronic hydrocephalus were assessed, and functional outcomes via modified Rankin Scale (mRS) scores were collected.

Results: 12 SAH patients were randomized, with 6 in each study arm. Baseline age and Hunt and Hess score were similar between groups. White blood cell counts were lower in the taVNS group at days 4 and 7 (p= 0.02, 0.03, respectively), and CSF nucleated cell count trended lower in the taVNS group after day 4. IL-1β was lower in the taVNS group by day 10 in plasma (p=0.043) and CSF (p<0.001). IL-17 was lower in the taVNS group on day 10 in plasma (p=0.048), and day 13 in the CSF (p=0.007). Levels of TNF-α in plasma and CSF trended lower in the taVNS group after day 4. Radiographic vasospasm was observed in 100% and 33.3% of patients in sham and taVNS arms, respectively (p=0.06). Permanent CSF diversion was required in 33.3% and 0% of patients in sham and taVNS arms, respectively (p=0.45). The change in mRS between admission and discharge was -0.67 for taVNS and +0.17 for sham patients (p=0.25). Rate of discharge to home or inpatient rehabilitation facilities was 83.3% and 50.0% for taVNS and sham groups, respectively.

Conclusion: Auricular VNS is a non-invasive, non-pharmacologic method of neuro- and immunomodulation. This pilot trial supports that taVNS following SAH can mitigate the inflammatory response, and potentially improve outcomes.
225: Middle Meningeal Artery Embolization for Chronic Subdural Hematomas: Predictors of Treatment Failure from Multicenter Experience of 368 Embolizations

International Travel Scholarship

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Introduction: Middle meningeal artery (MMA) embolization has emerged as a promising treatment option for chronic subdural hematoma (cSDH) patients, with reportedly lower recurrence rates compared to conventional open surgery. However, little remains known regarding predictors of treatment failure. Therefore, identification of these predictive factors would be of paramount importance to optimize patient selection for the success of these procedures.

Methods: Series of consecutive patients undergoing MMA embolization for chronic subdural hematomas at 7 North American centers (2018-2021) were included and analyzed. Treatment failure was defined as hematoma reaccumulation or neurological deterioration requiring rescue surgery, either during the same initial admission or on post-operative follow-up. A multivariate logistic regression model was constructed utilizing potentially significant variables (i.e., p<0.2) on univariate analysis and literature-known potential confounders to identify predictors of treatment failure (i.e., requiring rescue surgery).

Results: A total of 338 patients undergoing 368 embolization procedures (mean age 72 years, 27.4% females) were included, with 30 patients undergoing bilateral embolizations (8.9%). On presentation, median admission cSDH thickness was 14.9 mm (IQR 11-20), with 33.2% and 19.9% of patients were on antiplatelet and anticoagulation medications, respectively. Failure of therapy requiring rescue surgery was encountered in 33 patients (9.8%; median follow-up 5.2 months). On multivariate analysis controlling for confounders including concurrent surgical evacuation, presence of midline shift >5 mm, hematoma thickness >10 mm, pre-treatment baseline antiplatelet/anticoagulation therapy; independent predictors of treatment failure were older age (>75 years; OR 2.2; 95% CI: 1.02-4.73; p=0.045) female gender (OR 2.6; 95% CI 1.8-567,p=0.018), and MMA diameter of <2mm (OR 2.4; 95% CI 1.04-5.3; p=0.039).

Conclusion: Failure of MMA embolization for cSDH requiring rescue surgery was independently associated with older age, female gender and a smaller diameter of the MMA main trunk. Such factors could be used to guide individualized treatment selection and counseling in patients undergoing this procedure.
226: Socioeconomic Factors Associated with Pediatric Moyamoya Disease Hospitalizations: A Nationwide Cross-sectional Study

Robert Florin, MD

Kunal P. Raygor MD (San Francisco, California) Adib Abla, MD

Introduction: Healthcare disparities are widely described in adults, but barriers affecting access to care for pediatric patients with moyamoya disease (MMD) are unknown. Understanding socioeconomic factors impacting hospital access and outcomes is necessary to address pediatric healthcare disparities.

Methods: In this cross-sectional observational study, the Kids’ Inpatient Database was used to identify patients admitted with a primary diagnosis of MMD from 2003 to 2016. Patients ≤18 years with a primary diagnosis of MMD based on International Classification of Diseases (ICD) codes were included. Hospital admissions were queried for use of cerebral revascularization based on ICD procedure codes.

Results: Query of the KID yielded 1449 MMD hospitalizations. After multivariable regression, Hispanic ethnicity (OR 0.50 [95% CI 0.32-0.78, p=0.002) was associated with lack of surgical revascularization. Private insurance (OR 1.57 [1.15-2.14, p=0.004), admissions at medium- or high-volume centers (OR 1.97 [1.39-2.79, p<0.001 and OR 3.24 [2.23-4.60, p<0.001), respectively), and elective hospitalization (OR 3.08 [2.23-4.25], p<0.001) were positively associated with revascularization. Hispanic ethnicity was associated with increased mean (standard error of measurement [SEM]) length of stay by 2.01 ± 0.70 days (p=0.004) and increased hospital charges by $24333.61 ± $7918.20 (p=0.002) despite the decreased utilization of surgical revascularization. Private insurance was associated with elective admission (OR 1.50 [1.10-2.05], p=0.01) and admission to high-volume centers (OR 1.90 [1.26-2.88], p=0.002). Comorbid Sickle Cell Disease, observed in 67.9% of hospitalizations for African-American patients, was associated with the development of in-hospital complications (OR 2.72 [1.49-4.96], p=0.001).

Conclusion: Among pediatric MMD hospitalizations, multiple socioeconomic factors were associated with access to care, whether surgical treatment is provided, and whether in-hospital complications occur. These results suggest that socioeconomic factors are important drivers of healthcare disparities in children with MMD and warrant further study.
227: Brainterns 2.0: Durability of Webinar-based Education and Social Media Beyond the COVID-19 Pandemic

Byron Cone Pevehouse Young Neurosurgeon Resident Award

Randy S. D’Amico MD (New York, New York) Amanda Immidisetti, MBS – Medical Student, Rutgers, Robert Wood Johnson Medical School; Joshua Katz, Medical Student; Ashley Rosenberg, Student; John Boockvar, MD; Rafael Ortiz, MD; David Langer, MD

Introduction: “BRAINterns” is an open access webinar-based education platform that was produced by the Department of Neurosurgery at Lenox Hill Hospital to replace educational opportunities lost during the COVID-19 pandemic and showed previously that webinar-based education was effective at expanding access to careers in medicine, and in particular, neurosurgery. Interest in webinars has persisted despite a return to “in person” learning and BRAINterns 2.0 was established to assess the durability of web-based learning post-pandemic.

Methods: A modified 4-week webinar series was held during July of 2021 with 1 week delivered entirely in Spanish. A retrospective exit survey was distributed to participants and responses analyzed.

Results: A total of 16,045 people registered for BRAINterns 2.0 representing 103 countries. Survey responses were received from 3,765 participants (23% response rate), of which 34% of responders had participated in BRAINterns 1.0. Remarkably, 66% of participants were new. 342 unique students participated in the Spanish-only module. Females represented 81% of respondents. Participants identified that desirable elements of the program were opportunities to hear from women (53%) and people of color (44%) in healthcare. Participants heard about the series through TikTok (n=1251, 33%), Instagram (n=1109, 29%), and by word of mouth (708, 19%) using an ambassador program with 433 international members.

Conclusion: Webinar-based education programs play a valuable role in expanding access to careers in medicine, and in particular neurosurgery, to traditionally underrepresented populations despite a significant return to “in person” learning post-pandemic. Social media and the use of educational ambassadors are effective recruitment tools to improve visibility of educational programs across a diverse population of students. These data support the continued use of these programs throughout neurosurgery and medicine as a whole and hint at the role of web-based learning in the future of education.
228: Substance Use Disorders Are Independently Associated with Hospital Readmission Among Brain Tumor Patients

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Introduction: Research on the effects of substance use disorders (SUDs) on postoperative outcomes within neurosurgical oncology has been limited. The present study sought to quantify the effect of having SUDs on hospital length of stay (LOS), postoperative complications, discharge disposition, hospital charges, 90-day readmission, and 90-day mortality following brain tumor surgery.

Methods: The present study utilized data from patients who received surgical resection for brain tumor at a single institution (January 1st, 2017-December 31st, 2019). The Mann-Whitney U and Fisher’s exact test were used for bivariate analyses of continuous and categorical variables, respectively. Multivariate analyses were conducted using logistic regression models.

Results: Our study cohort included a total of 2,519 patients, 124 (4.9%) of which had at least one SUD. More specifically, 90 (3.6%) patients had an alcohol use disorder, 27 (1.1%) had a cannabis use disorder, and 12 (0.5%) had an opioid use disorder. Our patients had a mean age (± SD) of 55.27 ± 15.14 years, were predominantly female (53.4%), and were mostly White/Caucasian (70.4%). Most patients (95.2%) were not of Hispanic/Latino origin. A majority of patients were married (65.8%) and most had private health insurance (64.9%). On bivariate analysis, 90-day hospital readmission was the only postoperative outcome significantly associated with a SUD (OR=2.21, p=0.0011). When controlling for patient sex, race, marital status, insurance, brain tumor diagnosis, mFI-5 score, and ASA score, SUDs remained significantly and independently associated with 90-day readmission (OR=1.86, p=0.011). The three most common reasons for readmission in our cohort were altered mental status (n=34), weakness (n=32), headache (n=30).

Conclusion: In brain tumor patients, SUDs significantly and independently predict 90-day hospital readmission after surgery. Targeted management of patients with SUDs before and after surgery may optimize patient outcomes and improve the provision of high-value neurosurgical care.
229: Efficiency of Neurosurgical Operating Room According to Nursing Characteristics: A Cost-benefit Analysis

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Introduction: The aim of the study is to assess the impact of operating room (OR) nursing characteristics on operating time in neurosurgery. Subsequently, a cost-benefit analysis (CBA) is performed.

Methods: Operating time of adult elective neurosurgical procedures from 2018 and 2019 were collected and analysed according to surgeons, type of procedures (dichotomised in "simple" and "complex") and OR nursing characteristics (dichotomised in "dedicated" and "not dedicated" to neurosurgery). The related economic evaluation is based on the unitary cost per minute of the OR, the training cost for OR nurses and annual salary of trained OR nurses.

Results: For the category "complex" procedures, robust linear regression shows a reduced operating time of about 20 minutes with "dedicated" OR nursing staff than with "non dedicated" OR nursing staff. No significant difference in operating time was demonstrated among "simple" procedures, with or without "dedicated" OR nursing staff. If all procedures were assisted by "dedicated" OR nursing staff, this would lead to an annual cost reduction of CHF 68’144. CBA is carried out by comparing the current scenario with alternatives scenarios. Alternative scenarios are simulated by changing available human resources (OR nursing staff) and/or change at the organisational level.

Conclusion: This study compares operating time in adult elective neurosurgical procedures (quantitative variable) according to the OR nursing staff characteristics (qualitative variable). "Complex" neurosurgical procedures show a shorter operating time when performed with OR nursing staff "dedicated" to neurosurgery. Several hypothesis can be drawn to explain this phenomenon, possibly relating the level of specialisation of nursing staff to the complexity of the equipment used in neurosurgical procedures. Adapting human resources and changes at organisational level can generate a net benefit for the hospital.
230: The Political Polarization of Surgeons in the United States – an Analysis of Campaign Contributions Throughout the 2020 Election Cycle

Awinita Barpujari (Philadelphia, Pennsylvania) Rohin Singh, BS; Mehul Mehra, BS; Kendra Wang, BS; Benjamin Sherman, BS; Rhea Gopali, n/a; Vamsi Reddy, MD

Introduction: Political engagement by the physician workforce is necessary in order to assure continued representation of their interests in healthcare legislation. Objective: To analyze the magnitude and distribution of political donations across surgical specialties.

Methods: Contribution data were aggregated from the United States Federal Election Commission (FEC) database from January 1st, 2020, to December 31st, 2020. Contributions were labelled as Republican, Democrat, or Independent depending on the committee they were designated to.

Results: For the 2020 election year (January 1 - December 31st, 2020), a total of 53,944 donations were made by surgeons in the United States, amounting to $9,223,350.68. Among all surgical specialties, the top 5 highest number of contributions were made from orthopedic surgeons (15,081), ophthalmic surgeons (14,836), neurological surgeons (7,481), urologists (4,544) and plastic surgeons (4,060). Of these donations, 59.46% (32,107 donations) were made to the Republican Party ($5,420,326), 30.83% (16,644 donations) were made to the Democratic Party ($1,612,775), and 9.71% (5,243 donations) were made to non-partisan (i.e., independent) organizations ($2,190,250). Overall, pediatric surgeons reported the lowest average contribution amount of $59.43 whereas thoracic surgeons reported the highest average contribution amount of $225.19.

Conclusion: Healthcare legislation has an immense impact on how medicine is practiced and utilized. This analysis reveals a high degree of political activity of surgeons across different fields, and geographic regions.
231: Disparities in Screening for Alcohol and Drugs of Abuse After Traumatic Brain Injury: A TRACK-TBI Investigation

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Introduction: This study investigates variability in screening for alcohol and drugs of abuse (DA) after traumatic brain injury (TBI).

Methods: We analyzed data from adult patients enrolled in the prospective TRACK-TBI study cohort following presentation to 1 of 18 level-1 US trauma centers. Clinical and demographic data were reviewed, and participants grouped by those that received alcohol and drug screening and those that did not. Logistic regression modeling was performed to identify factors associated with screening. Results were then validated using the National Trauma Data Bank® (NTDB®).

Results: In the cohort of n=2,436, 1,699 (70%) participants underwent alcohol screening and 1,012 (42%) underwent screening for DA. Participants screened for alcohol and DA were younger on average (41.1y vs. 44.9y vs. p65y (OR=0.56, p=0.003), and Black race (OR=0.75, p=0.045) or Hispanic ethnicity (OR=0.45, p<0.001) were associated with not being screened for alcohol. Similarly, age >65y (OR=0.66, p=0.034) or Asian race (OR=0.52, p=0.013) was associated with not being screened for DA. Black race (OR=1.52, p=0.001) was associated with increased drug screening. The NTDB® data similarly showed decreased alcohol screening for Hispanic ethnicity patients and increased drug screening for Black patients and decreased screening for patients >65y old. When screening was performed, a substantial number of participants >65y were positive for alcohol over the legal limit (12%) and DA (22%).

Conclusion: There are significant biases influencing screening for alcohol and drug intoxication after TBI. We recommend universal screening in patients with suspected TBI, as failure can lead to mismanagement of care, unrecognized withdrawal symptoms, and missed opportunities to address issues related to ongoing substance abuse.
232: The Contrast Between Medical Student Interest in Neurosurgery and the Needs of the Neurosurgical Field of the Future: An Opportunity to Reevaluate Residency Selection Metrics

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Introduction: There are many advantages to having a Neurosurgery physician workforce that better reflects the population served. In this study, we characterize factors involved in medical students’ intention to pursue a Neurosurgery residency. Our aim was to determine the association between student demographics and medical school experiences with the intention to pursue Neurosurgery and serve the underserved.

Methods: Data from the Association of American Medical Colleges (AAMC) Student Record System (SRS) and Graduation Questionnaire (GQ) between academic years 2007-2008 and 2011-2012 were analyzed using chi-squared tests and multivariate logistic regression models.

Results: Our study cohort included 48,096 medical graduates, 607 (1.26%) of whom reported an interest in Neurosurgery. Compared to their peers, students intending for Neurosurgery were less likely to self-identify as female (115 [18.95%] vs. 22,880 [48.18%], p<0.001), report an intention to work with underserved populations (IWUP) (67 [11.07%] vs. 12,467 [26.37%], p<0.001), and participating in global health (133 [21.91%] vs. 14,427 [30.38%], p<0.001) and free clinic (421 [69.39%] vs. 35,180 [74.08%], p

Conclusion: Our study results suggest that efforts to diversify the Neurosurgery training pipeline, and subsequently the future physician workforce, may increase service of underserved patient populations in the field of Neurosurgery.
Gender of the Patient Does Not Correlate with Early Outcomes of Elective Lumbar Fusions

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Introduction: Existing literature demonstrates significant differences in morbidity and mortality measures between males and females undergoing various spinal surgeries, however, studies of lumbar fusion surgery are limited. The objective of this study was to investigate the impact of patient gender on 30-day perioperative outcomes of elective lumbar fusion spine surgery.

Methods: Patients who underwent lumbar fusion between 2015-2019 were reviewed from the ACS-NSQIP database. Propensity score matching was used to determine whether gender had an influence on perioperative complications.

Results: 20,115 PLF cases, 288,923 PLIF/TLIF cases, and 10,152 ALIF/LLIF cases met inclusion criteria and were reviewed. Females were of older age, functionally dependent, taking steroids for chronic conditions, and had a higher body mass index and lower preoperative hematocrit level. Males were more likely to be Caucasian, smokers, and have diabetes mellitus, hypertension, and bleeding disorders. In all cohorts, except for a slightly higher incidence of urinary tract infection in females and myocardial infarction in males, there were no significant differences in other postoperative outcome measures. These measures included complications: pulmonary embolism, blood transfusion, myocardial infarction, stroke, infections, reoperation, death, and hospital course data: operative time, length of hospital stay, ICU admission, non-home discharge, and readmission.

Conclusion: Several differences in demographics and baseline health status exist between males and females undergoing lumbar fusion. When attempting to control for comorbid conditions, we found that sex by itself is not an independent risk factor for higher perioperative morbidity or mortality in patients undergoing lumbar fusion surgery. We believe that these results are important findings for clinicians and spine surgeons while counseling patients undergoing these types of procedures. It is important to address patients’ concerns and to explain that the previously reported inferior perioperative morbidity and mortality outcomes in each gender might be due to differences in baseline health status, and not due to the gender difference itself.
234: Do Neurosurgeons Receive More Patient Complaints Than Other Physicians? Describing Who Is Most at Risk and How We Can Improve

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Introduction: Unolicited patient complaints (UPCs) about surgeons correlates with surgical complications and malpractice claims. Using a large national database, we sought to: 1) compare the distribution and rate of UPCs for neurosurgeons to other physicians, 2) analyze differences in risk of UPCs by individual neurosurgeon factors, and 3) describe the type of UPCs made about neurosurgeons.

Methods: Complaint reports among 36,265 physicians, including 423 neurosurgeons, 8,292 other surgeons, and 27,550 non-surgeons who practiced at 33 medical centers (22 academic; 11 regional) from 1/1/14 – 12/31/17 were coded using a previously validated algorithm used by the Patient Advocacy Reporting System (PARS).

Results: Among 423 neurosurgeons, 93% were male, and 71% practiced in academic medical centers; Neurosurgical subspecialties included: general (25%), spine (25%), tumor (16%), vascular (13%), functional (10%), and pediatrics (10%). Neurosurgeons had more complaints per physician (8.68; 95% CI: 7.68 to 9.67) than non-surgeons (3.40; 95% CI: 3.33 to 3.47) and other surgeons (5.01; 95% CI: 4.85 to 5.17) (p<0.001). Neurosurgeons also had a higher percentage of physicians receiving a UPC (71.6%; 95% CI: 67.3% to 75.9%) than non-surgeons (50.2%; 95% CI: 49.6% to 50.8%) and other surgeons (58.2%; 95% CI: 57.1% to 59.3%) (p<0.001). Factors associated with increased average UPCs were younger age, measured as median medical school graduation year (1990.5 in 0 UPC group vs. 1993 in 14+ UPC group, p = .009) and spine subspecialty (13.4 mean UPCs in spine vs 7.9 mean UPCs in others, 95% CI: 2.3 to 8.5, p<0.001). No difference in complaints was seen in graduates from non-U.S. vs. U.S. medical schools (p=0.605).

Conclusion: Neurosurgeons generate more UPCs than other surgical specialties, and more than two out of three neurosurgeons (71.6%) had at least one UPC during the study period. These results suggest that neurosurgeons have opportunities to reduce complaints and potentially improve overall quality of care.
235: Factors Associated with On-time First-start Elective Neurosurgical Cases

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Introduction: Effective surgical care coordination involves multiple Accreditation Council for Graduate Medical Education (ACGME) core competencies including Patient Care; Systems-Based Practice; Professionalism; and Interpersonal and Communication Skills. Starting operating rooms (ORs) on time is an important hospital quality metric. This study was performed to explore factors associated with On-Time First-Starts (OTFSs).

Methods: We retrospectively reviewed elective first-start cases between June 2015 and August 2021 in neurosurgery operating rooms at our safety-net hospital. Collected variables included operating room (OR) number, day of week, month of academic year, year of study, type of case (cranial or spine), and case duration. Multivariable logistic regression was used to identify associations with OTFS, defined as patient entering the OR within 5 minutes of first start time.

Results: There were 1465 elective first-start cases over the study period in neurosurgery ORs, of which 57% were cranial. OR duration was <2.5 hours in 27%, 2.5-5 hours in 43%, and >5 hours in 30%. Factors associated with poor OTFS included spine case (OR 0.54, 95% CI 0.40-0.72, p<0.001), day of week (Friday vs. Monday OR 0.17, 95% CI 0.11-0.28, p<0.001), OR number (p<0.014), longer case (>5 hours vs. <2.5 hours OR 0.59, 95% CI 0.42-0.83, p=0.003), and year of study (p<0.001). After adjustment for these variables, OTFS rate improved over the academic year (OR 1.08/month, 95% CI 1.04-1.12/month, p<0.001).

Conclusion: OTFS is affected by multiple factors. This metric informs multiple core competencies and may be considered as a tool by which to evaluate individual junior residents and resident teams.
236: Trends in Online Patient Perspectives of Neurosurgeons: A Sentiment Analysis

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Introduction: Patients increasingly rely on physician reviews to inform their provider choices. Sentiment analysis and machine learning techniques quantitatively analyze written prose to understand patient desires from physician encounters. Patient perspectives on their interactions with physicians has been understudied in neurosurgery. The goal of this study was to analyze patient reviews of neurosurgeons to uncover trends between patient ratings of their encounters and word content in their reviews.

Methods: Identification of neurosurgeons and demographic data were collected from 115 ACGME accredited programs using public data. Healthgrades.com was used to obtain online written and star-rating reviews which were analyzed using a machine learning sentiment analysis package. Student’s t-tests compared differences between demographics and outcomes from the sentiment analysis. Multivariate regression was performed to examine associations between sentiment rating and word/word-pair frequency.

Results: 1,284 neurosurgeons were found to have review profiles which consisted of 6,815 reviews. Analysis revealed a significant correlation between sentiment score and star-rating(r^2=0.554,p<0.0001). There were no differences in sentiment score based on neurosurgeon gender but a significant difference was found with respect to age as younger surgeons had more positive reviews(p=0.022). Word frequency analysis showed reviews were less likely to be positive if they included “pain”(OR:0.28,CI:0.24-0.32,p<0.0001) or “rude”(OR:0.03,CI: 0.01-0.06,p<0.0001). Reviews were more likely to be positive when they included “kind”(OR:3.7,CI: 2.6-5.3,p<0.0001), or “pain-free”(OR:3.1,CI:2.1-4.7,p<0.0001).

Conclusion: Top-rated reviews demonstrate the importance of compassion in patient satisfaction. The word “pain” arose for both negative and positive reviews. Therefore, pain management appears to be extremely important to patients, underscoring the importance of guiding patient pain expectations.
237: A Lack of Cost Awareness Amongst Neurosurgeon Faculty and Residents: A Need for Healthcare Sustainability Education to Improve Surgical Stewardship of Operating Room Costs

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Introduction: US healthcare expenditure makes up a major percentage of GDP, and operating rooms are one of the most resource-intensive and waste-generating areas in healthcare facilities. With the increasing demand for surgical procedures, there is a need to focus on supply costs and the ecological impacts among providers.

Methods: An electronic-based survey was distributed to attendings and residents in the University of California San Francisco (UCSF) Department of Neurosurgery. The 16-question survey contains free-text entry to estimate the cost of the 6 commonly used supplies in neurosurgery (e.g. 4-0 Nylon suture pack, microscope drape, ultrasonic aspirator microtip, 4 strip surface electrode) and questions to assess the general opinions of supply cost and waste generation in the OR (measured with a 5-point Likert scale). For cost estimation by the respondents, percent deviation from the supply acquisition cost was calculated.

Results: Thirty-two responses were obtained from 18 attendings and 14 residents. Among the 6 commonly used supplies, respondents on average overestimated the supply cost by 437% (SD ± 568%), particularly for the most inexpensive items. Neurosurgery attendings reported thinking about the supply cost more often than residents (p < 0.001). Similarly, attendings were much more likely to think about waste generation than residents (p = 0.002). 72% of all respondents and 93% residents rated their current knowledge of supply costs as “poor”, 88.2% of the respondents were “somewhat” or “very” interested in obtaining additional training to reduce OR costs and OR waste.

Conclusion: The overestimation and wide standard deviation indicates that residents and attendings are largely unaware of the cost of commonly used supplies in the operating room. Nonetheless, there is a strong interest across all training levels in receiving more education on surgical supply cost and operating room waste generation.
238: Reporting Policies in Neurosurgical Journals: A Meta-science Study of the Current State and Case for Standardization

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Introduction: Reporting quality within the neurosurgical literature is low, limiting the ability of journals to act as gatekeepers for evidence-based neurosurgical care. Journal policies during manuscript submission aim to improve reporting quality. We conducted meta-science study characterizing the reporting policies of neurosurgical journals and other related peer-reviewed publications.

Methods: Journals were retrieved in 7 searches using Journal Citation Reports and Google Scholar. Characteristics, impact metrics, and submission policies were extracted.

Results: Of 486 results, 54 journals were included, including 27 neurosurgical, 27 related topical journals. Thirty-eight (70.4%) adopted authorship guidelines and 20 (37.0%) disclosure standards of the International Council of Medical Journal Editors. Twenty-six (48.1%) required data availability statement and 33 (61.1%) clinical trials registration. Twenty-one (38.9%) required and 11 (20.4%) recommended adherence to reporting guidelines. Twenty (37.0%) endorsed EQUATOR network guidelines. PRISMA was mentioned by 30 (55.6%) journals, CONSORT by 28 (51.9%), and STROBE by 18 (33.3%). Among neurosurgical journals, factors associated with a requirement or recommendation to follow reporting guidelines among neurosurgical journals included impact factor (p=0.0013), Article Influence Score (p=0.0236), Scimago h-index (p=0.0152), Scimago journal rank (p=0.002), and CiteScore (p=0.0023), as well as recommendations pertaining to ICMJE authorship guidelines (p=0.0085), ORCID (p=0.014), clinical trials registration (p=0.0369), or data availability statement (p=0.0047). CONSORT, PRISMA, or STROBE delineations were significantly associated with the mention of another guideline (p<0.01).

Conclusion: Neurosurgical journal submission policies are inconsistent. Frameworks to improve reporting quality are uncommonly utilized. Increasing rigor and standardization of reporting policies across journals publishers may improve quality.
239: Vesalius and His Manikin: An Enduring Impact on Modern Anatomical Teaching

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Introduction: Anatomical teaching has long informed surgical knowledge, experience, and skills. Systematic advances in knowledge of human anatomy and physiology began in Hellenistic Alexandria, with the roots of modern anatomical teaching practices developed by Andreas Vesalius through unique and innovative means.

Methods: We examined the role of Vesalius in developing unique teaching practices through study of primary literature, library archives and classical manuscripts.

Results: Vesalius (16th century A.D.) carried on Herophilus’ model of experiential anatomy for his students, who were enthusiastic partners not only in cadaveric dissection but also the stealing of freshly deceased bodies to learn on, and in performing anatomic demonstrations for prominent persons under Vesalius’ supervision. While Vesalius’ 1543 Fabrica is more famous, the Epitome (published immediately before Fabrica) was the student’s anatomy manual. The Epitome (shorter, portable, foldable, with a leaf height of 55cm) revealed larger, exquisite illustrations of the dissected body. Largely ignored, special sheets within Epitome could be torn out and glued together creating a large, integrated paper manikin revealing organ and anatomic systems. This manikin was used by students tacked up to a nearby wall during dissection and likely represents the first ever 3D anatomical model designed for teaching. These models impacted 16th century surgeons, including Ambroise Paré, who, unknown before, knew Vesalius and acquired permission from Vesalius to use his anatomic illustrations for instructing revolutionary surgical skills. While Galenists such as Vesalius’ French mentor, Jacobus Sylvius, preferred to teach directly from Galen’s writings while students performed dissection for an audience, Vesalius made personal anatomical dissection, not mere observation of dissection, the standard of learning for aspiring students.

Conclusion: Vesalius put anatomical learning in the hands of the dissector, but also led revolutionary teaching methods, such as incorporating 3D models to guide his students, practices that are firmly rooted into the core experience of neurosurgical learning today.
240: The Brain and a Biological Basis for Violence: A Historical Retrospective

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Introduction: This study reviews the history of the surgical management of aggressive behavior and social violence.

Methods: Literature review

Results: On 9/11, 1967, the concept of “low violence threshold” (LVT) was linked to urban rioting. A letter to JAMA by Vernon Mark, William Sweet, and Frank Ervin construed LVT as a medical condition. Subsequently, Life magazine ran a cover story on the psychobiology of violence. In 1970, Mark and Ervin reported successful localization and ablation of areas associated with violence. Sweet commented: "The ability to treat these persons holds out the hope that knowledge gained... can be applied to combat the violence-triggering mechanisms in the brains of the non-diseased".

The introduction of human stereotaxis in 1947 enabled targeting limbic structures relatively safely. Indications included motional "instability" and violence. In the 1950s, José Manuel Delgado modulated aggressive behavior in animals using implanted electrodes. In 1963, he stopped a bull in mid-charge. In 1965, Hirotaro Narabayashi reported successful treatment of violent behavior by amygdalotomy. In 1966, Charles Whitman was found to have tumor around the amygdala after murdering 17 people in Texas. Thus, the case for a biological cause of aggressive behavior was made. Mark and Ervin postulated that the a hyperactive limbic focus could be identified and ablated, and offered proof of principle in man..

Vociferous opposition arose. In 1971, the psychiatrist Peter Breggin, published a condemnation of psychosurgery in the Congressional Record. The same year Anthony Burgess' published A Clockwork Orange and intensified the debate around the social implications of mind control.

Conclusion: Psychosurgery was attacked as a perversion of human rights. Further studies were blocked and the diagnosis of LVT condemned. The putative connection between violent behavior, street violence and a diagnosis justifying surgical intervention was deemed erroneous and retracted.

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Introduction: William Beecher Scoville (1906-1984) was an inexhaustible inventor of surgical instruments and techniques, a founder of neurosurgical associations, an outspoken proponent of psychosurgery, and a prolific teacher. He was "a sort of James Bond in scrubs who loved fast, expensive cars and motorcycles, a demanding dynamo in the operating room, brilliant at his craft." Nevertheless, there lacks biographical information about Scoville in the medical literature. Here, we present the most comprehensive biographical vignette available.

Methods: We interview Scoville's grandson and obtain unpublished family photos, unearth newspaper articles published about him spanning a century, leverage library resources to access historical papers, speak with neurosurgeons who knew Scoville, and obtain primary documents from the World Federation of Neurosurgical Societies (WFNS) and Connecticut Medicine.

Results: First, we describe his early life and career. Scoville originally wanted to be an auto mechanic but was pushed towards medicine by his father. Although initially training in psychiatry and neurology, Scoville eventually found his calling in neurosurgery. Shortly after residency, he founded neurosurgery at Hartford Hospital and served as departmental chief. Second, we outline his myriad surgical and technological innovations. Third, we describe his leadership and founding of neurosurgical societies. Paul Bucy notes that one of Scoville’s greatest achievements was his "almost singlehanded creation of the WFNS." Fourth, we describe Scoville's outsized role in the psychosurgical movement, driven by a personal motivation to cure his wife who suffered from schizophrenia. Scoville also became famous for his surgery on Patient H.M., which led to groundbreaking discoveries about memory.

Conclusion: Scoville met an untimely end while driving, and many awards have been named in his honor. The University of Connecticut neurosurgery chair is endowed in his name. Scoville leaves a legacy of myriad instruments and techniques, a new generation of preeminent trainees, flourishing neurosurgery organizations, hundreds of lobotomies, and countless lives saved.
242: Pre-incisional Radiographic Localization: An Overlooked Contribution by Ralph Bingham Cloward

Mark D. Johnson MD (Cincinnati, Ohio) Charles Prestigiacomo, MD, FAANS, FACS – Professor, Neurosurgery, University of Cincinnati

Introduction: Pre-incisional localization is a ubiquitous practice within spinal surgery and has served as the foundation for modern minimally invasive (MIS) techniques. Here we trace the origins of the use of radiographs to localize the pathologic level at the time of discectomy.

Methods: Pubmed and Ovid databases were searched using the MESH terms “spine” AND “localization”, “wrong level surgery”, “radiographs” for relevant articles. Original manuscripts of landmark studies on approaches to the cervical, thoracic, and lumbar spine for discectomy were reviewed for language on pre-incisional localization.

Results: Wilhelm Rontgen described x-rays in 1895, thirty years later modern spine imaging was catalyzed by Davis’ description of a standard technique for lateral projections. In the 1930’s myelography was preformed to localize herniated discs, however through the 1950’s two spinal levels were routinely explored during discectomy due to ambiguity over the involved level. Lindblom first described discography in 1941, and in 1955 Exum Walker applied this technique to the cervical spine. In his 1958 article, on what is now known as an anterior cervical discectomy (ACDF), Dr. Cloward comments on a case of wrong level surgery due to non-classical surface anatomy. He then goes on to describe a standard technique of cervical diskography performed with the patient under anesthesia in the operating room for localization of the pathologic level prior to skin incision. Contemporary reports by Mixter & Barr, Love, Yuhl, Hulme, Clark & Robinson, Mayfield, and Crafoord on approaches to the cervical, thoracic, and lumbar spine for discectomy lack reporting on pre-incisional localization techniques.

Conclusion: An anterior approach to the intervertebral space masks direct visualization of the pathologic foci, theoretically increasing the risk of wrong level surgery. This may have driven Dr. Cloward to describe the utility of pre-incisional radiographic localization, forming a foundation for progress towards modern MIS techniques.
300: Meralgia Paresthetica: A Large International Study on Prevalence and Treatment Pathways

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Introduction: Meralgia paresthetica (MP) is a mononeuropathy of the lateral femoral cutaneous nerve. No large multinational database study exists that measures the prevalence of MP or the procedures and treatments pursued by those with MP. This study describes its prevalence and the use of the most common procedures pursued.

Methods: A database spanning 11 countries and 66 academic medical institutions during 2002-2021 with a total of 86,224,051 patients was reviewed to study the prevalence of and pursued treatment pathways for MP.

Results: 53,585 (0.062%) of the 86,224,051 patients reviewed were found to have a diagnosis of MP. The mean age at diagnosis was 52.7±14.9, 56% were female, and mean BMI was 33.7±7.9kg/m2, with 8,457 (16%) having a BMI greater than 30kg/m2. 2,408 (8% of the female patients) were pregnant and 422 (0.7%) had a spinal surgery in the past 6 months. After diagnosis, 9,153 (17%) underwent an electromyography (EMG), nerve conduction study (NCS), injection with or without ultrasound guidance, neurolysis with or without ultrasound guidance, or neuroplasty. 5,204 (10%) underwent an EMG/NCS, 3,726 (7%) received an ultrasound guided needle placement, 2,386 (5%) received an injection, and less than 1% each of patients pursued neurolysis or neuroplasty. Of those who had a procedure done, 5,019 (55%) of patients had an EMG/NCS prior to other procedures, and 1,952 (21%) had an injection with or without ultrasound guidance prior to other procedures including EMG/NCS. With progression of the line of treatment and of all the listed procedures, there was a decrease in the percentage of patients who utilized EMG/NCS, and an increase in that of those who utilized neurolysis with or without ultrasound guidance.

Conclusion: An international study of over 80 million patients in 66 academic institutions provides novel information on the prevalence of MP and on the procedures and treatments pursued by those with the diagnosis.
301: A Retrospective Propensity-matched Patient Comorbidity Analysis Comparing Simultaneous versus Staged Bilateral Cubital Tunnel Release Surgeries

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Introduction: Cubital tunnel syndrome is a common peripheral nerve entrapment in the upper arm, often requiring surgical intervention. Simultaneous and staged bilateral cubital tunnel release surgeries are two common pain reducing procedures. The current understanding of preoperative factors and postoperative outcomes regarding these two interventions are limited. The purpose of this study was to determine pre- and post-operative medical comorbidities in patients undergoing simultaneous or staged bilateral cubital tunnel release.

Methods: We performed a retrospective analysis using the TriNetX database. Patients were identified undergoing simultaneous release, where two surgical procedures occurred on the same day, or staged release, where two procedures occurred within 3 months of each other. Propensity score adjustment was used to match cohorts on significant preoperative comorbidities. Post-operative outcomes, such as hematomas, orthopedic aftercare, elbow pain and others were measured within 180 days after surgery. Comorbidity and complication rates were compared between groups using t-tests and unadjusted odds ratios.

Results: This study included 10,776 patients undergoing simultaneous cubital tunnel release and 3,641 undergoing staged release. 3,641 patients remained in each cohort after matching. Overall the staged group had more preoperative comorbidities, including higher incidences of joint pain, hypertensive diseases, lipoprotein diseases, osteoarthritis, substance use disorders, obesity, chronic lower respiratory diseases, and mood/anxiety disorders. After matching, patients undergoing staged releases had significantly higher elbow pain (OR 1.344; 1.124 - 1.607), osteoarthritis post-procedure (OR 1.201; 1.069 - 1.351), and trigger finger (OR 1.411; 1.153 - 1.726). Additionally, patients undergoing simultaneous release had significantly more emergency room visits (OR 1.186; 1.054 - 1.336).

Conclusion: This analysis showed that patients who underwent staged bilateral cubital tunnel release had significantly higher rates of elbow pain, osteoarthritis, and trigger finger after matching for comorbidities. In addition, individuals undergoing simultaneous release had significantly higher emergency room visits.
302: Cortical Representation of Median and Ulnar Nerve Suggests Functional Reorganization Induced by Motor-eloquent Gliomas

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Introduction: Navigated transcranial magnetic stimulation (nTMS) has been applied in routine clinical practice to localize motor-eloquent regions. Yet, the cortical representation of peripheral nerves nor their alterations by gliomas were investigated so far. The current study therefore analyzes the impact and impairment of the median and ulnar nerve in patients with supratentorial tumors by nTMS motor mapping.

Methods: Patients with motor-eloquent gliomas within the left hemisphere were grouped according to the presence of motor deficits. Peripheral nerves-based hand mapping regions were analyzed in grouped patients with (n=20) and without (n=24) motor deficits. Cortical motor representations were analyzed, and corresponding motor evoked potentials (MEP) and their center of gravity (CoG) were calculated for intergroup comparison.

Results: Patient characteristics including gender (p=0.679), tumor type (p=0.158) and age (p=0.97) did not differ between groups. Total motor mapping regions (p = 0.043, 6.47±3.62 cm² vs. 4.69±1.92 cm²) and ulnar nerve-related mapping regions (p = 0.026, 4.03±3.27 cm² vs. 2.33±1.46 cm²) were both significantly extended in patients with motor deficits. Still, median nerve-related mapping regions were larger in patients with motor deficits showing borderline significance (p=0.057, 5.79±3.41 cm² vs. 4.16±2.10 cm²). There were no significant differences in the CoG of the median and ulnar nerve.

Conclusion: The present study shows similar intergroup CoG localizations, indicating the stability of hand motor function’s critical regions. The extended cortical representation of median and ulnar nerve in patients with motor deficits suggests a potential mechanism of compensation and functional reorganization induced by motor-eloquent gliomas.
303: Blood Ethanol Level Confounds Glasgow Coma Scale Interpretation and Increases Health Care Utilization Following Traumatic Brain Injury: A TRACK-TBI Study

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Introduction: This study investigates the effect of alcohol intoxication on the evaluation, management and outcomes in traumatic brain injury (TBI) patients.

Methods: We analyzed data from a subset of adult patients enrolled in the prospective TRACK-TBI study cohort following admission to hospital at 1 of 18 Level 1 US trauma centers. Clinical and demographic data were reviewed and participants were grouped by admission blood alcohol content (BAC).

Results: In the cohort of n=2032, admission BAC was available for 1520 participants; 24.3% of these had BAC>0.08 (+BAC). Rates of recreational drug use were identical for participants with +BAC and those with BAC<0.08 (-BAC). +BAC patients were more likely to have a positive Head CT (66% vs. 54%, p=0.001), a lower GCS at presentation (12 vs. 13, p<0.001), and were more likely to be categorized as severe TBI (GCS 3-8) at ED presentation (26% vs. 17%, p=0.001), despite no difference in injury severity scores (ISS) between the groups. Importantly, the effect of BAC on GCS remained significant on multivariable regression analysis after controlling for Marshall score, other drug use, and non-head ISS (β = -1.25, p<0.001). +BAC patients were more likely to be admitted to the ICU (64% vs. 55%, p=0.004) and underwent more CT scans during their hospitalization (2.52 vs. 2.33, p=0.007). There was no difference in the rates of ICP monitor placement, cranial operation, length of stay, complications, or seizure frequency between the two groups.

Conclusion: Patients with an elevated BAC are scored one point lower on GCS than patients with BACs under the legal limit even after controlling for Marshall score, other drug use, and non-head ISS, leading to more resource utilization (ICU admissions, CT scans). Providers should be aware of the interaction between BAC and GCS in the evaluation and initial management of TBI patients.
304: Full-endoscopic Transforaminal Discectomy Is Non-inferior and Cost-effective Compared to Microdiscectomy for Sciatica: Two-year Results of a Randomized Controlled Trial

Sanford Larson Award for Best Research Award

Pravesh S. Gadjradj MD, PhD (New York, New York) Biswadjiet Harhangi, MD PhD

Introduction: Open microdiscectomy (OM) is the current standard procedure to treat sciatica caused by lumbar disk herniation. Percutaneous transforaminal endoscopic discectomy (PTED) is an alternative procedure which is performed under local anesthesia. Here we report the long-term results.

Methods: A pragmatic, multicenter, non-inferiority, randomized controlled trial was conducted in which patients were randomized between PTED or OM in a 1:1 ratio. The primary outcome is self-reported leg pain measured by the 0-100 Visual Analogue Scale (VAS) with a non-inferiority margin of 5. Secondary outcomes include self-reported ODI, back pain, costs, QALYs, health-related quality of life and self-perceived recovery. Outcomes were measured the day following surgery, at 2, 4, and 6 weeks, and at 3, 6, 9, and 12, 24 months.

Results: A total of 613 were randomized to either PTED (n=304) or OM (n=309). At 24 months, 92% of the patients had follow-up data available. At 24 months, the adjusted between group difference of the VAS leg pain was 7.3 in favor of PTED (17.0 ± 22.4 vs. 24.3 ± 26.5). There was no difference in back pain at 24 months between both groups. All other secondary patient-reported outcomes showed small but statistically more favorable results for the PTED-group. Complications rates and rate of recurrent disc surgery appear similar between both groups. Except for costs of the surgery itself, all other costs were lower for PTED than OM. Cost-effectiveness acceptability curves indicated that the probability of PTED being cost-effective compared with OM was almost 100% for leg pain and QALYs, regardless of the willingness-to-pay.

Conclusion: PTED is non-inferior and cost-effective to OM in the treatment of sciatica at 24 months of follow-up and clinical outcomes appear to be more favorable for PTED albeit not exceeding established MCIDs. Therefore, based on these study results, implementation of PTED as a treatment option for sciatica is warranted.
305: Vagus Nerve Stimulation Paired with Rehabilitation for Upper Limb Motor Function After Ischemic Stroke

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Introduction: Vagus Nerve Stimulation (VNS) paired with rehabilitation has been explored as a potential approach to enhance neuroplasticity and support recovery of upper limb function after stroke. A recent pivotal trial tested the efficacy of rehabilitation paired with VNS or sham VNS in individuals with moderate to severe upper limb impairment 9 months to 10 years after ischemic stroke.

Methods: All participants (n=108) in the multisite, randomized, triple-blind, sham-controlled trial were surgically implanted with the VNS device and then randomized to receive rehabilitation paired with active (n=53) or sham VNS (n=55). Rehabilitation consisted of six weeks of in-clinic therapy involving a blinded therapist triggering active or sham VNS, followed by daily home exercises involving magnet-activated VNS stimulation.

Results: One day after in-clinic therapy, the mean Fugl-Meyer Assessment for Upper Extremity (FMA-UE) score increased by 5.0 points (SD 4.4) in the VNS group and by 2.4 points (3.8) in the sham group (between group difference 2.6, 95% CI 1.0–4.2, p=0.0014). Ninety days after in-clinic therapy, a clinically meaningful response on the FMA-UE score was achieved in 23/53 patients (47%) in the VNS group versus 13/55 (24%) in the control group (between group difference 24%, 6–41; p=0.0098). Adverse events including surgical complications were as expected and less than the reported rates in VNS for epilepsy and depression. There were no significant adverse events related to device stimulation reported. There was one serious adverse event related to surgery (vocal cord paresis) in the control group.

Conclusion: Participants with upper limb deficits after chronic ischemic stroke showed statistically significant and clinically meaningful improvements in motor impairment and function that was 2-3 times greater with VNS compared to intense rehabilitation alone. The trial results support the use of VNS paired with rehabilitation for the treatment of upper limb impairment in chronic stroke.
306: Future Grant Funding and Academic Achievement Following Neurosurgery Research and Education Foundation (NREF) Awards

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Introduction: The Neurosurgery Research and Education Foundation (NREF) provides diverse funding opportunities during the training and early careers of neurosurgeon-scientists. To describe the relationship of NREF to career trajectory and later funding of awardees, metrics of subsequent funding and academic productivity were surveyed.

Methods: A current curriculum vitae (CV) was requested from NREF award recipients from 2000 to 2015. In conjunction with demographic and award characteristics provided by NREF records, career information and research funding data were extracted from collected CVs. Outcomes included NREF funding impact ratio ($ NREF funds: $ subsequent grant funding), time to first grant as principal investigator, practice setting, highest academic position achieved, and academic productivity as assessed by number of publications and H-index.

Results: From 2000-2015, 158 neurosurgeons received 164 NREF awards totaling $8.2 million (M), with $1.8M awarded to 46 Young Clinician Investigators (YCI), $1.5 M to 18 Van Wagenen Fellows (VWF), and $4.9 M to 100 Research Fellowship Grants (RFG). Of all awardees, 73.4% have current academic appointments and the average number of publications and H-index were 71 (±82) and 20 (±15), respectively. The overall response rate to our data request was 70.3%. Of responders, 9% are department chairs, 26% are full professors, 82% received at least one subsequent research grant, and 66% became PI on a subsequent research grant. The respondents cumulatively obtained $776M post-NREF award grant funding, with the most common sources of funding including the NIH ($327M) and foundational awards ($306M). The NREF impact ratio for awardees was $1:$363 for YCI, $1:$75 for VWF, and $1:$42 for RFG. Awardees with NREF projects in functional neurosurgery, pediatric neurosurgery, and neuro-oncology had the highest NREF impact ratios of $1:$183 and $1:$185, and $1:$166, respectively.

Conclusion: This study demonstrates the significant impact NREF funding has on the academic careers of trainee and early career neurosurgeons.
Introduction: The genetic mechanisms regulating intracranial aneurysm (IA) formation and rupture are largely unknown. A number of Mendelian genetic diseases (Ehler’s Danlos, ADPKD, etc.) are associated with IA, but they comprise the minority of cases and are largely restricted to European populations. To identify germline genetic risk factors across ancestral populations, we perform a multi-national genome-wide association study (GWAS) of 155,154 individuals (3,132 cases and 152,022 controls) from the United Kingdom, Finland, and Japan.

Methods: Using GWAS summary statistics from UK Biobank, FinnGen, and Biobank Japan, we perform a meta-analysis of IA, containing ruptured and unruptured cases. Logistic regression was used to identify IA-associated single nucleotide polymorphisms (SNPs), minor allele frequency (MAF) > 3.0x10^-5. Effect size was calculated using the coefficient r. Genome-wide significance was set at 5.0x10^-8.

Results: Our cohort contained 155,154 individuals (3,132 IA cases and 152,022 controls). We identified 4 genetic loci reaching genome-wide significance and report the most significant genetic variants in each loci here: rs73392700 (SIRT3, MAF=0.12, Effect size=0.28, p=4.3x10^-12), rs58721068 (EDNRA, MAF=0.31, Effect size=-0.20, p=4.8x10^-12), rs4977574 (AL359922.1, MAF=0.47, Effect size=0.18, p=7.9x10^-12), and rs11105337 (ATP2B1, MAF=0.38, Effect size=-0.15, p=3.4x10^-8). Expression quantitative trait loci (eQTL) mapping suggests that our top SNP rs73392700 is associated with decreased expression of SIRT3 in arterial tissue. To our knowledge, loci containing SIRT3 and AL359922.1 have not been identified in prior GWAS of IA.

Conclusion: We perform a multi-national GWAS of IA and identify 4 genetic risk loci, including 2 previously unidentified risk loci. Given that activation of SIRT signaling has been shown to protect against cerebral ischemia and we identify decreased SIRT3 expression - at least in part - underlying IA risk, these findings may have direct translational relevance. Identification of high-risk genetic loci across genetic ancestries may instruct population-genetic screening approaches to identify patients with IA.
308: Preclinical Evidence for Deep Brain Stimulation of the Ventral Tegmental Area as a Potential Treatment for Addiction and Hyperdopaminergic Diseases

Philip L. Gildenberg Resident Award

Jason Yuen MSci, BM BCh, MRCS (Rochester, Minnesota) Abhinav Goyal, B.S.; Aaron Rusheen, B.S.; Abbas Kouzani, PhD; Michael Berk, PhD, MBBC, MMED, FF(Psych)SA, FRANZP; Jee Hyun Kim, PhD; Susannah Tye, PhD; Charles Blaha, PhD; Kevin Bennet, MBA PhD; Hojin Shin, PhD; Yoonbae Oh, PhD; Kendall Lee, MD, PhD

Introduction: Dopamine is a key neurotransmitter in many neurological and psychiatric diseases. For example, illicit drugs such as cocaine elevate extracellular dopamine levels in the nucleus accumbens (NAc), which contributes to their addictive properties. The ventral tegmental area (VTA) is a key source of NAc dopamine. We hypothesized that deep brain stimulation (DBS) of the VTA using clinical parameters would suppress NAc tonic extracellular dopamine levels and thus attenuate cocaine-induced dopamine release.

Methods: Male Sprague Dawley rats (approved by IACUC) were anesthetized (urethane, 1.5g/kg, i.p.) and implanted with carbon fiber microelectrodes in the NAc core and bipolar stimulating electrodes in the VTA. Electrode depths were optimized by analyzing VTA stimulation-evoked responses in the NAc with fast-scan cyclic voltammetry (60Hz, 2ms, 0.2mA, 2s). Tonic dopamine levels were then measured using multiple cyclic square wave voltammetry with high spatiotemporal resolution. Control and intervention groups (n=5/group) received saline i.v. (1mL/kg) and then cocaine i.v. (2mg/kg), with only the intervention group continuously receiving DBS-like parameters (130Hz, 200 s, 200mA) in the VTA during saline and cocaine administration.

Results: In the control group, saline did not significantly alter tonic dopamine levels (100.6+/−9.9nM vs 91.3+/−7.5nM; p=0.086); whereas cocaine rapidly increased dopamine levels (100.6  9.9nM vs 156.4  20.9nM, +56%; p=0.012). In the intervention group, VTA DBS not only suppressed tonic dopamine levels (112.4+/−5.2nM vs 65.1+/−10.5nM, −42%; p=0.002), but also alleviated cocaine-induced increases in tonic dopamine levels to small and non-significant levels compared to the new baseline (64.8+/−11.0nM vs 76.0+/−13.4nM, +17%; p=0.091).

Conclusion: Our study demonstrates that VTA high-frequency stimulation suppresses tonic dopamine levels and cocaine effects in the NAc. This may be due to axonal depletion and/or inhibition of DA release in the VTA. These results suggest the exciting possibility of abolishing dopamine release elicited by cocaine and other drugs of abuse by utilizing VTA deep brain stimulation, thereby treating drug addiction.
Decoding Neural Correlates of Speech Production from Intracranial Depth Electrodes

Tessy M. Thomas PhD (Houston, Texas) Latané Bullock, BS, BA; Aditya Singh, BE; Nitin Tandon, MD

Introduction: Brain-computer interfaces (BCI) are a promising tool for restoring speech to dysarthric patients. Prior speech BCI research primarily used electrocorticography (ECoG) to record neural activity, which has limited coverage and carries additional risks associated with large craniotomies. Stereoelectroencephalography (sEEG) can provide distributed coverage of speech and language regions in a less invasive manner than ECoG. However, the potential for decoding speech from sEEG depth electrodes is unclear.

Methods: We obtained sEEG recordings from multiple brain regions as a participant read sentences aloud. Broadband high-gamma (BHG: 70-150 Hz) power was computed for each electrode and annotated with word, phoneme, and articulator labels from speech production. These labels are representative of lexical and motor subprocesses of speech. The classification accuracy of decoding these labels from BHG power was evaluated using a linear discriminant decoding pipeline with 10-fold cross validation. A grid search was utilized with 10% of the data to optimize the peri-annotation window of data used by the decoding model.

Results: While both word and phoneme classification performances were above chance (8.12% across 36 words; 6.04% across 39 phonemes), classification of place (25.02%, 13 classes) and manner (30.74%, 5 classes) of articulation resulted in the highest accuracies. We observed that three regions (ventral sensorimotor cortex, inferior frontal gyrus (IFG), and mid-fusiform cortex) consistently contained the most discriminable information for all three sets of labels. However, neural encoding of articulator-specific features may have been the most separable in these regions. IFG and mid-fusiform cortex also showed increased and distinguishable BHG power for certain labels prior to word-articulation onset, suggesting that such multi-region recordings may play an important role in decoding intended speech.

Conclusion: This within-subject decoding comparison of different speech features sheds light on the distributed representations underlying speech processes, and the advantages of depth electrodes in safely accessing a wide range of cortical regions.
310: Seizure Source Propagation Patterns Mirror Interictal Spike Networks and White Matter Tracts

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Introduction: Treatment of patients with drug resistant focal epilepsy relies upon accurate seizure localization. Ictal activity captured in intracranial EEG (iEEG) has traditionally been interpreted to suggest that the underlying cortex is actively seizing. On the other hand, an emerging hypothesis suggests that seizures may in fact emerge from focal regions, which emit discharges that spread over the surface of the cortex via traveling waves.

Methods: 20 patients underwent placement of subdural electrodes for invasive monitoring at the National Institutes of Health, underwent surgical resection for epilepsy, and had at least 1 year of follow-up. Patients also underwent MRI with diffusion tensor imaging (DTI) for tractography. We measured the time delay in discharge receipt at adjacent electrodes during seizure, and used this time delay to compute the location of the seizure source. Similar algorithms have been used for signal source localization with sparsely-spaced sensors for over a century in geophysics, radar, and acoustics, but our lab is the first, to our knowledge, to use this approach in neuroscience.

Results: In patients with good outcome, but not in those with poor outcome, the seizure source tends to localize to the resection territory. The source is a dynamic entity that moves and evolves over the course of a seizure. Our approach also successfully localizes interictal spikes. Interictal spikes emerge from multiple distinct foci in each patient. Seizures either arise from or travel to interictal spike generators. Finally, both patterns of seizure spread and interictal spike networks respect white matter tracts. Only interictal spike foci which give rise to or receive seizures tend to be mutually connected via white matter tracts.

Conclusion: White matter pathways may be crucial for seizure onset and generalization. White matter pathways which connect interictal spike foci may serve as a possible therapeutic target.

Mahmoud Omidbeigi (Los Angeles, California) Jay Gill, University of California, Los Angeles; Emily Mankin, University of California, Los Angeles; Zahra Aghajan, University of California, Los Angeles; Itzhak Fried, University of California, Los Angeles; Nanthia Suthana, University of California, Los Angeles; Ausaf Bari, University of California, Los Angeles

Introduction: Delay (or temporal) discounting (DD) is a phenomenon where subjects demonstrate a preference for smaller immediate rewards over larger monetary rewards at variable delays. Pathological changes in DD are associated with several psychiatric disorders and behavioral traits including addiction and impulsivity. Understanding the neural basis of DD would guide the development of potential therapies for these disorders. Human imaging studies have identified an extensive network involved in DD processing that includes the amygdala and orbitofrontal cortex (OFC). We hypothesized that amygdala-OFC neuronal firing rates (FR) encode decisions when performing DD. Here, we aimed to evaluate the hypothesis that amygdala-OFC neuronal FR encodes decision-making during a monetary DD using direct human neuronal recordings.

Methods: We recorded single neuronal activity from the amygdala, OFC, and hippocampus in ten treatment-refractory epilepsy patients implanted with depth electrodes for seizure localization. Using a modified DD, participants were asked to repeatedly choose between a smaller immediate reward (less than $10) and a larger delayed ($10 after either 2, 30, 180, 365 days) reward. Trials were compared between those in which the participant chose an immediate reward against trials in which the subject chose the delayed reward.

Results: We isolated 52 amygdala, 50 OFC, and 70 hippocampus units. 16% of units in the OFC and 7.7% of units in the amygdala differentiated (P value

Conclusion: These findings confirm our hypothesis that amygdala-OFC neural activity encodes temporal choice and may underlie pathological conditions such as addiction and impulsivity. We also propose a mechanism for delay encoding in the hippocampus.
Cost Comparison for Open Surgery versus Middle Meningeal Artery Embolization in Patients with Chronic Subdural Hematomas: A Propensity Score Matched Analysis

Natus Resident/ Fellow Award for Traumatic Brain Injury

Mira Salih MD (Boston, Massachusetts) Nadia Mcmillan, MD, PhD; MirHojjat Khorasanizadeh, MD; Santiago Gomez-Paz, MD; Ajith Thomas, MD; Christopher Ogilvy, MD; Justin Moore, MD, PhD

Introduction: Chronic subdural hematoma (cSDH) can be treated with conventional surgery or with a minimally invasive endovascular technique middle meningeal artery (MMA) embolization. The cost profiles of open surgery versus MMA embolization have never been studied.

Methods: Patients treated with open surgery from 2006 to 2019 and those treated with MMA embolization from 2018 and 2020 were identified. Propensity score matching analysis was used to assemble a balanced group of subjects. The detailed hospitalization costs and follow up costs in each group were analyzed and compared.

Results: A total of 341 conventionally treated and 52 MMA embolization cases were identified. After propensity score matching, 33 patients in each group, in total 66 patients were included for analysis. Mean length of stay in conventional surgery group and MMA embolization group were 9.5±8.2 and 7.7±9.9, respectively. Direct procedural cost was significantly higher in MMA embolization group compared with open surgery group ($38255.48±$11859.7 vs $11206.83±$7888.13; P<0.001). Total cost for medication during hospitalization was also higher for MMA embolization group than surgery group ($6888.91±$6525.16 vs $4291.33±$3547.68; P=0.048). No significant difference was found in cost for imaging, ICU care, pharmacy, therapy, labs and emergency unit. Other total miscellaneous cost (such as wound care, pre-op and PACU hold) was higher in open surgery group (P=0.028). However, total hospitalization cost was not significantly different between the two groups (open surgery vs MMA embolization $60598.71±$61315.11 vs $71569.5±$37813.02, P=0.385). No significant differences in duration of follow ups, total number of follows or total costs for follow ups were found (P>0.05).

Conclusion: Open surgery and MMA embolization offer an overall equivalent economic cost-profile for chronic subdural hematoma when matching for potential cost confounders. Direct procedural costs and medication costs were significantly higher in MMA embolization group. However, total hospitalization costs follow up costs were not significantly different.
313: Predicting Intracranial Hypertension in Severe Traumatic Brain Injury Using Physiologic Data

Natus Resident/ Fellow Award for Neurocritical Care

Stephen P. Miranda MD (Philadelphia, Pennsylvania) Vinodh Mohan, BTech, MS; Christian Colon, BS, MS; Ramani Balu, MD, PhD; Ramon Diaz-Arrastia, MD, PhD; Dmitriy Petrov, MD

Introduction: Intracranial hypertension should be avoided after traumatic brain injury (TBI) to prevent secondary injury. Acute intracranial pressure (ICP) crises are often identified late and managed reactively. Accurate prediction of ICP crises would permit clinicians to proactively abort them.

Methods: 61 patients admitted to a Level I Trauma Center with severe TBI (GCS<8) who underwent intraparenchymal ICP monitor placement were retrospectively identified. Continuous data of the following parameters were extracted from each monitoring period (range: 4-96 hours): mean arterial blood pressure, heart rate, blood oxygen saturation, partial brain tissue oxygen tension, and ICP. An ICP crisis was treated as a binary outcome, defined as ICP>22 mmHg for at least 75% of the data within a five-minute interval. Physiologic data preceding each ICP crisis was grouped into four total datasets of one- and two-hour epochs, each with ten- and twenty-minute lead-time intervals before an ICP crisis. Data from 36 patients were randomly split into 70% for training and 30% for testing. Three machine learning algorithms were trained to predict ICP crises: light gradient boosting, extreme gradient boosting, and random forest. Accuracy and area under the receiver operating characteristics curve (AUC) were measured to compare performance. The most predictive algorithm was similarly trained and tested on 25 additional patients with severe TBI. Hyperparameter tuning using grid search was performed to avoid overfitting. Precision, recall, F1-score, and accuracy were measured.

Results: The random forest model demonstrated highest accuracy (0.82-0.88) and AUC (0.86-0.88) across all four datasets. Further validation testing revealed high precision (0.81), relatively low recall (0.49), and overall strong predictive performance (0.61, F1-score; 0.82, accuracy) for ICP crises.

Conclusion: Our algorithm can provide accurate and timely forecasts of ICP crises after severe TBI. If validated and implemented in clinical workflows, this algorithm can enable earlier intervention for ICP crises and potentially improve outcomes after severe TBI.
Comparison of Intraoperative Ultrasound with Postoperative MRI in the Assessment of Spinal Cord Decompression from a Posterior Approach

Charles Tator Spinal Cord Injury Resident Research Award

Timothy Chryssikos MD, PhD (Baltimore, Maryland) Jesse Stokum, MD, PhD – Resident, Neurosurgery, University of Maryland Medical Center; Phelan Shea, MD – University of Maryland Medical Center; Abdul-Kareem Ahmed, MD – Resident, Neurosurgery, University of Maryland Medical Center; Joshua Olexa, MD – Resident, Neurosurgery, University of Maryland Medical Center; Mani Sandhu, MD, MHS – Neurosurgery – Yale University; Gregory Cannarsa, MD – Resident, Neurosurgery, University of Maryland Medical Center; Nicholas Caffes, MD – Resident, Neurosurgery, University of Maryland Medical Center; Jeffrey Oliver, MD – Resident, Neurosurgery, University of Maryland Medical Center; Kenneth Crandall, MD – Assistant Professor, Neurosurgery, University of Maryland Medical Center; Charles Sansur, MD, MHSc – Professor, Neurosurgery, University of Maryland Medical Center; Gary Schwartzbauer, MD, PhD – Associate Professor, Neurosurgery, University of Maryland Medical Center; Bizhan Aarabi, MD – Professor, Neurosurgery, University of Maryland Medical Center

Introduction: Adequate decompression of the traumatically injured cervical spinal cord is associated with upward AIS grade conversion. In this study, the adequacy of spinal cord decompression was judged by intraoperative ultrasound at the time of laminectomy and retrospectively compared with the findings of postoperative MRI.

Methods: 29 patients with traumatic cervical spinal cord injury were retrospectively reviewed. Adequacy of spinal cord decompression was judged intraoperatively by the attending surgeon using the Aloka Prosound Alpha 7 Ultrasound System (Hitachi Aloka Medical, Ltd., Wallingford, CT). One trauma radiologist and four neurosurgeons retrospectively reviewed postoperative MRI studies to determine adequacy of decompression.

Results: Mean age was 59.4 (24 males, 5 females). AO Spine injury morphology (primary) was A0 in 14, B2 in 1, B3 in 12, and C in 2. AIS grade was A in 8, B in 4, C in 4, and D in 13. Mean number of laminectomy levels was 3.6. Ultrasound prompted additional level of laminectomy in 3/29 cases (10.3%) beyond the initial preoperative plan. At the end of all 29 cases, intraoperative ultrasound was judged to have demonstrated adequate spinal cord decompression. Mean and median time between surgery and postoperative MRI was 21:42 and 16:15, respectively. When postoperative MRI is considered the gold standard for evaluating surgical decompression, intraoperative ultrasound had an overall accuracy of 79.31% (23/29). Four of six (66.67%) cases that falsely predicted decompression occurred at the C2-3 level. Additionally, Four of six (66.67%) cases that falsely predicted decompression occurred in motor complete (3 AIS grade A and 1 AIS grade B) patients.

Conclusion: Intraoperative ultrasound is an auxiliary technique for evaluating decompression of the injured cervical spinal cord from a posterior approach but requires further prospective investigation. Intraoperative ultrasound may eventually serve as a reasonable, cost-effective alternative to postoperative MRI for the evaluation of spinal cord decompression.
315: Egfrviii Mutation Detection in Plasma Derived Extracellular Vesicle RNA

StacheStrong Award

Syeda Maheen Batool MD (Boston, Massachusetts) Leoonora Balaj, PhD – Associate Professor, Neurosurgery, Massachusetts General Hospital; Bob Carter, MD, PhD – Chief of Neurosurgery, Neurosurgery, Massachusetts General Hospital

Introduction: Glioblastoma (GBM) is the most common primary malignant brain tumor in adults with a median overall survival of 12-15 months. EGFR amplification is reported in 57% of GBM cases. Approximately, 30-50% tumors characterized by EGFR amplification are positive for EGFRvIII mutation. This prototypic oncoprotein, with a unique fusion sequence may serve as a potential tumor-specific target for immunotherapy. Furthermore, it can be utilized as a minimally invasive biomarker for blood-based diagnosis and monitoring of GBM.

Methods: Here, we developed a novel digital droplet PCR (ddPCR) assay to detect EGFRvIII deletion in plasma derived extracellular vesicle RNA (evRNA) of patients with glioma. A systematic approach was adapted to optimize the overall workflow in order to minimize false-positives whilst retaining high sensitivity. Reverse transcription was tailored to minimize the inhibitory role of RNA secondary structures using chemical additives. Measures were taken to ensure maximal ddPCR efficiency, including annealing temperature optimization, removal of inhibitors using cDNA purification, and use of additives to improve separation of mutant events.

Results: Performance of this assay was evaluated in tumor tissue and matched plasma samples. We first report that using our optimized assay, the prevalence of EGFRvIII in EGFR amplified gliomas is as high as 81% (95% CI, 77.0% - 85.0%) while the control group was determined at 35% (95% CI, 32.0% - 36.0%), similar to prior published reports. In patient plasma samples, we detected the EGFRvIII deletion in discovery and blinded validation cohorts, with an overall sensitivity of 73% (95% CI, 63.7% - 81.8%) and a specificity of 98% (95% CI, 87.6% - 100%) compared with gold-standard tissue biopsy.

Conclusion: Altogether, this study demonstrates the feasibility of detecting EGFRvIII mutation in patient plasma using a highly sensitive, novel ddPCR assay. The overall workflow is completed in less than 24h.
316: Matched Comparison of Hearing Outcomes After Stereotactic Radiosurgery or Observation Alone in Vestibular Schwannoma Patients

Lunsford & Leksell Radiosurgery Award

Zane Schnurman MD, MBA (New York, New York) Douglas Kondziolka, MD; John Golfinos, MD

Introduction: There remains considerable debate regarding the optimal treatment strategy for VS patients with intact hearing. Prior investigations comparing hearing outcomes after stereotactic radiosurgery (SRS) or a watch-and-wait strategy are limited by small sample sizes and no control for confounders. This study aimed to compare hearing outcomes for VS patients managed with SRS and observation, while controlling for potential confounders using propensity score matching.

Methods: 318 unilateral VS patients with serial audiometric data were reviewed. One-to-one nearest neighbor propensity score matching was used to compare 198 patients with initial serviceable hearing (99 after SRS, 99 observation alone) and 116 with initial Class A hearing (58 after SRS, 58 observation alone), matching between treatment cohorts by initial hearing status, initial tumor volume, patient age, and patient sex. Kaplan-Meier survival methods were used to assess and compare risks of hearing loss.

Results: There was no significant difference in loss of Class A hearing between the observation or SRS group (p = 0.88), with median time to loss of Class A hearing of 27.2 months (95% CI 16.8 – 43.4) for SRS patients and 29.2 months (95% CI 20.4 – 62.5) for observed patients. For loss of serviceable hearing, there was no significant difference in survival between observed and SRS patients (p = 0.18), with a median time to loss of serviceable hearing of 37.7 months (95% CI 25.7 – 58.4) for SRS patients and 48.8 months (95% CI 38.4 – 86.3) for observed patients.

Conclusion: After controlling for potential confounders, there was no significant difference in risk of losing Class A or serviceable hearing after SRS or with observation alone. These findings underline that SRS does not incur an increased risk of hearing loss. Combined with known tumor control rates, SRS may be the most conservative hearing preservation strategy for VS patients with intact hearing.
317: Single-cell Transcriptomic Analysis of Sporadic Cushing’s Adenomas and Adjacent Gland Reveals Novel Tumorigenic Pathways

Integra Foundation Award

David T. Asuzu MD, PhD, MPH (Bethesda, Maryland) Reinier Alvarez, MD; Patrick Fletcher, PhD; Debjani Mandal, PhD; Prashant Chittiboina, MD, MPH

Introduction: Sporadic pituitary adenomas are one of the most common human pathologies, found in more than 10% of the general population. The transcriptome of intra-vital human pituitary gland is unknown. We hypothesized that the normal human pituitary gland transcriptome would help identify novel mechanisms of tumorigenesis in sporadic adenomas.

Methods: We surgically annotated adenomas and en-route adjacent normal glands. We performed single cell RNAseq (scRNAseq; 10X Genomics Chromium 3’) and captured 28,724 cells in 6 patients (3 CD and 3 non-CD; 5 pairwise). We also performed bulk RNAseq (bRNAseq; Illumina Nextseq) in 7 patients (5 CD and 2 non-CD; 5 pairwise) and DNA methylation (DNAmeth) analysis in 6 patients (3 CD and 3 non-CD; Illumina Infinium MethylEPIC 850k probes). Transcriptomic/epigenomic data were analyzed with R packages and custom Python pipelines. Pairwise differential expression analysis was performed between cell types.

Results: We created the first transcriptomic map of the post-natal human pituitary gland at the single cell resolution and identified canonical resident pituitary cell classes in the human adult pituitary gland. CD corticotrophs displayed dominant expression of PCSK1, PPP1R17, EGLN, RSPO3 and PMAIP1 compared to surrounding tissues. We termed these Cushing’s adenoma signature genes. We confirmed over-expression of PCSK1, PPP1R17, RSPO3 and PMAIP1 by independent bRNAseq of CD and non-CD adenomas. DNA methylation analysis demonstrated hypomethylation at the promoters of PMAIP1, PPP1R17 and RSPO3 but not PCSK1 or EGLN1 in Cushing’s disease adenomas compared to non-Cushing’s adenomas.

Conclusion: We mapped the transcriptome of the adult human pituitary gland, identified novel signature genes for Cushing’s and highlighted DNA methylation as an epigenetic mechanism of transcriptional activation in several Cushing’s adenoma signature genes. We provide novel, targetable mechanistic pathways fort therapeutic intervention in Cushing’s disease.
318: Systemic Adoptive-Cell-Transfer Immunotherapy for High-Grade Meningiomas Targeting NY-ESO-1 Using TCR-transduced T-Cells

Synaptive Preuss Research Award

Matthew Z. Sun MD (Los Angeles, California) Joey Orpilla, B.S. – UCLA; Erick Contreras, B.S. – UCLA; Janet Treger, Ph.D. – UCLA; Sara Khattab, B.S. – UCLA; Jeremy Reynoso, B.S. – UCLA; Myungjun Ko, Ph.D. – UCLA; Marisa Imbroane, B.S. – UCLA; Linda Liau, M.D., Ph.D. – Chair, Neurosurgery, UCLA; Robert Prins, Ph.D. – UCLA; Richard Everson, M.D. – UCLA

Introduction: High-grade meningiomas have poor prognosis and lack effective adjuvant therapy. Cancer-Testis-antigens(CTA) are ideal immunotherapy targets, and NY-ESO-1 is the most frequently expressed CTA in meningiomas. Because NY-ESO-1 is expressed intracellularly, it's targetable by engineered T-cell-receptors-transduced T-Cells(TCRs) rather than by CAR-T's. To evaluate the feasibility of systemic adoptive-cell-transfer (ACT) for meningiomas, we tested the efficacy of NY-ESO-1 TCRs' against meningiomas in vitro and in vivo.

Methods: Immunohistochemistry for NY-ESO-1 was performed on meningioma samples (Grade I-III) from the OR. TCRs were generated by double-transfection with supernatants from PG-13 retroviral packaging cells encoding HLA-A2.1–restricted NY-ESO-1-specific TCR. We utilized HLA-A2.1 positive human primary meningioma cultures LB3750(Grade I) and LB3621(Grade II), and immortalized cultures SF1335(Grade I) and CH157-HLA-A2.1(Grade III) in vitro and in vivo. The CH157(Grade III) native culture lacked HLA-A2.1 and served as negative control. Immunodeficient NSG mice were intracranially implanted with meningioma cells, treated with ACT, and assessed for overall survival.

Results: NY-ESO-1 expression positively correlated with tumor grade in 30 samples based on immunohistochemistry(p=0.039). Grade I tumors SF1335 and LB3750 had low NY-ESO-1 expression; grade II LB3621 had moderate NY-ESO-1 expression; and both grade III tumors CH157 and CH157-HLA-A2.1 had high NY-ESO-1 expression. Co-culturing increasing meningioma grade tumors SF1335, LB3750, LB3621 and CH157-HLA-A2.1 with TCRs at a ratio of 1:1 resulted in 15%, 15%, 30% and 70% additional cytolysis in vitro compared to control T cells at 20 hours(all p<0.001), respectively, whereas the negative control CH157 had 0% increase. Systemic(intravenous) ACT of TCRs significantly increased median overall survival in NSG mice bearing intracranial xenografts of CH157-HLA-A2.1 by 30%(p=0.0001) and compared to SF1335 by 20%(p=0.06).

Conclusion: TCRs induced more effective NY-ESO-1/HLA-A2.1-specific cytolysis in high-grade compared to low-grade meningiomas in vitro, and systemic ACT statistically significantly increased survival in vivo for high-grade meningioma. Targeting NY-ESO-1 may be a clinically feasible immunotherapeutic strategy to treat high-grade meningiomas.
400: Development of Cerebral Vasospasm Following Traumatic Intracranial Hemorrhage: Incidence, Risk Factors, and Clinical Outcomes

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Introduction: Limited evidence exists characterizing the incidence, risk factors, and clinical associations of cerebral vasospasm following traumatic intracranial hemorrhage (tICH) on a large scale.

Methods: Weighted discharge data from the National Inpatient Sample were queried to identify tICH patients from 2015 to 2018 and subsequently those developing angiographically-confirmed cerebral vasospasm. Multivariable logistic regression analysis was performed to identify significant associations between clinical covariates and the development of vasospasm, and a tICH vasospasm predictive model (tICH-VPM) was generated based on the effect sizes of these parameters.

Results: Among 5,880 tICH patients identified, 375 developed vasospasm corresponding to an incidence of 6.4%. Multivariable adjusted modeling determined the following clinical covariates were independently associated with the development of PTV, among others: age (aOR 0.98, 95% CI 0.97 to 0.99; p<0.001), admission Glasgow Coma Scale score < 9 (aOR 1.80, 95% CI 1.12 to 2.90; p=0.015), intraventricular hemorrhage (IVH) (aOR 6.27, 95% CI 3.49 to 11.26; p<0.001), tobacco smoking (aOR 1.36, 95% CI 1.02 to 1.80; p=0.035), cocaine use (aOR 3.62, 95% CI 1.97 to 6.63; p<0.001), fever (aOR 2.09, 95% CI 1.34 to 3.27; p=0.001), and hypokalemia (aOR 1.62, 95% CI 1.26 to 2.08; p<0.001). The tICH-VPM achieved moderately high discrimination, with an area under the curve of 0.75 (sensitivity 0.61, specificity 0.81). Decision tree analysis identified IVH as a parent node and hypokalemia and age sub-groups as secondary nodes in a clinical prediction algorithm for vasospasm. Development of vasospasm was independently associated with lower likelihood of routine discharge (aOR 0.60, 95% CI 0.45 to 0.78; p<0.001) and extended length of hospital stay (aOR 3.53, 95% CI 2.78 to 4.48; p<0.001), but not with mortality.

Conclusion: This large-scale evaluation of of vasospasm in tICH identifies common clinical risk factors for its development and establishes an independent association between the development of vasospasm and poorer neurological outcomes.
Leveraging Machine Learning to Identify an Intraoperative Mean Arterial Pressure Threshold for Neurological Improvement in Patients Undergoing Decompressive Surgery for Acute Spinal Cord Injury

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Introduction: This retrospective study strives to utilize machine learning to define an optimal intraoperative mean arterial pressure (MAP) threshold after spinal cord injury (SCI) guided by clinical outcomes.

Methods: Seventy-four surgically treated patients were retrospectively analyzed as part of a longitudinal study assessing outcomes following SCI (TRACK-SCI). Each patient underwent intraoperative hemodynamic monitoring with recordings at five-minute intervals. Baseline clinical characteristics and hemodynamic parameters including type of vasopressor used, dose, drug-related complications, average intraoperative MAP, and time spent in extreme MAP ranges (<76 mmHg or >104 mmHg) were collected. Outcomes were evaluated by measuring the change in ASIA neurological impairment scale (AIS) score between admission and discharge. Features most predictive of an improvement in AIS score at discharge were determined statistically by generating random forests with 10,000 iterations. Recursive partitioning was used to establish clinically intuitive thresholds for the top features.

Results: There was a significant improvement in AIS scores by an average of 0.71 levels (p=0.0018) at discharge. Using random forests, the features most important in predicting this improvement were the amount of time intraoperative MAPs were in extreme ranges, the Brain and Spinal Injury Center AIS score at admission, and the average intraoperative MAP. Recursive partitioning revealed that patients with average intraoperative MAPs between 80 and 96 mmHg throughout surgery had improved AIS scores at discharge. Conversely, 12/12 of patients with MAPs >96 mmHg had unchanged or worse scores. A threshold of 93 minutes was identified as the maximum amount of time that should be spent in extreme MAP ranges. Finally, the use of dopamine as compared to norepinephrine was associated with substantially higher rates of significant cardiovascular complications (50% vs. 25%, p<0.001).

Conclusion: An intraoperative average MAP across surgery time between 80 to 96 mmHg is associated with improved neurological function at discharge among patients undergoing emergency surgical intervention for SCI.
402: PbtO2 Modification Using Designed Cardiac-Gated ICP Modulation Generated by an Intracranial Pulsating Balloon: A Swine Model Study

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Introduction: Brain oxygenation improvement is a sought-after goal in neurocritical care patients. Previously, we have shown that CBF improvement by cardiac gated ICP modulation using an intracranial pulsating balloon is feasible in a large animal study. We sought to explore specific ICP modulation protocols in order to augment as well as to reduce brain oxygenation using a clinically used PbtO2 probes to examine the validity of ICP modulation in relation to the cardiac cycle.

Methods: A cardiac-gated intracranial balloon pump in which volume, timing, and duty cycle of balloon inflation could be altered was used. Several protocols were tested in a swine model of normal and elevated ICP attained by continuous intracranial fluid infusion with continuous monitoring of systemic and cerebral physiological parameters, while measuring PbtO2.

Results: 5 swine were studied, at normal physiological status (ICP<20 and PbtO2 > 15) and at reduced brain perfusion status (ICP>20 and PbtO2<15). ICBP activation generated a consistent modification of the ICP waveform. In reduced brain perfusion status, while systemic physiological parameters remained constant, late-diastolic-early systolic (LaDES, Inflation/deflation) protocol showed elevation in PbtO2 (9% above baseline, p<0.01) with ICP reduction (12% under baseline, p<0.01). Early-systolic-late-diastolic (ESLaD, Inflation/deflation) protocol resulted in PbtO2 reduction (4% under baseline, p <0.01) coupled with ICP increase (5% above baseline, p <0.01). No significant changes were observed in PbtO2 at baseline of normal physiology status.

Conclusion: Specific protocols of ICBP activation can be used to modify cerebral oxygenation, and raise PbtO2 beyond ischemic threshold, specifically if brain metabolism and oxygenation are impaired. Study supports the concept of late diastolic pressure rise coupled with early systolic pressure drop as a potential mechanism of arterial inflow augmentation, compared with opposite activation mode which hampers oxygenated blood from entering the cranium. Further studies are required to assess the feasibility of ICP modulation in clinical practice.


Introduction: Medical advancements have led to an increased life expectancy, and thus an expanding and aging population. This study analyzes complications and outcomes in elderly patients following SCI using the established multi-institutional prospective registry Transforming Research and Clinical Knowledge in SCI (TRACK-SCI).

Methods: TRACK-SCI was queried for elderly individuals (>65 years old) with traumatic SCI from 2015 to 2019. Primary outcomes of interest included total hospital length of stay (LOS), perioperative complications, postoperative complications, and in-hospital mortality. Secondary outcomes included disposition location, and neurological improvement based on American Spinal Injury Association (ASIA) impairment scale at discharge. Multivariable regression analysis was performed.

Results: In the cohort of n=40 elderly patients, 30% of patients presented as an ASIA-A. Our study demonstrated a mortality rate of 10%. Every patient in this cohort experienced at least 1 complication, with an average of 6.6. The most common complication categories were cardiovascular (average of 1.6 complications) and pulmonary (average of 1.3) complications. Overall, 30 (75%) patients required vasopressor treatment for mean arterial pressure (MAP) goals maintenance. The use of vasopressors correlated with increased cardiovascular complications (p<0.001). Three patients (7.5%) of the total cohort had an improved ASIA grade upon discharge.

Conclusion: Given the increased frequency of cardiovascular complications associated with vasopressor use in elderly SCI patients, caution may be warranted when targeting MAP goals in elderly SCI patients. Further investigation around the use of lumbar drains to guide strict spinal cord perfusion pressure thresholds is warranted.
404: Prophylactic Levetiracetam and the Incidence of Early Post-traumatic Seizures Among Pediatric Patients with Traumatic Brain Injury

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Introduction: Traumatic brain injury (TBI) is the leading cause of death and disability in children. Anti-epileptic drugs (AEDs) are administered to both adults and children with TBI as the standard of care to prevent seizures 0-7 days post-trauma. However, in pediatrics, its effectiveness, appropriate dosing, and possible side effects are not well understood. This study examines the use of levetiracetam in a post-TBI pediatric population.

Methods: We performed a retrospective review of 361 pediatric patients with TBI at the Milton S. Hershey Medical Center between January 2011 and June 2021. Factors analyzed included age, sex, weight, injury mechanism, GCS, dosage, date of levetiracetam administration, presence of seizures, and medical and surgical management. The primary outcome was the prevalence of seizures within 7 days of injury.

Results: On logistic regression, the risk of having a seizure on levetiracetam is significantly increased in younger patients (p= .005; OR .687 [.528-.894]) and in those who had seizures prior to administration of levetiracetam (p= .001; OR 5.801 [2.004-16.789]). There were no significant differences noted in sex, etiology of TBI, the severity of TBI, intubation status, intracranial procedures, or dosage of levetiracetam. Furthermore, higher doses of levetiracetam (>10mg/kg) were more likely to be administered to younger patients (p= <.001; OR .907 [.867-.948]) and in those who had intracranial procedures (p=.021; OR 1.985 [1.110-3.551]). Seizures before levetiracetam administration as well as the severity and etiology of injury were not significant predictors of dosage.

Conclusion: Our study shows that younger age and presence of a seizure prior to levetiracetam administration are associated with increased risk of seizures despite prophylaxis. Increased dosage does not provide a significant decrease in seizure risk. However, younger patients are more frequently placed on a higher dosage. Further studies are needed to determine the optimal use of levetiracetam in managing pediatric patients with TBI.
405: Factors Associated with Hemorrhagic Progression of Cerebral Contusion After Traumatic Brain Injury: A Multicenter Study

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Introduction: Head trauma (TBI) is one of the most disabling traumatic injuries, capable of causing cognitive, physical, and behavioral dysfunctions. It encompasses several types of insults to the brain, and cerebral hemorrhagic contusion is one of the most serious. In this context, hemorrhagic contusion progression (HPC) is a secondary injury process related to the enlargement or appearance of a hemorrhagic parenchymal contusion due to delayed bleeding and corresponds to the enlargement of the hemorrhagic component of cerebral contusions visualized on imaging.

Methods: This is a prospective, multicenter study in which TBI victims admitted to the emergency room. Variables were collected related to demography, pathological history, medications in use, trauma characterization, laboratory tests, cranial CT on admission and controls, clinical management in the first 72 hours, prognostic scores in TBI and clinical judgment of the Neurosurgery team regarding the risk of HPC. The outcome was hemorrhagic contusion progression (HPC) defined as a relative increase of at least 30% and an absolute increase of at least 10 ml.

Results: There were 242 patients admitted with traumatic brain injury between January 2019 and May 2021. The patients were mostly male (n=214, 88.4%), with a mean age of 45 ± 20.8. In the analysis of the factors linked to cranial CT, the cisterns were compressed in 20.5% of the HPC group compared to 12.4% of the individuals in the non-HPC group, and they were obliterated in 12.8% of the HPC group x 0.8% of the non-HPC group (p=0.002).

Conclusion: A statistically significant association was observed between the development of HPC and SAH. There was a higher prevalence of SAH and the involvement of cisterns (compressed or obliterated) in patients who developed HPC. However, only SAH and obliterated cisterns remained as independent variables associated with HPC.
406: A Long-term Follow-up Study of Racial Disparities in Employment Status Following Traumatic Brain Injuries

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**Introduction:** Racial disparities in outcomes have been documented in patients with traumatic brain injury (TBI). Despite having equal access to care, minorities have been reported to have less community reintegration and less rates of competitive employment following TBI compared to non-Hispanic whites (NHW). The purpose of this study was to re-examine the progress we have made in community reintegration via examining employment rates of blacks and non-Hispanic whites following TBI.

**Methods:** Patients tracked in the Southeastern Michigan Traumatic Brain Injury System (SEMTBIS) were inquired. All patients hospitalized between 2001 and 2012 were included. Injury severity, as measured by CT scan findings and initial GCS, as well as employment status at years 1, 2, and 5 post-injury were assessed. Employment status categorized as competitive paid employment or non-competitive paid employment.

**Results:** NHW had higher rates of competitive employment (69.3%) compared to blacks (53%), and medium-high level of education (44.3%) compared to blacks (21.2%) prior to TBI. The of Black patients who were non-competitively employed pre-injury were more likely to regain non-competitive employment post-injury than NHW participants of the same pre-injury employment status at follow-up years 2 and 5 (p < 0.05 and p<0.01). NHW had significantly better competitive post-injury employment outcomes at follow-up years 2 and 5 (p < 0.005 and p<0.01). NHW patients experienced increasingly better competitive paid employment outcomes throughout the 5 years post-injury. Black patients experienced similar non-competitive employment outcomes than NHW regardless of follow-up year. Moreover, these employment outcome disparities were not explained by racial differences in injury severity.

**Conclusion:** Black patients experience worse employment outcomes than their NHW counterparts after TBI in higher education and competitive employment. Injury severity does not account for these differences. Further research is indicated to better understand the upstream factors driving these disparities and how social determinants of health affect these racial differences in long-term employment outcomes following TBI.
407: Impact of Age on Post-Operative Outcomes in Children with Type I Chiari Malformations Receiving Posterior Fossa Decompression: An Analysis of the Park-Reeves Syringomyelia Research Consortium

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Introduction: Chiari type I malformation (CM-I) with syringomyelia in pediatric patients may warrant a posterior fossa decompression (PFD), yet the impact of patient age at time of surgery has not been well-established.

Methods: We analyzed a registry of children with CM-I and syringomyelia across 36 institutions participating in the Park-Reeves Syringomyelia Research Consortium. Patient age was stratified as 0-3, 4-6, 7-9, or 10+ years, at time of initial PFD. Primary outcomes-of-interest included six-month postoperative complication risk (assessed after each surgery with sufficient post-surgical follow-up) and long-term redo PFD surgery risk (following the initial PFD). Multivariable logistic and Cox regressions were used to assess contribution of age to risk of complications and redo PFD, respectively.

Results: The cohort included 884 children (58.1% female) receiving 959 PFD with or without duraplasty. Overall, 70 (7.9%) patients required at least one redo PFD. Of all PFD performed, 99 (10.3%) were at age 0-3, 195 (20.3%) at age 4-6, 176 (18.4%) at age 7-9, and 489 (51.0%) at age 10+. Of all surgeries, 82.6% were performed with duraplasty; duraplasty was not associated with patient age. Postoperative complications were more common among the youngest patients (46.1% [age 0-3] vs 34.4% [age 10+]) and, adjusting for surgery characteristics, hospitalization features, and demographics, young age was significantly associated with increased risk of postoperative complications (age 0-3 vs 10+, OR=1.13, 95%CI 1.01-1.27). On multivariable analysis, risk of repeat PFD was higher among patients receiving surgery at a younger age, particularly among those aged 0-3 (vs 10+, HR=3.32, 95%CI 1.61-6.85). Risk of repeat PFD within two years was significantly higher for patients age 0-3 at initial surgery (20.0% [95%CI 8.9-29.8%] vs 5.7% [age 10+, 95%CI 3.1-8.2%]).

Conclusion: Extremely young patients with CM-I receiving PFD may be at higher risk of postoperative complications and redo PFD compared to children older at time of surgery.
408: Redefining Pediatric Cervical Spine Ossification Patterns

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Introduction: The seminal textbooks that define the ossification timeline of the cervical spine are flawed: frequently outdated, based on limited data, and have a wide range and variability. Most of these references do not mention the timeline for the ossification process for the subaxial cervical spine. Given that there are studies which attempt to estimate a pediatric patient’s age based on the ossification patterns, it is critical to have the most accurate description of the ossification pattern of the cervical spine.

Methods: In this IRB approved retrospective study, we analyzed a database of 100+ axial CT scans of the cervical spine in a normal pediatric population (0-18 years). Imaging was reviewed by two independent physicians who defined the presence of synchondroses at C1, C2, and C3.

Results: For C1, the presence of 1, 2, and 3 synchondroses were identified at 7.4, 4.8, and 1.9 years. At C2, 1, 2, and 3 synchondroses were identified at 6.1, 3.4, and 2.2 years. At C3, 1, 2, and 3 synchondroses were identified at 2.9, 2.0, and 0.4 years.

Conclusion: The presence of synchondrosis has been implicated in part of the mechanism for the increased flexibility and compliance of the pediatric cervical spine, and therefore it is critical to understand the ossification timeline. C3 consistently is the first to fuse, followed by C2, then C1. 95% of all patients have ossification of C1, C2, and C3 at 12, 9, and 5 years. This should update the previous parameters that state C1 completes fusion by 6-9 years. This is clinically important when reviewing pediatric trauma patients, in order to identify patients with fractures versus patients who have a high chance of having synchondroses. Future research will validate the current study in a prospective fashion.
409: Machine Learning Automated 3D Segmentation of Transependymal Cerebrospinal Fluid in Pediatric Patients

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Introduction: Transependymal movement (TEM) of cerebrospinal fluid (CSF) is a recognized imaging finding of periventricular hyperintensities on FLAIR MR sequences, often located adjacent to the frontal and occipital horns of the lateral ventricles. However, the specific ependymal regions capable of transmitting CSF migration have not been quantified nor have they been associated with disease pathology.

Methods: We retrospectively identified patients from St. Louis Children’s Hospital between 2008 and 2019 who had TEM of CSF on MRI. We excluded patients who underwent supratentorial craniotomies or were missing FLAIR and/or high-resolution T1 MR sequences. We generated volumetric WMH segmentation maps using a custom convolutional neural network-based deep-learning algorithm for automated detection of white matter hyperintensities (WMH) in 3D-FLAIR images. Individual WMH segmentation masks were co-registered to their respective high-resolution T1 images, then spatially normalized onto an MNI template for comparison. Image analysis was performed by creating a WMH frequency distribution map for each pathology with voxel intensity values indicating the WMH frequency in the standard brain template.

Results: 74 patients (40 females (54%), mean age 10.0 years old) met inclusion criteria. Pilocytic astrocytoma (PA) (n=21) and medulloblastoma (MB) (n=10) were among the most common diagnoses. PA was associated with a higher mean TEM of CSF in the region anterior to the frontal horns compared to MB (0.86 vs. 0.61, p<0.0001) while the opposite was seen in the region posterior to the occipital horns (0.43 vs. 0.61, p=0.0181). TEM of CSF was also frequently seen in the region rostral to the tela choroidea of the roof of the 3rd ventricle near the habenular commissure. Intensity in this region did not differ significantly between groups.

Conclusion: Our quantitative segmentation of TEM of CSF identifies region-specific ependymal areas that transmit CSF which differ based on tumor pathology. Neoplasms in particular may interact with distant brain regions through the CSF.
410: Comparison of the Safety and Efficacy of Hemispherotomy Techniques for Drug-resistant Epilepsy: A Systematic Review and Individual Patient Data Meta-analysis

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Introduction: In contemporary neurosurgery, hemispherectomy approaches favoring disconnection are termed hemispherotomy and preferred over more resective variants due to lower complication rates. Hemispherotomy techniques can be categorized by their plane of approach: lateral versus vertical. It is unclear whether one approach has superior efficacy or safety, thus, technique selection is dictated by surgeon preference. Since surgical technique is a modifiable factor that invariably influences outcomes, this meta-analysis aimed to determine whether differences in seizure outcomes or complications between hemispherotomy approaches exist.

Methods: CINAHL, Embase, PubMed, and Web of Science were searched from inception to September 9th, 2020 for studies reporting data for individual hemispherotomy patients. Articles were included if they reported time-to-seizure recurrence or complications including hydrocephalus, hemorrhage, infection, or mortality. Chi-squared test compared frequencies. Multivariate mixed-effects Cox regression controlling for known predictors of seizure outcome, including seizure onset age, bilateral EEG and MRI abnormalities, and etiology, was performed to identify predictors of time-to-seizure recurrence.

Results: Thirty-two articles reporting on 495 patients, of which 247 (49.9%) and 248 (50.1%) underwent lateral and vertical hemispherotomy, respectively, were included. More patients were seizure free at last follow-up in the vertical cohort (70% vs. 82%, p=0.002). Both approaches had similar rates of hydrocephalus (10.3% vs. 10.5%, p=1.000), hemorrhage (3.9% vs. 1.5%, p=0.625), infection (3.2% vs. 2.0%, p=0.808), and mortality (0.0% vs. 1.2%, p=0.313). Lateral hemispherotomy (HR=4.64, 95% CI=1.05-20.5, p=0.043) and contralateral MRI abnormalities (HR=3.47, 95% CI=1.14-10.56, p=0.029) independently predict faster time-to-seizure recurrence. Incomplete disconnection according to postoperative MRI was more common with the lateral approach (41% vs. 13%, p=0.034).

Conclusion: While vertical and lateral hemispherotomy have similar complication rates, real-world data suggests vertical approaches confer more durable seizure freedom. Lower rates of incomplete disconnection with vertical approaches may explain superior outcomes and be attributed to more complete disconnection of the perithalamic tissue and frontobasal region along the vertical plane.
411: Artificial Intelligence and Machine Learning Predicts the Need for Intervention in Premature Neonates with Intraventricular Hemorrhage

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Introduction: Among premature neonates with intraventricular hemorrhage (IVH), compare ventricular morphology from cranial ultrasound (cUS) of 2D slices and clinical data to predict need for cerebrospinal fluid (CSF) diversion in the setting of symptomatic post-hemorrhagic hydrocephalus (PHH).

Methods: This is a retrospective study of patients with IVH of prematurity (<37 weeks). We collected demographical information along with known predictors of need for CSF diversion. For image analysis, we chose the first cUS set provided by our institution regardless of transfer status. For each patient, we manually segmented a 2D cUS slice through the foramen of Monro for the area of intraventricular bleed, lateral ventricles, and germinal matrix hemorrhage. We extracted morphological features from the images, and compared the importance of features within differing predictive models.

Results: Fifty-eight neonates met inclusion criteria. Per protocol guidelines at our institution, twelve of 58 obtained intervention (temporary or permanent) for symptomatic PHH. We attained statistical significance for clinical data (birth weight, gestational age, age at presentation, all p < 0.05) that was included in the artificial neural network (ANN, e.g., machine learning algorithm). Using the ANN, cUS features and clinical data outperformed clinical data alone with an accuracy of 0.75 versus 0.67, respectively.

Conclusion: Evaluation of the first cUS in premature IVH patients presenting to an institution through image segmentation and machine learning can monitor for the need of intervention. This may be helpful for early surveillance. Further segmentation tasks, which extract more morphological features from images, also increase accuracy. Future work should be aimed at fuller analysis of images for increased accuracy in predicting clinical intervention.
412: Obstetric Management and Maternal Outcomes Among Patients with Myelomeningocele

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Introduction: With improvements in neurosurgical and obstetrical care, more women with myelomeningocele (MCC) are delivering children. Unfortunately, since the first published case report in 1973, the data on peripartum and postnatal outcomes are limited. The aim of this study was to examine obstetrical practices and outcomes in women with MMC in the United States.

Methods: A large, national database of privately insured patients, Clinformatics Data Mart Database (OptumInsight, Eden Prairie, Minnesota) was examined from 2001 to 2019. Women with MMC, were identified by ICD9 and 10 codes. Additional diagnoses of paraplegia, urinary retention and urinary incontinence were used as confirmatory codes. Demographic characteristics, type of delivery method, type of anesthesia, perinatal complications and postnatal outcomes including need for neurosurgical intervention were extracted.

Results: We identified 2,153 patients with MMC who had 2,724 deliveries. Compared to a cohort of known MMC patients, the positive predictive value of the diagnosis codes used to create this cohort from the national database was 75% (95% CI: 66.6 – 83.4%). Caesarian section (c-section) was the primary modality of delivery in 49% of patients (n= 1,335; 95% CI 47.2 – 50.8%) which is higher than the national average rate of c-section, 31.7%. Fifteen deliveries, or 1.1% of all vaginal deliveries, required forceps assistance, which is also higher than the national average of 0.5%. Abortion or miscarriage occurred in 26 (0.9%) delivery related hospitalizations. Shunt revisions occurred during 2.3% of hospitalizations for deliveries (n=58).

Conclusion: This study represents one of the largest database reviews of obstetric practices and outcomes in women with MMC in the United States. Women in this cohort were 1.6 times more likely to undergo c-section and twice as likely to undergo instrument assisted delivery than the national average. Additionally, neurosurgeons should be aware of the risk of shunt malfunction in the peripartum period in women with MMC.
413: The Impact of Social Risk Factors and Cerebral Spinal Shunting Procedures in Children

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Introduction: Socioeconomic adversity among children has been shown to be a subclinical biomarker of disease and associated with worse overall health, however, has not yet been established as a risk factor for increased healthcare utilization or poor postprocedural outcomes, namely among those undergoing cerebral spinal fluid (CSF) shunting.

Methods: In an all-payer claims database, records were analyzed to identify children undergoing CSF-shunting with and without social risk factors. Patients with social risk factors were compared to those without to study the implications of these factors on the rates of CNS-infection, shunt-related interventions, mortality, and the number of radiographic examinations performed within 5-years of their index-shunting procedure.

Results: Among the 5,420 children identified as having undergone first-time shunting procedures, 263 (4.9%) were identified to have social risk factors. Children identified to have social risk factors had an increased odds of central nervous system (CNS) infection (Odds Ratio [OR] 2.06, 95% Confidence Interval [CI] 1.45-2.91), revision (OR 2.43, 95% CI 1.89-3.12), and mortality (OR 2.86, 95% CI 1.23 to 5.72). The mean number of computed tomography (CT) studies (14.60±17.78 vs. 7.88±24.37, p...)

Conclusion: Social risk factors are associated with increased healthcare utilization, CNS-infection, shunt-related-interventions, and mortality. The identification of children with social risk factors can help to distinguish families for potential interventions to improve outcomes associated with patients undergoing CSF-shunting through intensive social programs.
414: How the Brain Anticipates: From Neurons to Networks

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Introduction: Anticipation of future events is a core component of human decision making. Measuring the neural processes that underlie anticipation is an important step towards developing novel closed-loop neuromodulation therapies for conditions that feature pathological decision making (e.g., opioid addiction, or problem gambling). However, measuring biomarkers of anticipation in the human brain is challenging because it requires recording neural activity with high spatio-temporal resolution and broad anatomical sampling.

Methods: To overcome these challenges, we studied 23 patients implanted with 2,934 intraparenchymal electrodes in widespread anatomical regions for intracranial encephalography (iEEG) evaluation of medically refractory epilepsy as they performed a simple anticipatory response task. We studied high frequency activity (70-200 Hz power) from bipolar electrode pairs as a surrogate of local population neural spiking activity. We combined quantitative modeling of response time distributions, unsupervised hierarchical clustering of electrode-level neural activity patterns and measurement of network state dynamics to link anticipatory processing with neural activity.

Results: We found that anticipatory processing was reflected in widespread neural firing patterns with distinct timing, form, and anatomical source locations. Although preparatory movement networks showed evidence of anticipatory increases in activity prior to stimulus onset, subject-to-subject variability in anticipatory behavior was not limited to these preparatory motor networks, but instead reflected in emergent network-wide neural dynamics across functionally heterogeneous networks.

Conclusion: These results suggest anticipation alters information processing across distributed brain networks rather than specific local neural populations. Thus, future efforts that aim to develop closed-loop neuromodulation technology for pathological decision making might benefit from broad anatomical sampling rather than targeting specific neural populations.
415: Discrimination of Normal Brain Tissue from Dysplastic Tissue in Focal Cortical Dysplasia Using Raman Spectroscopy

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Introduction: Focal cortical dysplasias (FCD), characterized by abnormal cortical architecture, are the most common cause of refractory focal epilepsy in the pediatric population. Only surgery can remove FCD lesions to cure focal epilepsy, but surgical success depends on the ability to resect the lesion completely while minimizing damage to perilesional normal tissues. Therefore, it remains extremely challenging to remove FCD lesions completely. Thus, better methods of delineating FCD lesions and their borders are needed to improve post-surgical seizure outcomes. Raman spectroscopy uses laser to induce vibrations in the molecules of a sample and the scattered radiation is then used to characterize the tissue composition. The goal of this in vitro prospective study is to use Raman spectroscopy to discriminate between normal brain tissue and dysplastic tissue using specimens of focal cortical dysplasia patients.

Methods: 70 stained sections of biopsy specimens from 35 patients with focal epilepsy were acquired and assessed by a pediatric neuropathologist. Raman map points were recorded from targeted abnormal regions with structures characterizing FCD: dysmorphic neurons, balloon cells and cortical dyslamination.

Results: With more than 2000 spectra acquired, significant spectral differences were observed between the dysplastic tissue regions and normal regions in the cortex. Indeed, FCD tissues exhibit significantly increased spectral at 1302 cm⁻¹, 1660 cm⁻¹ and 1156 cm⁻¹ peaks, indicating a higher intensity of protein components and abnormal stretching mode of protein, lower quantity of lipids and most interestingly, a higher intensity of glycogen in the dysplastic tissues, respectively. In addition, the fingerprint region between FCDIIa and FCDIIb differs in intensity in specific biomolecules.

Conclusion: These findings suggest the potential spectral fingerprint of dysplastic tissues as an aid to delineating FCD borders and improve surgical resection.
416: Normative Intracranial EEG Maps Epileptogenic Tissues in Focal Epilepsy

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Introduction: Accurately delineating the epileptogenic network is crucial to planning surgery for drug-resistant focal epilepsy. Many patients with discordant or inconclusive imaging findings undergo intracranial EEG (iEEG) monitoring to define the seizure onset zone (SOZ). We hypothesize that using a normative iEEG atlas to benchmark deviations from normal brain dynamics provides a data-driven method to identify surgical targets.

Methods: We constructed a normative iEEG atlas by augmenting a 106-subject normative iEEG atlas from the Montreal Neurological Institute (MNI) with 60 subjects carefully selected from the Hospital of Pennsylvania (HUP). This rigorously harmonized MNI-HUP normative iEEG atlas aggregates 2360 electrodes placed in brain areas located outside of epileptogenic tissue. We map each electrode to a predefined parcellated region of interest (ROI) and compute normative distributions of spectral power and coherence in each ROI. To demonstrate clinical utility, we selected a separate set of 2577 abnormal iEEG channels implanted in irritative or seizure onset areas across 60 patients. We quantitatively compared epileptic iEEG channels to normative data and mapped patient-specific abnormalities.

Results: We demonstrate that for seizure onset zones (SOZ) within the mesial temporal lobe, measures of connectivity abnormality provide greater distinguishing value than univariate measures of abnormal neural activity. We also find that patients with longer diagnoses of epilepsy have greater abnormalities in connectivity (Pearson r = 0.25, p = 0.03). By integrating measures of both single-channel activity and inter-regional functional connectivity, we predict SOZ versus normal brain (area under the curve = 0.78) with better accuracy compared to either group of features alone.

Conclusion: This study establishes a data-driven method to guide epilepsy surgery by aggregating iEEG studies. We believe that expanding this atlas with data from a large number of epilepsy centers, comparing individual patients to both normative data and matching abnormal patterns, will greatly improve this method and patient outcomes over time.
417: Cm/pf DBS Alleviates Tics in a Rat Model of Tourette’s Syndrome via Striatal Microcircuits


Introduction: Deep brain stimulation (DBS) of the thalamic centromedian parafascicular complex (CM/Pf) is an effective treatment for medical refractory Tourette's syndrome (TS). Here we test the hypothesis that CM/Pf DBS reduces tic frequency by modulating the thalamostriatal circuitry to induce striatal dopamine release in a rat model of TS.

Methods: TS was modeled in the rat by slowly infusing the GABA-A antagonist bicuculline into the striatum to elicit characteristic facial and forelimb tics. DBS-like stimulation (charge-balanced 0.4ms, 400mA waveform at 130 or 50 Hz) was applied in the parafascicular nucleus (analog of human CM/Pf) with an implanted bipolar concentric electrode. Striatal electrophysiological recording, and fast-scan cyclic voltammetry to record phasic dopamine release, were performed in response to 2-4s stimulation. Multiple-cyclic-square-wave voltammetry was used to record changes in tonic dopamine levels and tics were measured in response to 30min stimulation. Tics were monitored by electromyography in the face and forelimb. Pharmacologic studies were performed with nicotinic cholnergic antagonist mecamylamine, dopamine1-receptor (D1-R) antagonist SCH23,390, and D2-R antagonist sulpiride.

Results: Pf DBS elevated power in the alpha and beta frequency bands and decreased power in the delta and theta bands, which correlated with concurrent tic cessation. In addition, 2-4s DBS elicited 100.4±12.2 nM phasic dopamine release with concurrent tic cessation. Continuous (30min) DBS increased tonic dopamine levels by 10.6±3.0 nM while concomitantly reducing tic frequency by 28.4±6%. Nicotinic cholnergic receptor antagonism reduced theta and beta power changes, reduced phasic dopamine release, abated tonic dopamine elevations, and reversed tic reduction by DBS. Antagonism of D1-R and D2-R did not affect tonic dopamine activity. However, D2-R antagonism, but not D1-R, reversed the therapeutic effect of DBS.

Conclusion: These findings suggest that striatal dopamine release mediates the therapeutic mechanism of CM/Pf DBS. Further, our pharmacologic studies suggest that a disynaptic mechanism through cholnergic interneurons mediates dopamine release acting at D2-R.
418: A Randomized Trial of MR-Guided Focused Ultrasound Bilateral Medial Thalamotomies for Chronic Trigeminal Neuropathic Pain

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Introduction: MRgFUS thalamotomy has proven successful in patients with essential tremor, with a potentially impactful application in pain syndromes, as the medial thalamus is implicated in affective pain pathways. Trigeminal neuropathic pain is one such syndrome which can stem from trauma, infections, tumors, or iatrogenic causes, and is notoriously refractory to medical and surgical treatments. MRgFUS was thus proposed to perform medial thalamotomies for refractory trigeminal neuropathic pain.

Methods: This was a prospective, double-blinded, randomized trial in 10 subjects with trigeminal neuropathic pain, with sham procedures serving as controls. Subjects underwent assessments by a pain psychologist and pain management clinician, including the Numeric Pain Rating Scale (NPRS), patient-reported outcome measures (PROMIS), patient global impression of change (PGIC), and MRI at baseline, 1 day, 1 week, 1 month, and 3 months. Patients underwent bilateral MRgFUS thalamotomies targeting the central lateral nucleus. Controls underwent identical procedures with energy output disabled. Primary efficacy outcome measure was between-group differences in pain intensity (NPRS) at baseline and 3 months. Controls were eligible for treatment as an open-label extension of the study after 3 months. Lesion volumes were analyzed on 3-month MRIs.

Results: Mean NPRS change from baseline to 3 months was -0.2 1.1 for treated patients and 0.8 1.3 for controls; between-group change was not significantly different. PROMIS measures demonstrated decrease in “pain interference with enjoyment of life” at 3 months, but otherwise were not significantly different. Treated patients reported improvement more often than controls across PGIC assessments (8 vs 3); none reported worsening. MRIs demonstrated effective thalamic ablations with mean lesion volume of 77.0 35.1 mm3. Adverse events in the treatment group were all mild.

Conclusion: MRgFUS bilateral medial thalamotomy is safe and well-tolerated for refractory trigeminal neuropathic pain. While the overall group comparison was not significant, there were responders to the procedure in this small pilot study, warranting additional investigation.
419: Treating Hydrocephalus by Shunting to the Venous Intracranial Sinus - Sinushunt Project
849502 Supported by the European Union’s Horizon 2020 Programme

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Introduction: An ideal shunt for hydrocephalus treatment must maintain intracranial pressure within normal limits, drain the cerebrospinal fluid (CSF) without creating symptoms of overdrainage independent of body position/physical activity, and present a long-lasting solution without the need for reoperation. All these criteria can be met by shunting CSF to the venous intracranial sinus and several attempts have been made. However, in previous studies the silicone drain outlet in the sinus tended to become occluded, sometimes within a few months. This 15-patient study investigates an outlet designed to drain to the sigmoid sinus without occlusion or thrombus formation.

Methods: Patients diagnosed with hydrocephalus are treated with a standard ventricular drain, low pressure uni-directional valve and an outlet positioned at the junction of the jugular foramen/sigmoid sinus. The outlet is protected by a nitinol structure to hold it in the middle of the vein preventing it from touching the wall and keeping it away from the endothelium. Introduction of the outlet is via standard vascular techniques. Lung scintigraphy is performed pre-operatively and at 6-month endpoint. Shunts are tested for patency at 3 months and at 6 months by water column test. The study is expected to finish by December 2021.

Results: 9 patients have been operated as of 1 November 2021, of which 4 have passed 6-month endpoint and 2 have reached the 3-month milestone. All shunts were patent at follow-up, and clinical effect was satisfactory. No subdural effusion or haematomas were detected. No occlusions of the sigmoid sinus or jugular vein were observed. Lung scintigraphy at 6 months follow-up showed no signs of lung emboli.

Conclusion: Initial results are promising: the nitinol frame prevents outlet occlusion without provoking thrombosis. This study represents an important first step in demonstrating that shunting to the intercranial venous sinus is a safe, simple and long-lasting solution.
420: Thalamus Gates Progression of Mesial Temporal Seizures by Modulating Thalamocortical Synchrony

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Introduction: The anterior nucleus of the thalamus (ANT) regulates hippocampal seizures in experimental models of temporal lobe epilepsy (TLE) by altering synchronization, but a clinical study demonstrating this is lacking. Therefore, the objective of this study is to investigate thalamocortical coupling during seizures.

Methods: Following IRB approval, adults (N≥10) with suspected TLE undergoing stereotactic electroencephalography (SEEG) implantation were recruited prospectively. Seizures in which ANT recruitment was robust were selected for functional thalamocortical analyses using measures of synchrony and direct electrical stimulation of the ANT.

Results: Seizure onset was characterized by a decrease in alpha-band thalamocortical synchrony (p=0.024) whereas termination was characterized by an increase in theta-band synchrony (p<0.001). In addition, seizure termination in the thalamus displayed a stereotypical electrographic pattern of transition between a spike-and-wave signal to slow wave delta activity in the post-termination period. Furthermore, ictal thalamocortical synchronization patterns varied by seizure type (p=0.001). Electrical stimulation of the ANT with low and high frequencies produced distinct, opposite effects in the cortex: Low frequency stimulation resulted in cortical activation whereas high-frequency stimulation resulted in deactivation.

Conclusion: ANT facilitates seizure onset by decreasing inhibitory influences on the hippocampus. As the seizure evolves, inhibition within thalamotemporal networks is restored by theta synchrony that contributes to seizures termination. The ANT gates information flow to the temporal lobe, and this endogenous mechanism can be targeted for identifying stimulation parameters for thalamic deep brain stimulation in TLE.
421: Outcomes of Patients Undergoing Single-level Arthroplasty versus Anterior Lumbar Interbody Fusion

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Introduction: Lumbar degenerative disc disease (DDD) is most commonly treated with instrumented fusion, whereby there is a reduction in pain as a result of reduced motion. There is a concern that short segment fusions might increase risk of additional surgical intervention at adjacent segments due, in part, to biomechanical-fulcrum-motivated factors. To this end, artificial discs have been developed with the hopes of mitigating the potential motivators of adjacent segment disease and ultimately additional surgery. However, to date, no studies have compared the rates of post-operative complications and need for surgery at adjacent segments among patients who have undergone anterior lumbar interbody fusions (ALIF) versus those undergoing lumbar arthroplasty (LA).

Methods: Patient records were analyzed to identify individuals with lumbar fracture who underwent single level ALIF and LA for the treatment of DDD. Rates of complications following surgery, need for additional lumbar surgeries after the index procedure, length of stay (LOS), and opioid utilization following surgery were assessed. Logistic regression models were developed to evaluate factors that may independently impact rates of postoperative complications at 30-days and additional lumbar surgeries at 5-years following index-surgeries.

Results: A total of 846 patient’s records, were analyzed. No significant differences were noted among the rates or odds of postoperative need for subsequent lumbar surgeries at 5-years when comparing patients who underwent ALIF to those who underwent LA (8.24% vs. 5.67%, p=.18; Odds Ratio (OR) 0.70, 95% Confidence Interval (CI) 0.41-1.19, Log-Rank p=.4). Rates and odds of postoperative complications accessed at 30-days, were not found to be significantly different (p=.64).

Conclusion: The notion that single-level fusions might biomechanically motivate the development of adjacent segment disease that requires surgeries is not supported by our findings. This lends support that perhaps natural history of DDD might play more of a role in adjacent segment procedures rather than biomechanics alone in the lumbar spine. Further study should be undertaken to further evaluate this concept.
422: Comparison of Proximal Junctional Kyphosis Rates After L4 versus L3 Pedicle Subtraction Osteotomies

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Introduction: Some surgeons advocate pedicle subtraction osteotomy (PSO) at L4 for better corrective surgery. However, the rate of proximal junctional kyphosis (PJK) has not been compared to PSO at L3.

Methods: Patients with L3 or L4 PSO by 4 surgeons from 2005-2019 were retrospectively studied. Inclusion criteria were single-level L3 or L4 PSO, minimum 1-year follow-up, and comparison 36° films. Demographic variables, operative factors, and radiographic measurements were collected. Univariate analysis using was used to determine any baseline differences. Multivariate regression was performed to identify possible confounding variables.

Results: One-hundred three (64 female) met inclusion criteria. The mean age was 65.6 years, and mean follow-up was 3.28 years (1.01-8.09). PSO at L3 was performed in 75 patients and at L4 in 28 patients. Univariate analysis demonstrated significant differences in pelvic incidence (PI) (p = 0.03) between L3 PSO (47.98 ± 11.48) and L4 PSO (55.48 ± 15.95). There were no baseline differences in sex (p = 0.89), body mass index (p = 0.68), age (p = 0.80), estimated blood loss (p = 0.65), or surgical time (p = 0.75). Pre-operative SVA, central sacral vertical line (CSVL), pelvic incidence (PI), lumbar lordosis (LL), and PI-LL were not different between groups (all p values >0.05). Multivariate logistic regression showed no differences in rates of proximal junctional kyphosis after correcting for possible confounding variables (p=0.59). Furthermore, there was not any differences with respect to changes from pre-op to post-op L3 versus L4 SVA, CSVL, SS, PT, LL, PI-LL, and osteotomy angular correction.

Conclusion: We did not detect a difference in PJK rates between PSOs performed at L3 and L4.
423: Malpractice Litigation in Elective Lumbar Spinal Fusion Surgery: A Review of the past 50 Years

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Introduction: Spine surgery is disproportionately impacted by medical malpractice litigation. The purpose of this study is to provide a granular assessment of malpractice litigation in elective lumbar spinal fusion and identify factors associated with verdict outcomes.

Methods: Westlaw (Thomson Reuters, New York), a legal database containing litigation records for federal and state cases, was queried for verdict and settlement reports pertaining to lumbar spine surgery from 1970 to 2021. Data were collected regarding patient demographics, defendant specialty and training, state, procedure type, hospital type, alleged cause of malpractice, injury sustained, case outcome, and monetary award.

Results: A total of 322 cases were identified, yielding 181 (67%) defendant and 65 (24%) plaintiff verdicts, with 26 (9%) settlements. There were 77 single-level and 66 multilevel fusions, with defendant verdicts exhibiting a greater percentage of anterior fusion approaches compared to plaintiff verdicts (31% vs. 15%, p=0.056) with similar amounts posterior and lateral fusion approaches. The median award for plaintiff verdicts was $1.1 million ($8300-$22 million), while the median settlement award was $835,000 ($150,000-$23 million). Most cases were filed against surgeons operating in the private setting (defendant verdict: 100, 78%; plaintiff verdict: 54, 83%, p>0.05). A greater percentage of defendant verdicts were fellowship-trained when compared to plaintiff verdicts (73% vs. 48%, p>0.05). The most commonly alleged liabilities were intraoperative error (n=96, 36%) followed by failure to obtain informed consent (n=86, 27%). The most common injuries reported were excessive pain and suffering (n=133, 36%) followed by permanent deficits (n=98, 27%).

Conclusion: In our cohort, defendant verdicts had a greater percentage of surgeons practicing at academic institutions with fellowship training compared to plaintiff verdicts, suggesting a potential protective effect of these variables in the specialized field of spine surgery. As failure to obtain informed consent was the second most common alleged liability, clinicians must highlight patient education prior to surgery.
424: Using Smartphone-Based Accelerometry to Classify Peri-Operative Course and Outcomes in Spine Surgery

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Introduction: Spine surgery outcomes are currently assessed using patient-reported outcome measures (e.g., ODI, EQ-5D). However, such tools are limited by the inherent subjectivity of data collected at discrete timepoints without regard to each patient’s unique clinical course. In contrast, patient mobility data streamed from smartphones with built-in accelerometers offer a more objective and continuous measure of surgical outcome.

Methods: 14 patients who underwent elective decompressive surgery of the lumbar spine were included. Patient data was remotely exported from the Apple Health mobile application. A time series analysis was conducted on steps-per-day across a 2-year peri-operative period. Using a data-driven approach, up to five distinct temporal epochs were identified from each patient’s time series: 1) pre-operative baseline; 2) acute pre-operative decline, indicating either an acute event or an acute-on-chronic decline; 3) immediate post-operative recovery; 4) full recovery; 5) secondary decline from fully-recovered state.

Results: Mobility data revealed acute pre-operative decline in 10 patients (onset 11.8 ± 2.9 weeks prior to surgery); the remaining 4 patients demonstrated a chronic presentation (no Epoch 2). These presentations were concordant with clinical documentation in 13/14 patients. Following the immediate post-operative recovery period (duration 20.6 ± 4.9 weeks), 11 of 14 patients achieved a full recovery, indicating a return in mobility to levels commensurate to or better than Epoch 1. Of these, 2 patients subsequently experienced a secondary decline beginning 27.2.1 ± 9.9 weeks after surgery. During the full recovery period, subject-level daily steps improved by 80% ± 33% relative to before surgery (p = 0.002).

Conclusion: The peri-operative clinical course of spine surgery patients was classified from smartphone-based mobility data using a data-driven method. Our findings highlight the potential of using mobility data for pre-operative counseling, as an objective surgical outcome measure, and for remote follow-up beyond the immediate post-surgical period.
425: Evaluation of a Preoperative Adverse Event Risk Index for Patients Undergoing Spinal Tumor Surgery

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Introduction: Patients undergoing surgeries for spinal tumors are vulnerable to postoperative adverse events (AEs) and deaths. Accurately estimating surgical risks in these patients is critical for shared decision-making and optimization of outcomes. Therefore, we developed a preoperative risk index of short-term major postoperative AEs for patients undergoing spinal tumor surgery.

Methods: Prospectively collected data of patients undergoing spinal tumor surgery from multiple medical centers registered in ACS-NSQIP during 2006-2019 were analyzed. Sociodemographic, frailty-related, and surgical factors in the derivation cohort were evaluated using simple and multiple logistic regression. Risk factors were subsequently integrated into a preoperative spinal tumor surgery risk index (STSRI) and compared with existing models using the validation cohort. A composite variable of major postoperative AEs was used, including death within 30 days of surgery. Internal validation of the final model was done on a subgroup of patients from the ACS-NSQIP while the external validation was performed on an institutional cohort from Johns Hopkins Hospital.

Results: 14,982 operations were found using the ACS-NSQIP database. A total of 7,635 (51.2%) postoperative AEs occurred within 30 days of surgery with 4556 (16.5%) major AEs including 209 (4.5%) deaths. Older age, male sex, black race, smoking, steroid use, anticoagulation use, leukocytosis, anemia, disseminated cancer, weight loss, hypoalbuminemia, functional status, intradural intramedullary plane of the tumor, metastatic tumor, cervical or thoracic level of the surgery, combined anterior and posterior approach, and operative time >4 hours were independently associated with major AEs or death on multiple regression analysis (C statistic, 0.85). Using the validation cohorts, the STSRI produced an AUC of 0.86 (95% CI, 0.85-0.87) with a sensitivity of 80.1% (95% CI, 79.3%-80.9%) and a specificity of 74.3% (95% CI, 72.3%-76.2%). The STSRI outperformed existing risk models for prediction of AEs: modified frailty indices (mFI-1 & mFI-5), the American Society of Anesthesiologists classification, and the ACS risk calculator.

Conclusion: Among the present risk predictors, the proposed STSRI demonstrated the highest predictive performance for major postoperative AEs and death in patients undergoing surgeries for spinal tumors. STSRI can be used to counsel patients awaiting the index surgery.
426: Is It Better to Stop at C2 or C3/C4 in Elective Posterior Cervical Decompression and Fusion?

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Introduction: In patients undergoing elective posterior cervical laminectomy and fusion (PCLF), we sought to: a) compare operative variables, complications, and PROs in patients with an upper instrumented vertebrae (UIV) of C2 vs. C3/4, and b) assess outcomes based on C2 screw type.

Methods: A single-institution, retrospective cohort study from a prospective registry was conducted. All patients undergoing elective, degenerative PCLF from 12/2010-06/2018 were included. Patients were divided into a UIV of C2 vs. C3/4. Groups were 2:1 propensity matched for fusion extending to the thoracic spine. Demographics, operative, perioperative, complications, and 1-year PRO data were collected. Student’s t-tests and chi-squared tests were performed.

Results: 117 patients underwent elective PCLF and were successfully propensity matched (39 C2 vs. 78 C3/4). Groups were similar in fusion extending to the thoracic spine (p=0.588). Expectedly, the C2 group had more levels fused (5.63±1.89) compared to the C3/4 group (4.50±0.91) (p=0.001). The C2 group had significantly longer operative time (p < 0.001), yet no differences were seen in estimated blood loss (EBL) (p=0.494) or length of stay (LOS) (p=0.424). Both groups significantly improved all PROs at 1-year (EQ-5D; NRS-NP/AP; NDI). Twenty-one total adverse events (17.9%) were seen, with 12.8% in the C2 group and 20.5% in the C3/4 group (p=0.306). Both groups had the same percentage of surgical adverse events at 6.8% (p=1.00), including similar incidences of pseudarthrosis and implant failure 5.1% (p=1.00). Between C2 screw type, no differences were seen in operative time, EBL, LOS, complications, or PROs.

Conclusion: In patients undergoing elective PCLF, those instrumented to C2 had only longer operative times compared to those stopping at C3/4. No differences were seen in EBL, LOS, 1-year PROs, and complications. Type of C2 screw had no impact on outcomes. Besides increased operative time, instrumenting to C2 had no detectable difference on surgical outcomes or adverse event rates.
427: An Investigation of the Genetic Landscape of Invasive Spinal Schwannomas: Molecular Evidence of Upregulation of Proteoglycans Which Induce Bone Resorption

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Introduction: Invasive spinal schwannomas are Schwann-cell tumors that erode vertebral bodies and extend into the extraspinal space disrupting myofascial planes. Due to the rarity of these tumors, there is little known about their clinical, histological and biological characteristics.

Methods: An ambispective single-center study of consecutive spinal schwannomas (n=82) between 2003-2018 was performed. Tumors were graded as invasive Schwannomas (Sridhar V) (n =7) and non-invasive schwannomas (Sridhar I-IV) (n= 75). A random group of tumors (n=33) had whole exome sequencing, RNA sequencing, and methylation profiling performed.

Results: Invasive schwannomas significantly increased rates of neurological deficits (85.7% vs 45.3%, chi-square = 4.1785, p < 0.05), particularly urinary/bowel dysfunction (42.8% vs 13.3%, chi-square = 4.1834, p <0.05). Giant invasive schwannomas were significantly larger based on maximal diameter (6.64 cm vs. 2.84 cm, t-test, p < 0.01). There was no difference in rates of gross total resection (28.6% vs. 14.2%, chi-square 1.5137, p = 0.218). However, giant invasive schwannomas required higher rates of instrumented fusion (85.7% vs 32%, chi-square 7.9621, p<0.01). Invasive schwannomas did not demonstrate differences in the rates of mutations in common Schwannoma associated genes (NF2, ARID1A, ARID1B, TSC1, TSC2 and LZTR1). In addition, principal component analysis of the methylome profiles suggest that giant invasive schwannomas have the same cell of origin as other schwannomas. However, pathway analysis of differentially expressed genes identified upregulation of proteoglycan pathways which are known to regulate the osteolytic process. Computational drug screen suggests that anti-rheumatoid agents such as auranofin and hydroxychloroquine may be effective in treating giant invasive schwannomas.

Conclusion: Our study provides the first biological interrogation of invasive Schwannomas. Understanding how invasive Schwannomas activate the proteoglycan pathways and induce bone resorption and destruction will help identify potential therapeutic targets.
428: Development and Testing of a Photosensitive Liquid Polymer Embolization System for Neurovascular Diseases: Preliminary Animal Results

Best international Abstract Award

Jerry C. Ku MD (Toronto, Canada) Yuta Dobashi, PhD Candidate – Institute of Medical Science – University of Toronto; Christopher Pasarikovski, MD, PhD – Division of Neurosurgery – University of Toronto; Joel Ramjist, MASc Candidate – Department of Electrical, Computer, and Biomedical Engineering – Ryerson University; John Madden, PhD – Department of Electrical and Computer Engineering – University of British Columbia; Konrad Walus, PhD – konradw@ece.ubc.ca – University of British Columbia; Victor Yang, MD, PhD – Division of Neurosurgery – University of Toronto

Introduction: Embolization represents a minimally invasive treatment modality for arteriovenous malformations (AVMs), tumors, and hemorrhagic blood vessels, but can be limited by currently available embolic agents, in terms of safety and efficacy. Discovery of new and improved agents could lead to better treatment outcomes. The goal of this project was to develop and test a novel embolization strategy using photosensitive liquid polymers.

Methods: We formulated low-viscosity, injectable liquid polymers which were mixed with a photo-initiator agent and non-ionic contrast medium. We utilize photo-crosslinking at the tip of the microcatheter with an integrated optical fibre to induce rapid solidification of the embolic agent. The UV intensity can also be adjusted, in real-time, to dynamically modulate the degree of crosslinking and thus the viscosity of the polymer. We utilized the swine rete mirabile as an animal model for AVMs, the swine renal arterial tree (inferior segmental artery) as a model for tumors, and swine blood vessels (branches of the subclavian artery). 5 animals were utilized without prior preparation. Embolization was graded based on degree of obliteration of the vascular target, and any complications were recorded. Follow-up angiography was performed at the 4-week interval.

Results: With a combination of shear-thinning properties and modulation of photo crosslinking, we were able to deliver an embolic agent with an end-product viscosity range of up to $10^4$ Pa·s with a single low viscosity precursor. Using this methodology, embolization was technically successful in all animals. 4/5 rete mirabile, 5/5 inferior renal arterial trees, and 5/5 blood vessels were graded as completely obliterated, and there were no instances of clinical or angiographic complications.

Conclusion: We demonstrated a novel method of dynamic photomodulation and delivery of bioengineered liquid polymers to address current limitations of endovascular embolization therapies. This promising technology will be investigated further with longer-term comparative animal trials.
429: Interleukin 6: An Emerging Mechanistic Target for Cerebral Vasospasm Following Subarachnoid Hemorrhage

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Introduction: A key unknown is how cerebral vasospasm (CV) is triggered following subarachnoid hemorrhage (SAH). Utilizing a pre-clinical c57/bl6 SAH model, we investigate the role of interleukin-6 (IL-6) in the pathogenesis of CV and the beneficial effects of IL-6 blockade.

Methods: C57/bl6 females were used: saline injected, SAH, SAH + IL-6 blockade, SAH IL-6 KO, SAH IL-6 KO + IL-6 administration. For SAH, 50micromilliters of blood was collected from tail puncture and administered into the basal cisterns via right frontal burr hole. CV was measured via india-ink/gelatin vessel ratios. Turning test and Garcia’s modified score were utilized. IL-6 receptor, IL-6, blood brain barrier markers, microglial markers, toll-like receptor 4, caspase-3, and tunel staining were measured via Western Blot or Immunohistochemistry. Graphpad prism was utilized for analysis with p<0.05 for significance.

Results: IL-6 expression peaked 3 days following SAH (p<0.05). Receptor upregulation was perivascular in distribution. A significant increase in endothelin 1 (3.5-fold) and occludin (2.2-fold) were noted following SAH day 3, but were reduced with IL-6 blockade (p<0.01). CV occurred day 5 post SAH but was absent in the IL-6 KO mice and mitigated with IL-6 blockade (p<0.05). The SAH mice had impaired performance on the turn test and a poor Modified Garcia Score of 14 compared to 17.25 for controls. A M2 phenotype was noted day 5 in the SAH group with overlap coefficients r=0.96 and r=0.94 for Arg1 and iNOS, respectively. At day 7, a significant increase in toll-like receptor 4, Stat3, and Caspase 3 were noted, but reduced by IL-6 blockade (p<0.05). Ventricular dilation consistent with hydrocephalus and increased tunel positivity were noted day 9, but reduced in the IL-6 blockade group (p<0.05).

Conclusion: Correlation between IL-6 and CV has been well documented. We present the first mechanistic connection and show IL-6 blockade providing benefit in reducing CV and its consequences.
430: Fetal Radiation Exposure Risk in the Pregnant Neurointerventionalist

Stephanie Chen MD (Miami, Florida) Marie-Christine Brunet, MD

Introduction: The prevalence of women physicians is steadily rising, however, the field of neurointervention remains one of the most male dominated subspecialties in medicine. A fear of radiation exposure, particularly during pregnancy and child-bearing years may be responsible for deterring some of the best and brightest. This is the first study, examining the amount of maternal and fetal radiation exposure during a pregnant neurointerventional fellow’s training.

Methods: We retrospectively analyzed the radiation exposure of a neurointerventional fellow prior to and during pregnancy from February 2018 to May 2019 in 758 neurointerventional cases. The collar dosimeter was used to measure overall maternal exposure and an additional fetal dosimeter was worn under two lead apron skirts to estimate fetal radiation exposure.

Results: There was not a significant difference between pre and post pregnancy overall maternal radiation exposure as measured by the collar dosimeter (151 mrem pre-pregnancy and 105 mrem during pregnancy, p=0.129). Mean fluoroscopy time and fluoroscopy emission per procedure also did not differ prior to and during pregnancy. Recordings from both the Mirion Genesis Ultra TLD dosimeter as well as the Mirion instadose dosimeters worn under double lead apron skirts were 0 mrem for all 6 months.

Conclusion: These findings suggest that when optimal radiation safety practices are implemented, the fetal dose of a pregnant neurointerventionalist is negligible. Further studies and education are necessary to encourage women to choose neurointervention and allow practicing women neurointerventionalists to maintain their productivity during their reproductive years.
431: Prospective Study on Embolization of Intracranial Aneurysms with the Pipeline Device (PREMIER Study): 3-year Outcomes and Evaluation Using a Specific Flow Diverter Occlusion Classification

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Introduction: Flow diverters proved to be a safe and efficacious approach for the management of large intracranial lesions. The long-term outcomes of the technique for the management of small- and medium-sized aneurysms remain uncertain. We present the 3-year results of the PREMIER trial.

Methods: The PREMIER was a prospective, single-arm study, including patients with a target wide-necked aneurysm of ≤ 12mm, located in the internal carotid artery or vertebral artery. The primary effectiveness endpoint (complete aneurysm occlusion without significant parent vessel stenosis or retreatment) and primary safety endpoint (major stroke in the supplied territory or neurologic death) were independently monitored and adjudicated. Additional angiographic evaluation to highlight the natural history of aneurysms treated with flow diverters was performed using the modified Cekirge-Saatci Classification (mCSC).

Results: According to CRL review, of 141 patients treated with PED, 25 (17.7%) required angiographic follow-up after the first year due to incomplete aneurysm occlusion. Three (12%) of these patients progressed to complete occlusion, resulting in a complete aneurysm occlusion rate at 3-year of 84.0% (116/138), and an effectiveness endpoint of 79% (109/138, 95% CI, 71.2%–85.4%). Angiographic evaluation using mCSC demonstrated that complete occlusion, neck residual, or aneurysm size reduction occurred in all cases with consecutive available follow-ups (97.8%). One (0.7%) major safety event occurred after the first year, which was non-disabling at 2-year follow-up. Overall combined safety endpoint at 3-year was 2.8% (4/141). There was one case of aneurysm recurrence but no cases of delayed rupture in this series.

Conclusion: A high rate of aneurysm occlusion, low morbidity, and absence of aneurysm rupture emphasize the PED as a safe treatment strategy for small and medium-sized aneurysms located along the ICA and VA in the long term. Aneurysm stability and long-term remodeling also reinforce the favorable natural history of aneurysms treated with flow diverters.
432: Association of External Ventricular Drain Removal and Prophylactic Anticoagulation in Aneurysmal Subarachnoid Hemorrhage: A Propensity Adjusted Analysis

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Introduction: Aneurysmal subarachnoid hemorrhage (aSAH) patients frequently require external ventricular drains (EVDs) for intracranial pressure monitoring. Since aSAH patients often have prolonged hospital stays with an increased risk for deep vein thrombosis (DVT), prophylactic anticoagulation (AC) is recommended following aneurysm treatment. However, no guidelines currently exist for AC administration during EVD removal. The use of prophylactic AC was analyzed during EVD removal.

Methods: All patients in the Post-Barrow Ruptured Aneurysm Trial (PBRAT) treated for an aSAH from 1/1/2014 - 7/31/2019 with an EVD were analyzed and compared based on number of doses of prophylactic AC that was held for EVD removal (>1 vs)

Results: Of the 271 patients who meet inclusion criteria, 139(51.3%) were started on SQH and 132(48.7%) on enoxaparin. At least a dose of prophylactic AC was held for EVD removal in 171(63.1%) patients and >1 dose was held in 116(42.8%) patients. A hemorrhage due to EVD removal occurred in 6 patients(2.2%) and a DVT/PE was found in 17(6.3%) patients. Patients with >1 AC dose held were found to have an increase percentage of SQH(59.5%, N=369 vs 45.2%, N=310; p=0.02), number of U/S performed(1.1, sD 1.2 vs 0.7, sD 1.0; p=0.005), longer hospital stays(24.4 days, sD 8.8 vs 21.3 days, sD 7.1; p=0.002), and DVT/PEs found(N=313, 11.2% vs N=314, 2.6%; p=0.005) compared to 1 dose versus 1 dose of AC held to be associated with DVT/PE (OR 4.8, 95% CI 1.5 to 15.7, p=0.009)

Conclusion: In aSAH patients with EVDs, holding greater than one dose of prophylactic anticoagulation for EVD removal is associated with an increased risk of developing deep vein thrombosis or pulmonary embolism. Continuation of prophylactic anticoagulation was not associated with increased hemorrhagic risk. The present study supports the safe practice of continuation of prophylactic anticoagulation during EVD removal.
433: Diagnosis and Treatment of CSF-Venous Fistulas: A Single Institution Surgical Outcome Study and Proposed Management Algorithm

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Introduction: Spontaneous intracranial hypotension (SIH) is a debilitating condition characterized most often by orthostatic headaches. Cerebrospinal fluid-venous fistulas (CVF) are an increasingly recognized cause of SIH. Here we present a large series of patients who underwent surgery for CVF at our institution. We also propose a diagnostic and treatment algorithm for suspected CVF.

Methods: Patients who had undergone surgical treatment for suspected CVF between 2015 and 2020 were identified retrospectively from the surgical database at our tertiary referral center. Patients were excluded if the CVF diagnosis was not confirmed intraoperatively. Demographic and clinical data were extracted from the electronic health records. All imaging studies related to SIH symptoms or treatment were reviewed. Surgical, clinical, and radiological outcomes were noted. Change in pre- and post-operative Bern scores was calculated with immediate pre- and post-operative MRI, and a T-test or ANOVA was used to assess its correlation with clinical resolution after surgery.

Results: A total of 91 patients underwent surgery for the treatment of CVF. The median number of imaging studies per patient before an accurate diagnosis was 11. While conventional CT myelogram showed a CVF in only 4/81 patients, lateral decubitus digital subtraction myelogram (LDDSM) showed a CVF in 51/65. A total of 61 patients had complete resolution of symptoms at first surgical follow-up, 11 patients had partial resolution, and 15 patients had no improvement. 74 patients required no further treatment for CVF. Among the 17 patients who underwent additional treatment, 10 had repeat surgery, 4 received additional epidural blood patches, and 3 had both surgery and blood patching. An improvement in post-operative Bern scores were associated with resolution of symptoms and lack of further treatment. A management algorithm is also suggested.

Conclusion: The diagnosis of CVF may be expedited by early performance of LDDSM, and symptoms usually improve after surgery.
434: Continuous Blood Flow Visualization with Laser Speckle Contrast Imaging During Cerebrovascular Surgery

Ramsey Ashour MD (Austin, Texas) David Miller, PhD; Colin Sullender, PhD; Andrew Dunn, PhD

Introduction: Cerebral blood flow (CBF) monitoring is routine during cerebrovascular surgery to inform decision making. The technology indocyanine green angiography (ICGA) is often used to determine patency in vessels, and successful aneurysmal obliteration or arteriovenous malformation (AVM) resection. The optical imaging technique laser speckle contrast imaging (LSCI) has emerged as a promising tool to non-invasively monitor CBF because it produces real-time, full-field blood flow maps without any contrast agents. We aimed to evaluate if LSCI could perform continuous and real-time visualization of CBF during cerebrovascular surgery.

Methods: The LSCI hardware – a laser, camera, and imaging optics - were attached to the surgical microscope prior to the start of surgery and did not interfere with the sterile draping of the microscope. LSCI images were overlaid on the white light images from the microscope and displayed in real-time to the surgeon on a monitor. All n=5 surgeries were performed at Dell Seton Medical Center at The University of Texas at Austin by author R.A.

Results: LSCI was performed throughout each surgery when the microscope was positioned over the patient, providing the surgeon with real-time visualization of blood flow changes before, during, and after aneurysm clipping or arteriovenous malformation (AVM) resection in humans. LSCI was also compared with indocyanine green angiography (ICGA) to assess CBF during aneurysm clipping and AVM surgery; simultaneous acquisition of LSCI and ICGA was performed to compare sensitivity and specificity.

Conclusion: The results suggest that LSCI can provide continuous and real-time CBF visualization during cerebrovascular surgery without affecting the surgeon work-flow or requiring a contrast agent. The results also demonstrate that LSCI and ICGA provide distinct, yet complementary information about vessel perfusion.
435: The Utility of Invasive Blood Pressure Monitoring in Microvascular Decompression

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Introduction: The utility of arterial lines in microvascular decompression is not well described.

Methods: We retrospectively reviewed patients undergoing MVD from 2012-2020. Patients were grouped by procedure date from 2012-2014 and 2015-2020, reflecting our institution’s decreasing trend in arterial line placement around 2014-2015. Patient features, intraoperative characteristics, and postoperative complications were collected for all cases. Statistical differences were evaluated via Chi-squared analyses and t-tests.

Results: 858 patients underwent MVDs, with 204 between 2012-2014 and 654 between 2015-2020. Over time, the frequency of arterial line placement decreased from 64.2% to 30.1%, p<0.001. Arterial lines involved 11 additional minutes of pre-incision time, p<0.001. Patients with arterial lines required both increased doses and costs of vasoactive medications intraoperatively. Patients receiving arterial lines demonstrated no significant differences in complications compared to patients with NIBP monitoring. On average, patients with arterial lines incurred $802 increased costs per case compared with NIBP monitoring.

Conclusion: NIBP monitoring in MVDs provides neurologically and hemodynamically safe outcomes compared to invasive blood pressure monitoring. For patients without significant cardiopulmonary risk factors, NIBP monitoring may be a cost-effective alternative in MVDs.
436: Bilateral Nervus Intermedius Sectioning for Geniculate Neuralgia: Case Report and Operative Video

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Introduction: Geniculate neuralgia is a rare condition characterized by excruciating ear pain. Surgical options for geniculate neuralgia include microvascular decompression and sectioning of the nervus intermedius. We report herein a case of bilateral geniculate neuralgia treated by nervus intermedius sectioning without prior microvascular decompression. To our knowledge, this is the first report of this treatment strategy with subsequent description of the side effects of bilateral nervus intermedius disruption.

Methods: This case report is adherent with CARE guidelines and included a literature review that did not yield any similar published cases.

Results: Case Presentation: A 54-year-old woman presented with bilateral geniculate neuralgia, worse on the left, refractory to medical therapy. Surgical treatment options were reviewed including microvascular decompression and sectioning of the nervus intermedius. She opted for left nervus intermedius sectioning. The procedure was uncomplicated and no compressive vascular loop was identified during surgery. Postoperatively, she had complete symptom resolution with no discernable side effects. Three years later, the patient developed worsening geniculate neuralgia on the contralateral side. After discussion of treatment options, she opted again for sectioning of the contralateral nervus intermedius with successful resolution of all symptoms after surgery. Following surgery, the patient identified partial impairment of lacrimation and gustation. She continued to have functional taste of the anterior two-thirds of the tongue, lacrimation, and hearing bilaterally.

Conclusion: Bilateral sectioning of nervus intermedius may provide benefit in patients with bilateral geniculate neuralgia without egregious side effects. However, lacrimatory and gustatory alterations are a potentially significant effect with a wide range of symptomatology.
Surgical Technique: The “paddle-under-bridge” Technique for Safe Thoracic Spinal Cord Simulator (SCS) Paddle Lead Placement in Patients with Thoracic Stenosis

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Introduction: Thoracic placement of spinal cord stimulator (SCS) paddle lead can be difficult in patients with thoracic stenosis. Neurologic deficit is a rare complication that can be caused by spinal cord injury, spinal cord compression, and/or epidural hematoma. The authors propose the “paddle-under-bridge” surgical technique to ensure adequate spinal canal diameter for safe paddle lead placement.

Methods: Patients undergoing thoracic laminectomy for new SCS paddle lead were identified from January 2018 to October 2021. Surgical techniques used were: 1. A single-level ligamentum flavum removal with SCS paddle lead passed superiorly (“Standard”); 2. Aggressive under-cutting of lamina (“Aggressive laminectomy”); or, 3. “Paddle-Under-Bridge,” which entails a two-level ligamentum flavum removal at and below the level of final SCS lead placement, leaving a bony bridge for the paddle lead to pass under (Figure 1).

Results: A total of 112 patients were identified; a standard technique was used in 95 (85%) patients, aggressive laminectomy in 5 (4%), and Paddle-Under-Bridge in 12 (11%) (Table 1, Figure 1). There were two cases (2%) of transient neurologic deficit in the standard laminectomy group, but none in the aggressive laminectomy or Paddle-Under-Bridge groups.

Conclusion: The authors describe the “Paddle-Under-Bridge” technique for use in patients in whom thoracic SCS lead paddles are difficult to pass because of epidural adhesions or thoracic stenosis (Figure 1). This technique offers the advantage of providing a bony bridge to keep the paddle lead positioned midline and opposed to the spinal cord for optimum stimulation.
438: A Quantitative Analysis of Quality of Life Improvement of Neurolesioning Procedures for Refractory Cancer Pain

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Introduction: Malignant cancer pain is a major cause of decreased quality of life in patients with cancer. Current non-invasive therapies are not always effective. Surgical options exist that may be effective in controlling refractory pain in this population. Our objective is to determine the benefit of various surgical lesioning techniques in the treatment of refractory cancer related pain.

Methods: The PubMed database and the EBSCOhost database were utilized to find articles that met the set search criteria. Relevant full text articles written in the English language and including human subjects were reviewed and used for data collection. Data collection was carried out according to PRISMA guidelines. Pain reduction data were converted into quality adjusted life years (QALY) using a standardized scale. QALYs of the included surgical lesioning procedures were compared.

Results: 11,062 relevant abstracts were identified initially. After screening for relevance reduced to 215 remained. A full text review found that 42 of the 215 articles met all established criteria and were assessed for pain management outcomes. All neurolesioning procedures identified were associated with improvements in quality of life.

Conclusion: Surgical neurolesioning procedures can be a beneficial treatment option for refractory cancer related pain. As technology progresses these benefits, as well as the number of patients seeking them, will likely increase.
439: Evaluation of a Multimodal Pain Protocol After Craniotomy

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Introduction: Post-operative pain is an important quality-of-care metric. It is estimated that 60% of patients undergoing craniotomy report severe pain within the first 24 hours of surgery. However, there is a dearth of evidence investigating standardized multimodal regimens for post-craniotomy pain control. In addition, post-operative opioids pose a risk for developing substance use disorders, a significant public health issue in our society. Here, we present the results of a multimodal post-craniotomy pain protocol at our institution.

Methods: We performed a cohort study of 65 patients who underwent craniotomy by a single neurosurgeon. Patients were selected to receive either 1.) scheduled acetaminophen 650 milligrams every 6 hours as needed, morphine 2 milligrams every 2 hours as needed for breakthrough pain, oxycodone 5/10 or hydrocodone/acetaminophen 7.5 milligrams every 6 hours for severe pain (standard pain management) or 2) the aforementioned protocol plus as needed intravenous ketorolac and scheduled gabapentin 300 mg three times daily (experimental group). A retrospective chart review of post-operative pain scores (numeric 1-10) and oral morphine equivalent (OME) usage was analyzed to assess the efficacy of the protocol. Data is reported as mean +/- standard error.

Results: Twenty-nine patients received the experimental protocol. Our experimental group had 13.5% lower post-operative pain scores at 8 hours (3.03±0.50 vs. 2.62±0.48) and 19.4% lower at 24 hours (2.52±0.44 vs. 2.03±0.47). In addition, the experimental group required 17.4% fewer post-operative OMEs at 4 hours (13.9±1.9 vs. 11.4±2.9) and 32% lower OMEs in the first 24 hours (35.8±4.5 vs. 24.2±4.2).

Conclusion: Our experimental multi-modal protocol resulted in a reduction in post-operative pain scores and OME utilization. The addition of gabapentin and as needed ketorolac may help achieve sufficient control of post-operative pain. Further analysis of our data will aim to elucidate its efficacy in the context of specific demographics, prior medical history, and surgical data.
Comparison of Low Dose Intrathecal Morphine Delivery in the Treatment of Chronic Pain Syndrome and Post-laminectomy Syndrome

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Introduction: The use of low dose intrathecal morphine via a morphine drug delivery system has gained further interest as a promising alternative to oral analgesics in the treatment of chronic pain. Though, chronic pain can be caused by different etiologies. For example, post-laminectomy syndrome (PLS) is chronic pain following spinal surgery and chronic pain syndrome (CPS) is generalized chronic pain with poorly understood etiology. This study sought to compare the efficacy of intrathecal morphine delivery in the treatment chronic pain caused by both PLS and CPS.

Methods: This was a retrospective chart-review. Patients were enrolled at St. James Mercy Hospital, University of Rochester, New York from February 2016 to February 2020. Patients were weaned off oral analgesics completely and an out-patient intrathecal morphine trial was performed by injecting a single dose of 0.1-0.2 mg of preservative free morphine in the lumbar intrathecal space. Following at least 60% reduction in pain, a permanent intrathecal catheter and morphine pump was implanted. Follow up visits occurred between 12 and 60 months.

Results: 51 patients were enrolled (median age 59, 53% female). 21 patients were diagnosed with CPS and 30 were diagnosed with PLS. Median intrathecal morphine dose was 0.1750 mg / day. There was a significant reduction in pain following treatment on the 10-point scale (median: 10 vs 2, p < 0.001). Interestingly, pain reduction following treatment did not differ based on underlying diagnosis of PLS or CPS (median: 8.5 vs 8, p: 0.91). There were no infections or complications present in the study.

Conclusion: Low dose intrathecal drug delivery was shown to significantly reduce pain following treatment regardless of CPS or PLS diagnosis. This study further characterizes the efficacy of the use of low dose intrathecal morphine delivery in the treatment of chronic pain. A future multi-center study is desired.
Introduction: Superior semicircular canal dehiscence (SSCD) is a rare skull base disorder described by an aberrant bony defect between the floor of the middle cranial fossa and the superior semicircular canal. The dehiscence in the otic capsule structure results in the development of a “third mobile window” which elicits debilitating vestibular and auditory symptoms that require surgical intervention. Conventional methods in the management of SSCD include plugging, resurfacing, and capping of the canal. Sealing of the canal with bone wax is an updated resurfacing technique applied for SSCD repair. We present a novel approach to surgical sealing for SSCD repair with IQ Dome (named after the two senior authors), a titanium mesh plate that overlies the arcuate eminence, and evaluate its efficacy compared to traditional sealing methods.

Methods: A retrospective analysis of patients undergoing SSCD surgical sealing repair with IQ Dome compared to a cohort of patients with traditional sealing methods was performed. Data including patient demographics, pre- and post-operative symptoms, neuroimaging, neurosurgical technique, perioperative complications, clinical outcomes, and follow-up length was collected.

Results: A total of 92 patients with SSCD, 35 (38.1%) male and 57 (61.9%) female, were surgically repaired at our institution from June 2020-September 2021. 80 patients received SSCD repair with the novel IQ Dome method and 12 patients underwent SSCD repair with traditional sealing methods. All cases with IQ Dome led to no additional perioperative complications or inhibition of symptom resolution.

Conclusion: IQ Dome may offer an alternative and effective intervention for surgical sealing repair of SSCD. This innovative technique may help improve post-operative outcomes. Future studies are warranted to further assess the efficacy of this novel surgical approach.
442: Socioeconomic Status Predicts Disproportionate Healthcare Utilization Following Elective Spine Surgery

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Introduction: A significant portion of healthcare spending is driven by a small percentage of the overall population. Understanding risk factors predisposing patients to disproportionate utilization of healthcare resources is critical. We aimed to identify risk factors leading to a prolonged length of stay (LOS) following elective spine surgery.

Methods: Patients who underwent elective anterior cervical discectomy and fusion from 2015-2021 at a single institution were identified. Multivariate logistic regression evaluated the effects of sociodemographic factors including Area of Deprivation Index (a measure to quantify income, education, employment, and housing quality), along with procedural and discharge characteristics on postoperative LOS. Extended LOS was defined as greater than the 90th percentile for the study population.

Results: There were 686 patients eligible for our study, with a mean age of 57 years (range 26-92), average procedure duration of 126 minutes (45-370 minutes), and 1.6 levels (median, 1 level) were fused. After adjusting for confounders, patients had increased odds of extended LOS if they were highly disadvantaged on the Area of Deprivation Index (ADI, OR=2.60, 95% CI=1.24-5.46; p=0.012); were insured by Medicaid (OR=2.33; 1.04-5.22; p=0.040); had surgery on Thursday or Friday (OR=1.96; 1.03-3.73; p=<0.039); had a concomitant corpectomy performed (OR=3.15; 1.46-6.83; p=0.004); were evaluated by physical therapy (OR=3.60; 1.59-8.14; p=0.002) or speech and language pathology (OR=23.06; 6.69-79.45; p=<0.001). Patient age, race, primary language spoken, procedure start time and duration, number of levels instrumented, and surgeon experience did not predict prolonged LOS. Patients with an extended LOS were more likely to present to the emergency department or be re-admitted within 30 days after discharge (p=0.047).

Conclusion: After adjusting for potential cofounders, patients most disadvantaged on ADI or insured by Medicaid were more likely to have an extended LOS following elective anterior cervical spine surgery. Strategies to improve peri-operative care of patients with elevated socioeconomic stressors are needed.
443: Current Trends in Subspecialty Fellowship Training for 1687 Academic Neurological Surgeons

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Introduction: Neurosurgical subspecialty fellowship training has become increasingly popular in recent decades, particularly to advance personal knowledge and professional development. To date, there is no study that evaluates the recent trends in postgraduate education among neurological surgeons. Here, we provide a detailed analysis of subspecialty fellowship training for U.S. academic neurosurgeons.

Methods: Academic clinical faculty (M.D. or D.O.) teaching at accredited neurosurgery programs were included. Gender, academic rank, leadership, and fellowship training history were determined using departmental physician profiles. The American Association of Neurological Surgeons (AANS) membership database provided residency start year information. Relative citation ratio (RCR) scores for each surgeon were retrieved using the NIH iCite tool. Distributions of all variables were determined for each subspecialty.

Results: A total of 1,687 neurosurgical faculty (1,756 fellowships) were included. The majority (79.13%) reported fellowship training. Spine was the most popular subspecialty (16.04%), followed by pediatrics (11.18%) and oncology (8.92%). The least common was peripheral nerve (1.26%). Spine and endovascular grew in popularity over time. Completion of at least one fellowship was more common among recent graduates (residency year >2000), as was training in multiple subspecialties (p<0.0001). Among females, pediatrics was most popular, whereas spine was most popular for males. Fellowship training correlated with higher weighted, but not mean, RCR scores among associate (p=0.002) and full professors (p=0.005).

Conclusion: There is an emerging proclivity for additional fellowship training among young neurosurgeons, often even in multiple subspecialties. These findings may help guide professional decision-making for academic institutions, fellowship directors, and trainees alike to optimize the delivery of postgraduate training in the U.S.
444: Mapping migratory workforce trends in the United States: an analysis of 4,075 neurosurgeons

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Introduction: Characterizing changes in the geographical distribution of neurosurgeons in the United States (US) may inform efforts to address lack of access to neurosurgical care. A comprehensive analysis was performed of the geographic movement and distribution of the neurosurgical workforce.

Methods: A list containing all board-certified neurosurgeons practicing in the US in 2019 was obtained from the American Association of Neurological Surgeons membership database. Chi-square analysis and post hoc comparison with Bonferroni correction were performed using Stata 17 (College Station, TX) to assess differences between geographical movement throughout their career and demographic variables.

Results: The study cohort included 4,075 neurosurgeons practicing in the US, including 3,830 male and 245 female neurosurgeons. By US Census Bureau region, 781 practiced in the Northeast, 810 in the Midwest, 1,562 in the South, 906 in the West, and 16 in a US territory. The trending association between gender and region of current practice (P=0.077) was predominantly accounted for by variation in female practice location as indicated by the relative contribution to the Chi-square test statistic (F: 6.4, M: 0.4); moreover, female neurosurgeons made up the highest percentage of the workforce in the South (31.4%). Male and female neurosurgeons exhibited no difference in movement by state or region from medical school to residency to current practice location (P=0.465). Following Bonferroni correction, region of current practice had a strong association with completing medical school and residency in that same US region as follows: Northeast (322/781, 41.2%) followed by the Midwest (305/810, 37.7%), South (577/1562, 36.9%), and West (141/941, 15.0%) (P <0.001).

Conclusion: Female neurosurgeons were proportionately more likely to practice in the South than any other US region. Although no association with any particular gender, practicing in the same region as completing training was most associated with neurosurgeons practicing in the Northeast.
445: Venous Sinus Stenting: Single Institution Safety and Healthcare Cost Review

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Introduction: Increasing evidence has shown the effectiveness and safety of venous sinus stenting. Few have looked at optimal postoperative recovery area for patients that maintains maximum patient safety while cutting healthcare costs. At this institution, all patients recover in an intensive care unit (ICU), raising costs and decreasing bed availability.

Methods: Single institution retrospective review of elective venous sinus stenting procedures performed from May 2008 to February 2021. All patients were screened with venous sinus manometry prior to stenting. Primary data included hospital length of stay (LOS), ICU LOS, and need for ICU/surgical interventions. Secondary data included demographics, stent location, diagnosis, and postoperative neurological deficit. Financial data was supplied by the hospital financial team.

Results: There were 53 patients (98.1% female) that met inclusion criteria. Mean LOS was 1.04 days (range, 1-2 days) and mean ICU LOS was 1.02 days (range, 1-2 days). There were 51 patients (96.2%) discharged on post-operative day (POD)-1. There were 2 patients discharged on POD2 both due to minor complications of groin hematoma from femoral artery access. The total estimated cost for room and direct cost to the patient on the initial recovery day is $4,200 for the neuroscience ICU versus $2,000 for the neurosurgery/neurology ward. Transferring directly to a neurosurgery/neurology ward without ICU care would save an estimated $127,200 for bed placement alone in our cohort. There were no complications requiring ICU level of care or surgical intervention. There were no mortalities. There were 8 patients (15.1%) that were lateralized to other ICUs or remained in the post-anesthesia care unit due to the neuroscience ICU being at capacity.

Conclusion: This institution’s data reaffirms the safety of venous sinus stenting. It also reveals the ability for these patients to recover on a trained neurosurgery/neurology ward, which would save healthcare and patient costs as well as increase ICU bed availability.
446: Resident Education in Ethiopia: Opportunities for Global Neurosurgery Collaborations

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Introduction: Neurosurgery is a rapidly developing specialty in Ethiopia. In 2006, a neurosurgery residency program was established by partnering local teaching hospitals with Norwegian universities and Foundation for International Education in Neurological Surgery (FIENS). In the past 15 years, the neurosurgery workforce density has leaped from 0.0022 to 0.045 neurosurgeons/100,000 population. Currently, three 5-year residency programs are training 80 residents in two major cities.

Methods: A survey was sent to all current neurosurgery residents (May 28-August 6, 2021). Responses were analyzed to identify opportunities for global neurosurgery partnerships focused on resident education.

Results: The response rate was 86% (69/80). 98.6% were 25-35 years old (7.3% female). The top three subspecialties of interest were spine (30%), skull base (28%), and cerebrovascular (14%). While 99% used textbooks as their primary study resource, 72% utilized the official journals and other resources of neurosurgical societies. 93% found skills lab sessions organized in collaboration with international partners either very helpful or extremely helpful. Similarly, 88% and 91% deemed virtual training sessions and multidisciplinary training programs hosted in partnership with international collaborators very helpful or extremely helpful, respectively. Residents chose cerebrovascular (91%), endoscopy (88%), and epilepsy (87%) as the top procedures for more training opportunities. While 77% agreed that training sessions led by foreign neurosurgeons were applicable to low-income settings, 70% agreed that visiting neurosurgeons considered the local sociocultural relevance of the training they provided. 25% of residents would like international collaborators to provide advanced training at local institutions, and the remaining respondents desired to gain advanced skills via training opportunities abroad.

Conclusion: International partnerships were essential for the surge in the Ethiopian neurosurgery workforce. Resident education and advanced training in subspecialty procedures are both in high demand and could serve as potential collaboration avenues with neurosurgeons and institutions that have an interest in global neurosurgery.
447: Geographic Variations in Continuous Insurance Duration in the United States

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Introduction: Health insurance plays a significant role in neurosurgical practice and reimbursement in the United States. While equitable access to high quality neurosurgical services has been discussed in the past, important aspects regarding individual insurance subscribers have yet to be analyzed, including average length of continuous health insurance coverage; geographic variations in the duration insurance coverage; factors associated with longer coverage and higher payment. We provide the first retrospective analysis of these factors.

Methods: The Stanford Redivis was used to access the Truven Health Marketscan Database containing patient insurance data. A random 1% of three datasets were selected and combined. Only patients with one consistent region and state were included. ANOVA analysis was used to compare age, gender distribution, days of enrollment, and total payments for admissions among regions.

Results: 1,168,751 patients were identified. Regions were divided into the Northeast (209,741, 17.95%), North Central (263,332, 22.53%), South (465,421, 39.82%), West (206,847, 17.70%), and Unknown (23,410, 2.0%). North East had the highest mean total payments at $11874.81 (±$43517.30), mean days of enrollment 1033.16 (±824.47). West was second, with mean total payments at $11343.39 (±46228.50), mean days of enrollment 1060.55 (±856.78). North Central was third, with mean total payments at $11315.74 (±38124.44), mean days of enrollment 1037.62 (±851.60). South was fourth with mean total payments at $10802.90 (±39510.69), mean days of enrollment 1008.78 (±861.81). The three states with longest mean days of enrollment were Puerto Rico 1799.82 (±1260.57), Delaware 1454.09 (±1182.85), and Michigan 1321.86 (±1042.57). The three with the shortest were Washington DC 731.52 (±481.64), Hawaii 746.46 (±639.15), and Montana 770.17 (±568.47).

Conclusion: This study demonstrates significant variations in duration of insurance coverage and payments depending on geographic location in the US. Understanding these variations is vital as neurosurgeons continue to advance policies and practices that ensure access to quality neurosurgical services.
448: Neurosurgical Responses to Evaluation of the Virtual Recruitment Cycle

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Introduction: Applicant and program perceptions concerning the new virtual neurosurgery residency recruitment methods due to the COVID-19 pandemic during the 2020-2021 recruitment cycle were analyzed and informed changes in neurosurgical recruitment.

Methods: A national survey of neurosurgical residency applicants from the 2020-2021 application cycle was performed. This survey was developed in cooperation with the Society of Neurological Surgeons (SNS) and the American Association of Neurological Surgeons Young Neurosurgeons Committee (YNC) and sent to all applicants (n=280) who submitted academic video submissions to the SNS repository.

Results: 44.3% of applicants and 70% of programs responded to the survey. 84% of faculty expressed that the standardized letter of recommendation template facilitated candidate comparison, but nearly all identified areas for optimization. 72.6% of applicants and 74.6% of faculty did not find the application video submissions helpful. Approximately 60% of faculty, program coordinators and applicants agreed that “preference signaling” would be beneficial for programs to elucidate which applicants harbor a strong desire to match at their program. 61.3% of faculty and 64.8% of applicants agreed that an interview “cap” for applicants to decrease the number of interviews accepted would be favorable. While 71.3% of applicants agreed that standardized interview release dates would improve the process, only 37.7% of faculty and 43.1% of program administrators agreed.

This data was used to improve the standardized letter of recommendation, and implement standardized interview release dates on each Friday of October starting at 4pm, with a commitment to hold each invitation open for 48 hours. The SNS is exploring options of interview caps and preference signaling.

Conclusion: The SNS undertook an intensive study of the first virtual recruitment cycle and recommended changes to optimize future cycles, like improved standardized letters of recommendation and single release date. The 2021-2022 cycle will be similarly evaluated to continue to improve equity, diversity and fiscal integrity.
449: The Legacy of Ambroise Paré: Advancements in Neurosurgery and Traumatic Brain Injuries from the 16th Century Battlefield

Marian Park BS; Giancarlo Mignucci-Jiménez, MD; Lena Mary Houlihan, MD; Mark Preul, MD

Introduction: During the 1536 siege of Turin in northern Italy, a young French barber-surgeon abandoned the conventional treatment of battle-inflicted wounds, launching a revolution in military medicine and surgical techniques. Ambroise Paré (1510-1590) was born into a working-class family in Laval, France during an era when surgery was not considered a respectable profession. He rose from humble origins as a barber-surgeon, a low-ranked occupation in the French medical hierarchy, to become a royal surgeon (“chirurgien ordinaire du Roi”) serving 4 consecutive French monarchs. While Paré’s contributions to functional prosthetics and treatment of warfare injuries are well-documented, a deeper understanding of his role in military neurosurgery is yet to be uncovered.

Methods: We examined primary archival texts and written accounts by Paré that reveal patient cases highlighting his innovative contributions to neurotrauma and neurosurgery during demanding and harrowing circumstances of both the battlefield and medical field in 16th century France.

Results: Paré’s innovative ideas and surgical practice emanated from the demands of the immediate environment of new military technology on 16th century European battlefields, i.e., gunpowder weapons. Advances in military weaponry led to unfamiliar and complicated injuries, which challenged Paré to develop new surgical instruments and techniques. We also discuss his contemporary connection to Vesalius and the circumstances that established the conditions for multi-disciplinary interactions with artisans that were crucial for the neurologically-associated restoration of functionality, including development of prosthetics and surgical tools.

Conclusion: In a life filled with adventure, and serving in horrendous conditions during a time when Galenic dogma still dominated medical practice, he developed a reputation for logic, empiricism, technology, and careful treatment. “I have [had] the opportunity to praise God, for what he called me to do in medical operation, which is commonly called surgery, which could not be bought with gold or silver, but by only virtue and great experimentation.”
450: Endoscopic Endonasal Resection of Rathke’s Cleft Cysts: A Single Institution Analysis of 113 Consecutive Patients

Mizuho Minimally Invasive Brain Tumor Surgery Award

Hanna N. Algattas MD (Pittsburgh, Pennsylvania) Pradeep Setty, MD; Eric Wang, MD; Georgios Zenonos, MD; Carl Snyderman, MD; Paul Gardner, MD

Introduction: Sellar Rathke’s cleft cysts (RCC) are generally treated with an endoscopic endonasal approach (EEA) for fenestration, but suprasellar RCCs offer unique challenges to appropriate management.

Methods: Retrospective review was performed on 113 consecutive patients with RCCs that underwent EEA at a single institution between October 2003 and April 2017.

Results: A total of 113 patients underwent EEA for RCCs. Drainage and marsupialization was performed in 87 (77.0%) cases and cyst wall resection in 26 (23.0%). Cysts were classified as purely sellar (52.2%), sellar with suprasellar extension (29.2%), or purely suprasellar (18.9%). Radiographic recurrence occurred in 15 cases (13.3%), 3 (20%) of which were asymptomatic (mean follow-up 40 months). Purely suprasellar cysts demonstrated radiographic recurrence in 19.0%, sellar cysts with suprasellar extension in 12.1%, and purely sellar cysts in 10.2%. Cases with cyst wall resection had lower recurrence rates (3.8% vs. 16.1%; p=0.11), but increased rates of new/worsened pituitary dysfunction (15.4% vs. 5.7%; p=0.11). Cyst wall resection was significantly more common in suprasellar cysts (16/21 vs. 8/33 vs. 2/59) (p<0.001). Of the 21 purely suprasellar cysts, cyst wall resection improved recurrence risk compared to fenestration alone (6.3% vs 80%, p=0.0007). However, among the 92 cysts which were sellar or sellar with suprasellar extension, there was no significant change in risk of recurrence (p=0.765). Specifically, for sellar cysts recurrence was 0% (0/2) in cases of cyst wall resection and 10.5% (6/57) in cases of marsupialization (p=0.31) whereas sellar cysts with suprasellar extension recurred in 0% (0/8) of cases of cyst wall resection and 16% (4/25) of those with marsupialization (p=0.11).

Conclusion: Endoscopic endonasal fenestration of sellar RCCs may be the ideal treatment strategy whereas purely suprasellar cysts may require cyst wall resection to avoid recurrence. Cyst wall resection reduced recurrence with a trend towards increased hypopituitarism, which should be balanced depending on cyst location.
**451: ERK1/2 Phosphorylation Predicts Survival Following anti-pd-1 Immunotherapy in Recurrent Glioblastoma**

**Journal of Neuro-Oncology Award**

Victor A. Arrieta González MD/PhD (Chicago, Illinois) Christina Amidei, PhD; Uttiya Basu, PhD; Daniel brat, MD/PhD; Jeffrey bruce, MD; Kirsten Burdett, MS; Jared Burks, PhD; Peter Canoll, MD; Andrew Chen, MD; Li Chen, MD/PhD; David Cieremans, MD; Timothy Cloughesy, MD; Lee Cooper, PhD; Crismita Dmello, PhD; Andrew Gould, BS; Amy Heimberger, MD; Craig Horbinski, MD/PhD; Fabio Iwamoto, MD; Dinesh Jaishankar, PhD; Joshua Kane, BS; Seong Jae Kang, PhD; Cynthia Kassab, MD; Brice Laflleur, PhD; Catalina Lee-Chang, PhD; Xiaoyang Ling, PhD; Rimas Lukas, MD; Matthew McCord, MD; Robert Prins, PhD; Raul Rabadán, PhD; Gerson Rothschild, PhD; Joseph Shilati, BS; Peter Sims, PhD; Adam Sonabend, MD; Pavan Upadhyayula, MD; Jonathan Yamaguchi, MD; Jinhao Yuan, PhD; Bin Zhang, PhD; Daniel Zhang, BS; Hui Zhang, PhD; Junfei Zhao, PhD; Wenting Zhao, PhD

**Introduction:** PD-1 checkpoint inhibition has led to remarkable clinical responses in several cancer types. Whereas PD-1 blockade has not shown an overall survival (OS) benefit for glioblastoma (GBM) patients, a subset of them exhibit long-term responses to this immunotherapy. Previously, we reported an enrichment of BRAF/PTPN11 activating mutations in 30% of recurrent GBMs that responded to PD-1 blockade, but the molecular profile of the majority of responders remained elusive. Given that BRAF and PTPN11 promote MAPK/ERK signaling, we investigated whether activation of this pathway is associated with response to PD-1 inhibitors in recurrent GBM, including patients that do not harbor BRAF/PTPN11 mutations.

**Methods:** Immunohistochemistry for ERK1/2 phosphorylation (p-ERK), a marker of MAPK/ERK pathway activation, was performed in a discovery cohort including pre-treatment specimens of 29 recurrent GBM patients treated with adjuvant PD-1 blockade, and 33 patients who did not undergo immunotherapy. Furthermore, we evaluated the phenotypic and cellular differences of the tumor microenvironment of patients with elevated ERK1/2 activation through multiplex immunofluorescence staining and single-cell RNA-seq (scRNA-seq) of human GBMs.

**Results:** p-ERK was predictive of response and OS following PD-1 blockade. Yet p-ERK was not associated with OS in patients not treated with immunotherapy. p-ERK was also associated with OS in a validation GBM cohort treated with adjuvant anti-PD-1 therapy. Single-cell RNA-seq and multiplex- immunofluorescence analyses revealed that p-ERK was mainly localized in tumor cells and high p-ERK GBMs contained tumor-infiltrating myeloid cells and microglia with elevated expression of MHC class II and associated genes.

**Conclusion:** These findings indicate that ERK1/2 activation in recurrent GBM is predictive of response to PD-1 blockade and is associated with a distinct myeloid cell phenotype. This may offer an opportunity to apply immunotherapy with a personalized approach for GBM, providing therapeutic benefit for a subset of patients while avoiding futile treatments for others.
452: Gammatile Brachytherapy in the Treatment of Recurrent Glioblastomas

Brainlab Neurosurgery Award

Clark C. Chen MD, PhD (Minneapolis, Minnesota) Kathryn Dusenbery, MD; Clara Ferreira, PhD; Joseph Levine, MD; Rena Shah, MD; Jim Shanks, MD; Jun Ma, MD – University of Minnesota; Liam Chen, MD; Mark Folkertsma, MD; Mehmet Gencturk, MD – University of Minnesota; Dominic Gessler, MD; Elizabeth Neil, MD; Can Ozutemiz, MD; Margaret Reynolds, MD – University of Minnesota; Bell Robert, MD; Christopher Wilke, MD; Shunqing Zhang, MD – University of Minnesota

Introduction: GammaTile (GT) is a brachytherapy platform cleared by the U.S. Food and Drug Administration (FDA) for use in the treatment of recurrent brain cancer in 2019. Here, we provide the first report of clinical outcomes for recurrent glioblastoma patients after GT treatment following maximal safe resection.

Methods: We prospectively followed twenty-two consecutive Isocitrate Dehydrogenase (IDH) wild-type glioblastoma patients (six Methylguanine-DNA methyltransferase methylated (MGTMt); sixteen MGMT unmethylated (MGMTu)) who underwent maximal safe resection of the recurrent tumor followed by GT placement.

Results: The cohort consisted of 14 second and eight third recurrences. In terms of procedural safety, there was one 30-day re-admission (4.5%) for an incisional cerebrospinal fluid leak, which resolved with lumbar drainage. No other wound complications were observed. Six patients (27.2%) suffered a decline in Karnofsky Performance Score (KPS) after surgery due to worsening existing deficits. One patient suffered a new-onset seizure post-surgery (4.5%). There was one (4.5%) 30-day mortality from intracranial hemorrhage secondary to heparinization for an ischemic limb. The mean follow-up was 698 (range 329-1571) days from the time of initial diagnosis. Six-month local control (LC6) and twelve-month local control (LC12) were 78 and 50%, respectively. Median progression-free survival (PFS) was 240 days for both MGMTu and MGMTm patients. Median overall survival (OS) was 734 days for the MGMTu patients and was not reached for MGMTm patients (estimated >1200 days). These outcomes compared favorably to data in the published literature and an independent glioblastoma cohort of comparable patients without GT treatment at our institution during the study period (LC: 52%; OS MGMTu: 462 days; OS MGMTm: 821 days; p=0.0089 and p=0.0271, respectively when compared to the GT treated patients).

Conclusion: This clinical experience suggests the efficacy of brachytherapy in the setting of recurrent glioblastoma and supports GT brachytherapy as a treatment option in a multi-modality treatment strategy for recurrent glioblastomas.
453: Dissociating Broca’s Aphasia from Broca’s Area

Elekta Tumor Section Award

John P. Andrews MD (San Francisco, California) Nathan Cahn, BA; Benjamin Speidel, MS; Jason Chung, MD PhD; Stephen Wilson, PhD; Mitchel Berger, MD – Professor, Neurological Surgery, University of California-San Francisco; Edward Chang, MD – Chair, Neurological Surgery, University of California-San Francisco

Introduction: Language deficits after neurological surgery can be devastating for patients. Patient safety depends on neurosurgeons’ knowledge of the functional consequences of lesions to areas of the brain. Broca’s aphasia is a syndrome of impaired fluency with retained comprehension. In the largest prospectively evaluated series of language We used an unbiased algorithm to examine which neuroanatomic areas are most likely to result in Broca’s aphasia following surgical lesions.

Methods: Patients were prospectively evaluated with standardized language batteries before and after surgery. Resections were outlined from MRIs to construct 3D-volumes of interest. These were aligned using a non-linear transformation to MNI brain space. A voxel-based lesion-symptom mapping (VLSM) algorithm was used to test for areas statistically associated with Broca’s aphasia when incorporated into a resection, as well as areas associated with deficits in fluency independent of Western Aphasia Battery classification. Post-operative MRIs were reviewed blindly to estimate percentage resection of Broca’s area compared to areas identified through the VLSM algorithm.

Results: 289 patients had early language evaluations, of whom 19 had postoperative Broca’s aphasia. VLSM analysis revealed an area highly correlated (P<0.001) with Broca’s Aphasia, spanning ventral sensory-motor cortex and supramarginal gyri. Reduced fluency scores were significantly associated with an overlapping region of interest. Fluency score was negatively correlated with fraction of resected pre-central, post-central, and supramarginal components of the VLSM area.

Conclusion: In contrast to neurosurgical historical cannon regarding lesion-deficit associations, resection of Broca’s Area frequently does not lead to Broca’s Aphasia, and Broca’s Aphasia does not typically arise from resection of Broca’s Area. Ventral sensorimotor cortex and supramarginal gyri are an area critical for fluent speech production. The new area described here should be considered an eloquent language area and incorporated into language mapping paradigms.
454: Evaluation of Immunologic Parameters in Canine Glioma Patients Treated with an Oncolytic Herpes Virus

Southeastern Brain Tumor Foundation (SBTF) Award

Dagoberto Estevez-Ordonez MD (Birmingham, Alabama) Melissa Chambers, MD; Jeremy Foote, PhD, DVM, DACVP; R. Timothy Bentley, BVSc (Dist), MRCVS, ACVIM; Davide Botta, PhD; David Crossman, PhD; Deborah Della Manna, MS; Jey Koehler, DVM, PhD, DACVP; Catherine Langford, MS; Margaret Miller, DVM, PhD; James Markert, MD MPH – University of Alabama Birmingham Neurosurgery; Alicia Oliver, PhD, DVM; Nidal Omar, MD – University of Alabama Birmingham Neurosurgery; Simon Platt, BVM&S; Daniel Rissi, DVM, MS, PhD, DACVP; Andy Shores, DVM, MS, PhD; Donald Sorjonen, DVM, MS; Eddy Yang, MD PhD; Amy Yanke, VM, MS; Yancey Gillespie, PhD – University of Alabama Birmingham Neurosurgery

Introduction: To molecularly characterize the tumor microenvironment (TME) and evaluate immunologic parameters in canine glioma patients before and after treatment with oncolytic human IL-12-expressing herpes simplex virus (M032).

Methods: We assessed 22 pet dogs with sporadically occurring gliomas that were enrolled in Stage 1 of an ongoing veterinary clinical trial to establish the safety of intratumoral oncoviral therapy with M032, a genetically modified oncolytic herpes simplex virus (oHSV) between January 2018 and August 2020. Pre- and post-treatment specimens were evaluated with immunohistochemistry, NanoString, Luminex cytokine profiling, and multi-parameter flow cytometry.

Results: The majority of tumors exhibited morphologic and immunohistochemical features consistent with oligodendroglioma (12/18 high-grade) and astrocytomas comprised a smaller proportion (~21%; 2/4 high-grade). Treatment-naive canine glioma subject tumor microenvironment had enrichment of Iba1 positive macrophages with minimal numbers of T and B cells, consistent with previous studies identifying these tumors as immunologically “cold.” Pre-treatment NanoString mRNA profiling revealed enrichment for tumor intrinsic pathways consistent with suppression of tumour-specific immunity and support of tumor progression. Oncolytic viral treatment induced an intratumoral mRNA transcription signature of tumor-specific immune responses in 83% (5/6) of canine glioma patients. Changes included mRNA signatures corresponding with interferon signaling, lymphoid and myeloid cell activation, recruitment, and T and B cell immunity. Multiplexed protein analysis identified a subset of oligodendroglioma subjects with increased concentrations of IL-2, IL-7, IL-6, IL-10, IL-15, TNFα, GM-CSF between 14 and 28 days after treatment, with evidence of CD4+ T cell activation and modulation of IL-4 and IFNγ production in CD4+ and CD8+ T cells isolated from peripheral blood.

Conclusion: These findings indicate that M032 modulates the tumor-immune microenvironment in the canine glioma model, specifically effecting a shift from TH2 (IL-4) to TH1 (IFNγ) cytokine production within recirculating T cells after M032 treatment.
455: Plasma Circulating Tumor DNA Enables Detection of Temozolomide Resistance in Glioma

AANS/CNS Joint Section on Tumors Neuro-Oncology Trainee Award

Jordan J. Jones MD (Melbourne, Australia) Kate Drummond, MD, FRACS – Professor, Head of Department, Neurosurgery, University of Melbourne, Royal Melbourne Hospital; Andrew Morokoff, MBBS, PhD, FRACS – Associate Professor, Neurosurgery, Neurosurgery, University of Melbourne, Royal Melbourne Hospital

Introduction: Liquid biopsy based on circulating tumor DNA (ctDNA) is a novel tool in clinical oncology to assess prognosis, tumor burden and treatment resistance. Despite significant progress seen in other cancers, ctDNA analysis in glioma has been limited by low levels of circulating DNA and poor sensitivity. In the following study, we report the use of a novel next generation sequencing technique in one of the only longitudinal ctDNA studies in glioma, providing evidence that mutations can be reliably detected in the blood of patients with glioma including those associated with temozolomide resistance.

Methods: In a prospectively collected cohort of gliomas, we analysed 49 plasma samples from 10 patients with tumor tissue available from at least two operations. Circulating cell free DNA was extracted from the plasma and analysed with the CAPP-seq next generation sequencing platform. Matched tumor tissue was sequenced with the TruSight Oncology 500 Assay. Droplet Digital PCR was performed to validate the sequencing findings.

Results: We found glioma associated mutations in 93% of plasma samples including common drivers such as EGFR amplification. Concordance between plasma and tissue was 52%, with 25% of mutations detected in the plasma only, suggesting ctDNA may complement tissue biopsy in providing a complete genomic characterisation of a tumor and overcome the spatial heterogeneity encountered on biopsy. Mutations in the mismatch repair genes (MMR) were most frequently detected following temozolomide treatment and were observed prior to their appearance in tissue at the time of progression.

Conclusion: We show that contrary to previous reports, ctDNA can be reliably detected in the plasma of gliomas using a novel NGS platform. We found that ctDNA offers complementary information to tissue biopsy alone, as well as providing early evidence of temozolomide resistance through mutations in MMR genes. These results support further evaluation of plasma ctDNA in glioma clinical trials.
456: Survival Outcomes of Molecular Glioblastoma: A Multicenter Study

Rosenblum-Mahaley Clinical Research Award

Andres Ramos-Fresnedo MD (Jacksonville, Florida) Michael Pullen, BS – Neurosurgery – Mayo Clinic Florida; Carlos Perez-Vega, MD – Postdoctoral Research Fellow, Neurosurgery, Mayo Clinic Jacksonville; Ricardo Domingo, MD – Postdoctoral Research Fellow, Neurosurgery, Mayo Clinic Florida; Kaisorn Chaichana, MD – Professor, Neurosurgery, Mayo Clinic Florida; Daniel Trifiletti, MD – Associate Professor, Radiation Oncology, Mayo Clinic Florida; Mark Jentoft, MD – Assistant Professor, Laboratory Medicine and Pathology, Mayo Clinic Florida; Alfredo Quinones-Hinojosa, MD – Professor, Neurosurgery, Mayo Clinic Florida; Ricardo Domingo, MD; Erik Middlebrooks, MD – Professor, Radiology, Mayo Clinic Florida; Wendy Sherman, MD – Assistant Professor, Neurology, Mayo Clinic Florida

Introduction: The updated 2021 WHO classification of brain tumors now considers astrocytic tumors without the histological features of glioblastoma (GBM) but harboring a TERT promoter mutation, EGFR amplification, or chromosomal +7/-10 copy changes as GBM, IDH-Wildtype (WHO Grade 4). The objective of this study is to explore and compare the survival outcomes between classical or histological GBM (histGBM) vs. molecular GBM (molGBM).

Methods: Medical records of patients diagnosed with glioblastoma at the three main sites of our institution (Rochester, Arizona, and Florida) from November 2017 until October 2021 were reviewed. Only patients who underwent chemoradiation after surgery were included. Patients without molecular feature testing or with an IDH mutation were excluded from the analysis. A log-rank test was performed to compare the overall survival (OS) and progression-free survival (PFS) between histGBM and molGBM. An exploratory sub-analysis on the molecular GBM group only to evaluate for any associated factors to OS or PFS was performed through a multivariable Cox regression taking into consideration age >65 years, sex, KPS <70, location in the cortex, contact with the lateral ventricles, and extent of resection.

Results: 231 consecutive patients were included; 166 with histGBM and 65 with molGBM. Median OS was 21 (histGBM) months and 26 months (molGBM) (p=0.507) and median PFS was 8 months (histGBM) and 13 months (molGBM) (p=0.0043). On multivariable analysis for OS in the molGBM group only, contact with the lateral ventricles was the only factor associated with a significantly decreased survival (HR 3.462 [CI 95% 1.040-11.518], p=0.043). Multivariable analysis for PFS in the molGBM group only, showed no significant association with any of the input variables.

Conclusion: In our multicenter experience, molecular GBM had a significantly improved PFS when compared to classical or histological GBM. Contact with the lateral ventricles is the only variable associated with a decreased OS within the molecular subgroup.
457: Risk Factors for Chronic Depression Following Aneurysmal Subarachnoid Hemorrhage: A 17-year Experience

Joshua Catapano MD (Phoenix, Arizona) Stefan Koester, MS; Ethan Winkler, MD; Robert Rudy, MD; Tyler Cole, MD; Jacob Baranoski, MD; Visish Srinivasan, MD; Christopher Graffeo, MD; Ruchira Jha, MD; Ashutosh Jadhav, MD; Andrew Ducruet, MD; Felipe Albuquerque, MD; Michael Lawton, MD

Introduction: Aneurysmal subarachnoid hemorrhage (aSAH) is associated with substantial morbidity. Besides physical and/or neurological disabilities, aSAH patients often suffer from psychological sequelae including depression. However, the prevalence and risk factors for chronic depression in aSAH remains largely unknown.

Methods: Patients with an aSAH treated at the Barrow Neurological Institute from 2003 to 2019 with long term follow-up were analyzed for chronic depression. Data for patients in the BRAT(2003-2007) were extracted from 6-year follow-up and those from 2007-2019 from the Post-Barrow Ruptured Aneurysm Trial (PBRAT) via long-term phone follow-up. Chronic depression was defined as >/=5 positive answers for >2 weeks using the SIGECAPS depression screening questionnaire. Patients were dichotomized into depression and no depression. Primary outcome was risk factors for depressions via a logistic regression analysis with significance of p<0.05.

Results: During the 17-year study period 1,419 patients were treated for an aSAH, with 514(36%) having follow-up depression data available. Of the 514 patients, 152(30%) were found to have major depression with an average follow-up over 6-years post-aSAH. Following a multivariable logistic regression analysis, modified Rankin Scale(mRS)>2(OR 2.44, 95% CI 1.49-3.97,p<0.001) and tobacco use(OR 2.25, 95% CI 1.46- 3.51, p<0.001) were found to be predictors of depression in this population. A multivariate logistic regression analysis was then performed for patient’s discharged with an mRS of 0-2, finding tobacco use(OR 2.19, 95% CI 1.29-3.79,p=0.004) and the presence of a DVT or PE in the hospital(OR 2.67, 95% CI 1.00-6.86,p=0.043) to be significant predictors of depression in patients with good outcomes.

Conclusion: In this long-term study, a substantial percentage of patients demonstrated symptoms of depression on follow up highlighting the importance of evaluating for and managing mood disorders in the aSAH population. Tobacco use and poor neurological outcomes were significant predictors of depression. Future studies analyzing mental health and aSAH is warranted.
458: Shorter Reproductive Lifespan and Early Age at Menopause Are Associated with Aneurysmal Subarachnoid Hemorrhage in Women

Pui Man Rosalind Lai MD (Boston, Massachusetts) Monik Jimenez, Sc.D. – Assistant Professor of Medicine, Medicine, Brigham and Women’s Hospital/Harvard Medical School; Rose Du, MD, PhD – Director of Cerebrovascular Surgery, Professor of Neurosurgery, Neurosurgery, Brigham and Women’s Hospital/Harvard Medical School; Kathyrn Rexrode, MD, MPH – Chief, Division of Women’s Health, Department of Medicine, Brigham and Women’s Hospital/Harvard Medical School

Introduction: Subarachnoid hemorrhage from cerebral aneurysm remains a devastating disease with high mortality and morbidity. Cerebral aneurysm and its rupture are more prevalent in post-menopausal women and have been postulated to be hormonally influenced. The goal of this study was to investigate the associations of female-specific factors, including reproductive life span, age at menarche, and age at menopause, with the incidence of aneurysmal subarachnoid hemorrhage (aSAH) in women.

Methods: A total of 97,398 postmenopausal women with reproductive lifespan data in the Nurses’ Health Study were prospectively followed from 1980 or the time of reaching menopause until 2018, Only women with natural menopause or surgical menopause due to bilateral oophorectomy were included. Reproductive life span was defined by subtracting the age at menarche from the age at menopause. A total of 138 participants developed aneurysmal subarachnoid hemorrhage which was confirmed on medical record review by a physician. Multivariate stratified proportional hazards models were used to study reproductive life span, age at menarche and age at menopause with the incidence of aSAH. Multivariate models were adjusted for age, race, smoking, hysterectomy, hypertension, hyperlipidemia, body mass index, hormone therapy use, oral contraceptive use, and parity.

Results: A shorter reproductive lifespan (≤35 years) was associated with a two-fold higher incidence of aSAH after multivariable adjustment (HR=2.0 [95%CI 1.4-2.8]). Early age at menopause (age<45) was similarly associated with a higher risk of aSAH (HR=2.1 [95%CI 1.4-3.1]), but age at menarche was not. The use of oral contraceptives and postmenopausal hormone therapy were not associated with the incidence of aSAH.

Conclusion: An earlier age at menopause, as well as a shorter reproductive life span duration (≤35 years), were associated with a higher risk of incident aSAH in women.
**459: Non-invasive Low Pulsed Electric Fields Induce Transient BBB Disruption, Depicted by the Trams, Enabling Efficient Delivery of Biologics into the Brain**

Yael Mardor PhD (Tel-Hashomer, Israel) David Last, PhD – Advanced Technology Center – Sheba Medica Center; yael Bresler, Student – Sackler Faculty of Medicine – Tel Aviv University; Dianne Daniels, PhD – Advanced Technology Center – Sheba Medica Center; Itzik Cooper, PhD – Head of the BBB lab, The Joseph Sagol Neuroscience Center, Sheba Medica Center; Shirley Sharabi, PhD – resaetcher, Advanced technology center, Sheba Medica Center

**Introduction:** Brain diseases are extremely hard to treat, mainly due to poor penetration of therapeutics across the BBB. We have developed a method to induce non-invasive transient/safe BBB disruption (BBBd) using low pulsed electric fields (L-PEFs) and demonstrated feasibility/efficacy in-vitro and in-vivo.

**Methods:** In-vitro: 10 pulses (7-150V/cm, 50µs at 1Hz, total 10sec) were applied to a human in-vitro BBB model. BBB function was measured using trans-endothelial-electric-resistivity (TEER) and permeability+efficacy assays to different therapeutics (chemotherapy, proteins, antibodies, siRNA and cells).

In-vivo: 25-400 pulses (100-300V, 50µs pulses at 4Hz, total 25-100sec) were applied non-invasively to mice brains using 2-plate electrodes pressed against the skull. Contrast-enhanced T1-weighted MRI and treatment response assessment maps (TRAMs, based on delayed-contrast MRI) were used to depict BBBd. Evens-blue/Doxorubicin were used to quantify drug penetration into the brain.

**Results:** In-vitro: Significant increase in permeability to Fluorescein and decrease TEER were found at fields >15V/cm (p<5E-24). 40±7% increase in transmigration of immune cells was also found at 45V/cm. In-vitro efficacy studies with Taxol and glioma cells and with Kadcyla and Her2+ breast cancer cells showed that L-PEFs induced BBBd resulted in significant therapeutic effects (tumor cells-kill) compared to control (p<2.2E-9, p<0.01).

In-vivo: Treatment with 100 pulses (25sec) induced subtle BBBd (fully recovered after 1-4hrs), depicted on the TRAMs but not on conventional T1-Gd. BBBd intensity/volume increased linearly with the voltage and number of pulses. Based on a finite-elements simulations, the electric field in the disrupted regions was 28-87 V/cm. The MRI BBBd results were consistent with the Evens Blue results. Following L-PEFs with IV Doxorubicin, the Doxorubicin brain concentration reached 885±85 µM, X230 its IC50 in GL261 glioma cells.

**Conclusion:** Our results demonstrate the feasibility for efficient/non-invasive/reversible BBBd using short L-PEFs treatments, enabling efficient delivery of Biologics, thus leading the way to new means for non-invasive drug delivery into the CNS.
460: Sympathetic Nervous System Hyperactivity Results in Potent Cerebral Hypoperfusion in a Swine Model of Cerebral Vasospasm

Wi Jin (Jason) Kim MD (Los Angeles, California) Michael Dacey, MD; H. Milan Samanage, MBBS; David Zarrin, BS; Keshav Goel, BS; Christopher Chang, BS; Xin Qi, BS; Anthony Wang, MD; Kalyanam Shivkumar, MD PhD; Jeffrey Ardell, PhD; Geoffrey Colby, MD PhD

Introduction: Cerebral vasospasm is a complex disease resulting in reversible narrowing of blood vessels, and a leading cause of preventable stroke and poor outcomes following aneurysmal subarachnoid hemorrhage. Sympathetic-mediated vasoconstriction is thought to be a significant contributor to cerebral vasospasm. We sought to demonstrate that stimulation of the superior cervical ganglion (SCG) and sympathetic activation in swine can cause ipsilateral cerebral hypoperfusion similar to that of human cerebral vasospasm. Furthermore, we aimed to show that inhibition of SCG can reverse the effects sympathetic-mediated cerebral hypoperfusion.

Methods: SCG was surgically identified in 15 swine and was electrically stimulated to achieve sympathetic activation. CT perfusion scan was used to assess for changes in cerebral blood flow (CBF), cerebral blood volume (CBV), mean transit time (MTT) and maximum recorded temperature (TMax). Syngo.via software was used to determine regions of interest and quantify perfusion measures.

Results: SCG stimulation resulted in significant ipsilateral cerebral hypoperfusion. There was approximately 20-30% reduction in mean ipsilateral CBF and CBV compared to its contralateral unaffected side (p<0.001). Additionally, ipsilateral MTT and TMax increased with SCG stimulation. Injection of lidocaine to the SCG inhibited the effects of SCG stimulation and restored perfusion comparable to that of baseline (p>0.05).

Conclusion: In swine, electrical stimulation of SCG resulted in a significant cerebral perfusion deficit, and this was inhibited by prior local anesthetic injection into the SCG. Inhibiting sympathetic activation by targeting the SCG may be an effective treatment option for cerebral vasospasm.
461: Inflammasomes in Large Vessel Occlusion Thrombi

Stephanie Chen MD (Miami, Florida) Xavier Scott, B.S.; Juan Pablo de Rivero Vaccari, PhD; W. Dalton Dietrich, PhD; Robert Keane, PhD; Eric Peterson, MD; Robert Starke, MD; Dileep Yavagal, MD

Introduction: Inflammation and coagulation are closely related processes wherein inflammatory mechanisms initiate clotting and clotting increases inflammatory responses. Previous studies have shown that the inflammasome, an innate immune complex involved in the activation of interleukin (IL)-18 and IL-1 through caspase-1 may play a critical role in the inflammatory response after stroke in humans [1] and rodents [2]. In this study, we assess the presence of inflammasome proteins in cerebral thrombi and their association with clinical and procedural outcomes of mechanical thrombectomy for acute ischemic stroke.

Methods: Between November 2018 and November 2019, we conducted a prospective study investigating thrombi retrieved from mechanical thrombectomy procedures in acute ischemic stroke patients admitted to Jackson Memorial Hospital/University of Miami Hospital. Patient demographics, clinical presentation, neurological exam, procedural details, and follow-up data were collected. Simplex assay analysis was used to evaluate the relative concentration of inflammasome proteins caspase-1, ASC, IL-1β, and IL-18 in cerebral thrombi as compared to the plasma of stroke patients and healthy controls. Multivariate regression models were used to identify predictors of functional independence, vessel recanalization, and time to reperfusion.

Results: There is significantly increased expression of ASC (p<0.0001), caspase-1 (p<0.0001), IL-1β (p=0.0013) in cerebral thrombi and significantly decreased expression of IL-18 (p<0.0001) as compared to serum and plasma of healthy controls. On multivariate analysis, IL-1β was correlated with poor functional outcome (p=0.05) and number of passes (p=0.049). ASC, caspase-1 and IL-18 were correlated with time to recanalization.

Conclusion: These results provide evidence for inflammasome activation in cerebral thrombi. Furthermore, inflammasome protein level is associated with number of thrombectomy passes, time to recanalization, and worse outcomes, which reflects the role of inflammasomes in clot formation and stabilization.
462: Rescue Stenting for Acute Ischemic Stroke with Refractory Emergent Large Vessel Occlusion in the Modern Thrombectomy Era

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Introduction: Despite the recent and remarkable advances in treatment for large vessel occlusions, successful recanalization is not achieved in about 12-29% of the mechanical thrombectomies (MT). Rescue stenting is used as a bailout technique in select stroke patients. We present findings of our experience with rescue stenting for refractory emergent large vessel occlusion (RELVOs) and compare with patients in which we were unable to achieve recanalization.

Methods: We identified all patients who underwent a mechanical thrombectomy for a large vessel occlusion between January 2010 and October 2019. Subjects with mTICI 0-2A after at least three passes were defined as failed MT and constituted the control group (NSG). Patients that received a rescue stent (RSG) formed the study group.

Results: Comparative analysis of patient demographics between NSG and SRG was performed. Baseline characteristics and comorbidities were not significantly different between both groups. NIHSS at admission and IV t-PA were not significantly different among both groups (16.5 vs. 14.2, p=0.19) and (39.4% vs. 29.4%, p=0.30), respectively. There was no significant difference in procedural and post-procedural complications between both the groups. In the RSG, 24 patients (82.4%) achieved favorable revascularization outcomes. NIHSS at discharge (p=0.01) was higher in the NSG, while favorable functional outcome at three months (12% vs. 39.2%, p=0.01) was observed at a higher proportion in the RSG. There was also a significant mortality difference, with 15.2% mortality in the RSG compared to 35.1% mortality in the NSG (p=0.03). In multivariate analysis, stenting was an independent predictor of favorable outcome (OR: 10.0, p=0.009).

Conclusion: Herein, we demonstrated that rescue stenting is a feasible, safe, and effective procedure to improve stroke outcomes and should be seriously considered if the primary mechanical thrombectomy is not successful.
463: Laparoscopic Omental-cerebral Transposition for Repeat Revascularization of Refractory Moyamoya Disease

Benjamin Yim MD (Palo Alto, California) Matias Bruzoni, MD – Associate Professor, Pediatric Surgery, Stanford University; Sanjeev Dutta, MD MA – Pediatric Surgery – Stanford University; Andrew Gauden, MBBS PhD – Stanford University; Gary Steinberg, MD PhD – Stanford University

Introduction: Despite the success of traditional revascularization techniques for moyamoya disease, there remains a subset of patients for which failure of these procedures results in progression or recurrence of symptoms. While the use of omental grafts has largely been abandoned in recent decades, the modernization of laparoscopic techniques has improved the safety and viability of the omentum as an additional source for intracranial perfusion, particularly in stances where traditional modalities have failed.

Methods: A retrospective chart review was performed for 21 consecutive patients (mean 27.5± 7.3 yo, 7 patients ≤ 18 yo) undergoing omental-cerebral transposition for Moyamoya disease between 2011 to 2021. All patients had recurrent or progressive ischemic symptoms despite prior revascularization procedures with a mean inter-procedural time of 4.15 ± 1.3 years. Pedicled omental grafts were procured and tunneled laparoscopically by general surgeons for 20 patients with a single patient requiring a free flap anastomosis of omentum gastroepiploic artery & vein to the superficial temporal artery & vein.

Results: All patients had preserved or improved Modified Rankin Scores and improvement of frequency and/or severity of ischemic symptoms with 13 patients having complete resolution during a mean follow-up period of 3.5 ± 1.02 years. 20 patients were discharged home following 4.16 ± 0.97 hospitalization days with 1 patient transferred to an acute rehabilitation unit. 13 of the 17 digital subtraction angiograms obtained at 6 months post-procedure demonstrated contrast filling of the graft. Notable complications included vascular injury to the transverse colon (1), incisional hernia (2), granuloma formation at the neck (1), aspiration pneumonia (1), and acute tubular necrosis (1).

Conclusion: Laparoscopic omental-to-cerebral revascularization is effective and safe in managing the difficult cohort of patients with Moyamoya disease refractory to traditional surgical techniques.
464: Factors Associated with Intracranial Aneurysm Rupture: A HEAT Trial Secondary Study

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Introduction: The risk of intracranial aneurysm rupture is dependent on multiple patient-related and aneurysm-related factors. Understanding these improves patient selection for appropriate aneurysm treatment. Using the Hydrogel Endovascular Aneurysm Treatment (HEAT) database, we evaluated factors associated with aneurysm rupture at presentation and developed a risk model for predicting hemorrhage.

Methods: The HEAT trial enrolled 600 subjects with a single intracranial aneurysm eligible for endovascular coiling. The dataset was randomly divided into training and validation sets. In the training set, we evaluated potential risk factors for aneurysm rupture using univariate and multivariate regression analyses. Factors significant at the multivariate analysis level were integrated into a regression-based model and validated with receiver operating curves. The final score model was constructed using multivariate analysis of the total dataset.

Results: 593 aneurysms were included and 169 (28.5%) were ruptured. Dome-to-neck ratio > 2.5, irregular shape, daughter sac, and anterior and posterior communicating artery locations were associated with higher rates of hemorrhage. The use of aspirin was associated with a lower rate of hemorrhage. The validation set yielded an area-under-the-curve > 0.8. Data on aspirin use (OR=0.16, 95% CI [0.09-0.28]), dome-to-neck ratio > 2.5 (OR=3.66, 95% CI [2.10-6.37]), irregular shape (OR=3.79, 95% CI [1.97-7.30]), daughter sac (OR=5.89, 95% CI [2.98-11.64]), anterior (OR=3.32, 95% CI [1.70-6.49]) and posterior communicating (OR=3.56, 95% CI [1.83-6.91]) artery locations were implemented in a regression-based model. Predictive factors were assigned as 1 point; aspirin use was assigned –1 points. Cumulative scores were associated with the probability of aneurysmal hemorrhage ranging from 1.5% to 70%.

Conclusion: In the HEAT trial population, aneurysm shape, location, and dome-to-neck ratio were associated with increased rate of aneurysm rupture at presentation while aspirin use was associated with a decreased rate. The development of a hemorrhage risk model allowed us to assess the probability of hemorrhage in patients with these risk factors and to assist clinical judgement.
465: Vessel Wall Imaging and Quantitative Flow Assessment in Arteriovenous Malformations: A Feasibility Study

Laura Stone McGuire MD (Chicago, Illinois) Mark Rizco, MD, MS; Denise Brunozzi, MD; Fady Charbel, MD; Ali Alaraj, MD

Introduction: Cerebral arteriovenous malformations (AVMs) draining vein stenosis is associated with higher rate of AVM rupture. Several architectural factors influence rupture rate, and a recently theorized model describes the role of vessel wall inflammation that predisposes to stenosis and nidal hemorrhage. A novel imaging modality, vessel wall imaging (VWI), has been developed to study cerebral aneurysms and inflammatory processes in vessel wall foci and but has not been examined in AVMs or their draining veins.

Methods: This retrospective chart review studies prospectively collected data in patients with both ruptured and unruptured AVMs between 2019 to 2021. Inclusion criteria included adult patients (>18 years) with radiographically confirmed AVM diagnosis who underwent VWI protocol. Patients who could not undergo VWI due to contraindication to MRI or gadolinium were excluded from analysis. Charts were reviewed for medical history, including clinical presentation, hospital course, and follow-up.

Results: Nine patients underwent VWI, aged 37.7 +/- 9.9 years, and 4 presented with hemorrhage (44.4%). Seven (77.7%) received glue embolization, and 6 (66.7%) underwent surgical resection. Of baseline characteristics, all patients (4/4) with hypertension presented with hemorrhage (p=0.0027). Size and Spetzler-Martin grade were not associated with hemorrhage presentation (p=0.47, p=0.59). Net AVM blood flow was higher in patients presenting with hemorrhage, although non-significant (p=0.19). With VWI, 3 (75%) hemorrhagic AVMs demonstrated positive post-contrast wall enhancement in at least one draining vein; conversely, only 2 (40%) non-hemorrhagic AVMs demonstrated post-contrast wall enhancement in any draining vein (p=0.090). There was a non-significant trend toward circumferential enhancement in walls of draining veins of hemorrhagic AVMs relative to non-hemorrhagic AVMs (p=0.47).

Conclusion: This pilot study successfully demonstrated capture of venous walls in AVMs using VWI. It also suggested that VWI may be used to prognosticate AVM stability. Particularly notable is the nearly significant association between draining vein enhancement and AVM rupture and venous volumetric flow.
466: Angiographic Study of Cranial Venous Outflow Patterns at the Skull Base in Patients with and Without Idiopathic Intracranial Hypertension

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Introduction: Several venous collateral pathways exist that provide cranial venous outflow, in addition to the internal jugular vein (IJ) and may be termed extrajugular networks (EJN). With the increasing role of venous sinus stenting in idiopathic intracranial hypertension (IIH), greater attention is being paid to venous hemodynamics. However, the angiographic pattern of venous drainage via EJN has not been compared previously between patients with and without IIH.

Methods: A retrospective imaging review of 100 cerebral angiograms at a single academic medical center was performed: 50 consecutive patients diagnosed with IIH (IIH group) and 50 patients undergoing angiography for other indications (non-IIH group). Based on the size and opacification of the EJN on AP and lateral images in relation to the IJ (randomly assigned 5 points), points in ascending order ranging from 0-6 were assigned for: Pterygoid, Clival plexus, Inferior Petrosal Sinus, Condylar/Mastoid Emissary and ‘Other’ (torcular or occipital emissary vein). Mann-Whitney U test was used for comparison of individual EJNs between the 2 patient groups.

Results: The inter-rater reliability between the raters was substantial (Cohen kappa coefficient k =0.869) for each EJN on either side and for assessment of sinus dominance. Significant difference in distribution of extrajugular venous drainage was noted between IIH group and non-IIH group for several EJN, implying more robust extrajugular venous drainage at the skull base in patients with IIH.

Conclusion: This study was able to characterize significantly increased anterior and posterior extrajugular venous outflow in IIH patients in both supra- and infratentorial compartments. Whether this finding has an etiopathogenic basis or is simply an epiphenomenon needs to be elucidated. Objective flow estimation of both jugular and extrajugular venous outflow in physiological and pathological conditions may lend itself to development of a points based system with potential diagnostic and prognostic value in selection of patients for appropriate therapy.
467: Between Scylla and Charybdis: A Neuroanatomic & Clinical Assessment of Safe Navigation Routes Through the Middle Cerebellar Peduncle for Brainstem Cavernous Malformation Resection

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Introduction: Brainstem cavernous malformations (BSCM) resection is challenging, due to deep location and proximity to key structures. The middle cerebellar peduncle (MCP) offers a versatile approach for many BSCM; however, outcomes after trans-MCP resection as a function of neuroanatomic trajectory have not been studied.

Methods: Single-surgeon cohort study of all primary trans-MCP BSCM resections during the study period, 7/1/2017-6/30/2021. Pre- and postoperative MRIs were reviewed by 3 independent, blinded investigators, using a standardized rubric to define zones of BSCM involvement and resection trajectories.

Results: Thirty-one patients underwent primary trans-MCP BSCM resection during the study period. Median age was 40 (range 5-83); 19 were female (61%); 7 had familial cavernoma syndromes (23%). Median follow-up was 6 months (range 6-37); no mortality occurred. Median preoperative modified Rankin scale (mRS) was 1 (range 1-4); immediately after surgery, 4 patients experienced an mRS decline ≥2 (13%), 2 of whom improved by ≥1 point as of 6-month follow-up (50%). Twelve had immediate postoperative new/worsened cranial neuropathy or hemiparesis (39%); 11 experienced at least partial recovery in follow-up (92%). After adjusting for lesion size and baseline deficits, resection trajectories involving the ventral midbrain, ventral medulla, or contralateral ventral pons were associated with unfavorable outcomes.

Conclusion: Trans-MCP resection is a safe and effective treatment strategy for many patients with BSCM. Involvement of ventral regions in the mesencephalon or medulla may convey increased risk of new postoperative deficit, especially if the operative trajectory extends contralateral to the entering MCP.
468: Pre-operative Brain Mapping Supports Clinical Decision and Guides Surgical Management in Eloquent Arteriovenous Malformation. A Clinical Prospective Study

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Introduction: A considerable number of cerebral arteriovenous malformations (AVMs) occur adjacent to the eloquent cortex, and the heterogeneity of cortical plasticity and functional reorganization presents a challenging scenario for clinical management. Surgical management of AVMs is often associated with significant risk causing postoperative functional deficits. A greater understanding of the developmental progression and intrinsic plasticity in AVMs will inevitably help advance the discovery of treatments and surgical management. Although developmental neural plasticity is known to play a critical role in AVMs, to date, brain mapping has not been implemented to assess its impact on eloquent areas of AVM patients. Indeed, brain mapping has not even been utilized for pre-operative decision-making to enhance outcomes in AVM patients.

Methods: Here, we use transcranial magnetic stimulation (TMS), electroencephalography, electromyography, phosphene induction, and neurobehavioral outcomes to functionally map language, motor, and vision in AVMs patients.

Results: The results of pre-operative mapping and detailed neurobehavioural outcomes demonstrate a significant developmental functional plasticity and downgraded the Spetzler Martin score in patients. These AVM patients underwent surgical resection without postoperative deficits. In summary, this study proves that neuronavigation TMS can be used to map motor, language, and visual function (for the first time) accurately and allowing for personalized functional plasticity-based surgical plans for the treatment of AVMs.

Conclusion: This modern approach allows for precise surgical management of AVMs using multiple complementary approaches to surgically treat AVMs to preserve motor, language, and visual functions.
469: Pilot Study of a Randomized, Blinded, Placebo-controlled Trial of Shunt Surgery in Idiopathic Normal Pressure Hydrocephalus

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Introduction: While multiple prospective non-randomized studies have shown that 60-70% of patients improve with shunt surgery, no multi-center placebo-controlled trial has been performed. Without this evidence some have called for a restriction or cessation of idiopathic normal pressure hydrocephalus (iNPH) shunting. While multiple prospective non-randomized studies have shown that 60-70% of patients improve with shunt surgery, no multi-center placebo-controlled trial has been performed. Without this evidence some have called for a restriction or cessation of iNPH shunting.

Methods: Five sites of the Adult Hydrocephalus Clinical Research Network, enrolled 18 patients scheduled for ventriculoperitoneal shunting based on response to CSF drainage. Patients were randomized to a Codman® Certas® Plus valve with SiphonGuard® at either setting 4 (Active, N=9) or setting 8 "virtual off" (Placebo, N=9). Patients and assessors were blinded to the shunt setting. Outcomes included 10-meter gait velocity (primary outcome), cognitive function, bladder activity, depression, Modified Rankin scale, and Lawton ADL/IADL scores. The primary analysis was gait velocity improvement in the Active versus Placebo groups at 4-months. Afterwards all shunts were blindly adjusted to the active setting. The long term evaluation of active shunting in all patients is ongoing.

Results: At the 4-month primary outcome evaluation, gait velocity increased by 0.28 ± 0.28 m/s in the Active Group and 0.06 ± 0.15 m/s in the Placebo Group (p=0.078), a treatment difference of 0.21 m/s (95% CI: -0.03, 0.45). Overactive Bladder (OAB-q) significantly improved in Active versus Placebo (p=0.007). No significant between-group differences were found for the other outcome measures.

Conclusion: This multi-center, randomized pilot study demonstrates the feasibility of a placebo controlled trial in iNPH and a trend suggesting gait velocity improves more at an active shunt setting than a placebo shunt setting. A larger, sufficiently powered, study is indicated and planned to confirm the efficacy of shunting.
470: A Role for Steroids in Acute Pain Management in Patients with Trigeminal Neuralgia

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Introduction: Effective therapies for acute pain management in trigeminal neuralgia (TN) are limited. Here, we investigate the role of steroids in TN patients experiencing acute pain flares.

Methods: We retrospectively reviewed patients presenting to the emergency room of a tertiary care institution between 2014-2020 for acute trigeminal neuralgia pain flares. Patients were dichotomized into those who received steroids versus those who did not. General presenting characteristics, admission and surgical intervention rates, Barrow Neurological Institute (BNI) pain and numbness scores upon presentation and discharge, pain recurrence rates, and surgical intervention within 6 months of discharge were obtained for each patient.

Results: Our cohort consisted of 151 patients presenting to the emergency room, of which 40 (26.5%) received steroids prior to admission and/or discharge. Patients who received steroids were less likely to undergo surgical intervention to treat their acute pain flare, p=0.023. Specifically, these patients were less likely to undergo combined glycerin and radiofrequency rhizotomy compared to patients who did not receive steroid treatment, p=0.012. Upon discharge, patients in the steroid group were more likely to be prescribed steroids upon discharge compared to patients in the non-steroid group, p<0.001. Additionally, the steroid treatment group demonstrated a lower average BNI pain score on discharge compared to the non-steroidal group, p=0.013. Patients who received steroids for acute pain management were less likely to undergo surgical intervention within 6 months of discharge than those who did not receive steroids (p=0.033). Steroid administration did not show any significant reductions in admission rates or 30-day readmission rates following discharge.

Conclusion: Our findings suggest that steroid administration in these cases may reduce the likelihood of surgical intervention both during admission and within 6 months of discharge. Future prospective studies should examine the efficacy of steroids as an adjunctive medication in acute trigeminal neuralgia pain management.
471: Interventional Therapies for SUNCT/SUNA: A Review

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Introduction: Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) and short-lasting unilateral neuralgiform headache with autonomic symptoms (SUNA) are disabling primary headache disorders. While the medical therapies for SUNCT/SUNA have been well documented, there exists a paucity of data regarding the outcomes for interventional therapies in patients who fail medical management. This literature review sheds light on the current evidence available for interventional therapies in medically intractable SUNCT/SUNA.

Methods: PubMed, EMBASE, and the Cochrane Library were searched for publications between 1978 and 2021. Inclusion criteria were SUNCT/SUNA studies reporting outcomes following occipital nerve stimulation (ONS), sphenopalatine ganglion stimulation, stereotactic radiosurgery (SRS), deep brain stimulation (DBS), or microvascular decompression (MVD) of the trigeminal nerve.

Results: Of the 194 studies screened, 31 were selected. For the purposes of this review, a greater than 50% reduction in severity or frequency was defined as a successful response. For ONS, 19/26 (73.1%) patients were considered responders. 9 patients received pulsed radiofrequency (PRF) of the sphenopalatine ganglion, with 5 patients (55.6%) being successful. In DBS of the posterior hypothalamus, 12/14 (85.7%) responded. Radiosurgical (SRS) treatment to the sphenopalatine ganglion and/or trigeminal nerve resulted in a 7/9 (77.8%) response rate. MVD was successful in 24/33 (72.7%) patients. Mean follow-up time in months was 39.5 (ONS), 24.8 (PRF), 28.2 (DBS), 24.6 (SRS), and 15.5 (MVD). The patients treated with SRS and MVD were more likely to reach complete resolution of symptoms without requiring supplemental medications.

Conclusion: Ultimately, a significant proportion of SUNCT/SUNA patients remain unresponsive to medical therapy (45-50%). This review discusses the current data available for interventional approaches including neuromodulation, gamma knife radiosurgery, and microvascular decompression. The encouraging outcomes from these techniques emphasize the need for further research in order to develop a robust surgical management algorithm.
472: The Effect of Intraoperative Intrathecal Morphine Administration on the Length of Stay and Postoperative Pain Control for Patients Undergoing Lumbar Interbody Fusion

Kara Beasley DO; Ewell Nelson, MD; Hash Taha, BA; Sharad Rajpal, MD; Sigita Burneikiene, MD

Introduction: To control postoperative pain more effectively in spinal fusion patients, the intraoperative intrathecal morphine (ITM) administration is gaining popularity and acceptance with clinicians. The main objective of this study was to determine the impact of intraoperative intrathecal morphine administration on postoperative pain control and length of hospitalization.

Methods: The retrospective analysis of prospectively collected data was performed. The study compared patients undergoing one- or two-level transforaminal interbody fusions between 2019 and 2021 and intraoperatively received two different ITM doses (n=89) vs. the reference group (n=48) that did not receive ITM. The ITM group was further divided into two subgroups: 50mg (n=44) or 175mg (n=44) morphine equivalent dosage (MED). The effect of ITM was evaluated for the first four postoperative days (POD) on pain scores (Visual Analog Scale), length of stay (LOS, hours), and opioid requirement.

Results: In the ITM group, a significant reduction of postoperative pain scores (t(99) = 4.3, p = < 0.001) and opioid intake (t(70) = 2.47, p = < 0.05) was noted on POD1; there was also a tendency for lower opioid intake on POD 2 - 4 (p>0.06), which was partially offset by the increased post-operative acetaminophen administration. Mean LOS was 15.4 hours less in the ITM group (63.4 ± 37.1 vs. 78.8 ± 39.6; p = 0.06). Analyzing the effect of dosage (50mg vs. 175mg MED), no significant differences were found in length of stay (LOS), pain scores, or post-operative MED intake.

Conclusion: In patients undergoing lumbar spinal fusion, intraoperative ITM administration predicts a significant decrease in pain scores and opioid intake for POD1 with no increase in adverse events. There was also a tendency of lower opioid intake for the following postoperative days, but no benefits were noted in patients who received a higher ITM dose.
Introduction: Trigeminal Neuralgia (TN) is characterized by brief episodes of unilateral, electric shock-like pain in the distribution of the trigeminal nerve that typically is triggered by cutaneous stimuli. Percutaneous Radiofrequency Ablation (PRT) remains the first-line invasive treatment following medical treatment. Outcomes for 3rd branch are well documented as successful however, TN of multiple or the remaining branches are not as successful. Internal structure of the Gasserian Ganglion (GG) is thought play a major role for this variance in outcomes despite the similar surgical technique. Therefore, the anatomical structure of GG and its divisions on cadavers are investigated to understand their contribution to PRT outcomes.

Methods: Six cadaveric heads were following Klingler’s method and each GG and middle fossa were dissected under microscope using Rhoton Surgical Instruments. Dissections were carried out at Department of Neurosurgery, “Center for Advanced Simulation and Education (CASE), Neuroanatomy Lab” at Acibadem MAA University. After the fiber dissection of the GG, PRT procedure were done using a hollow metallic introducer gauge 14 with a sharp tip. Fluoroscopy images were taken to compare results as well as the dissection photographs after the catheter is introduced.

Results: Within the GG, major bundles of each branch can be divided into two segments and these segments make their separation twice, once in the proximal area and once in the distal area before the exit. Furthermore, in all ganglions (n=12), there are fiber components of V2 present that have not been possible to penetrate with the catheter.

Conclusion: The dissections along with the PRT procedure on the cadavers leads to two major outcomes: 1) Each branch inside the GG has major bundles which divide twice. Therefore, it can be assumed that ablation of the correct area as confirmed by stimulation during PRT may leave some branches intact depending on the location. 2) The chances of a single lesion generation for V2 TN is very low for covering all bundles exiting from the V2.
**Introduction:** Complex facial pain syndrome (CFPS) is a debilitating condition with varying etiologies that responds poorly to medical and surgical management. Motor cortex stimulation (MCS) with spinal paddle electrodes, placed via functional magnetic resonance imaging (fMRI) and diffusion tensor imaging (DTI) guidance, represents a unique and novel alternative intervention for patients suffering from CFPS who have failed traditional treatments.

**Methods:** All relevant patient charts and imaging were reviewed and summarized for inclusion. Relevant literature was reviewed and included for augmentation of the conclusion.

**Results:** A 56-year-old male presented for evaluation of CFPS. His past surgical history was significant for multiple facial reconstructive surgeries. The patient was diagnosed with trigeminal neuralgia and underwent microvascular decompression without significant improvement in symptoms. He developed left-sided complex facial pain syndrome after a stroke, which was refractory to medical management and peripheral nerve stimulation. Given the failure of traditional management, it was decided the patient was a candidate for MCS. Areas of the motor cortex corresponding to facial and tongue motor areas were identified using fMRI and DTI. Intraoperatively, phase reversal was used to identify corticospinal tracts and stimulus mapping confirmed the location before the epidural placement of two spinal paddle electrodes. Postoperatively, the patient reported significant reduction in pain levels, burning dysesthesias, and symptom frequency. This trend continued, and the patient experienced equivalent levels of relief at four months.

**Conclusion:** We report effective treatment of refractory CFPS with MCS. Utilization of DTI and fMRI was central to accurate placement of leads. Additionally, we demonstrate that spinal epidural paddles can be effectively employed in intracranial locations.
475: Augmentation of Postoperative Pain and Opioid Consumption Following Craniotomy: A Study of Subcutaneous Sumatriptan

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Introduction: Traditional pain management pathways following craniotomy are predicated on opioid medications which may confound critical neurological examination in the postoperative period. Alternative medication regimens to better address pain while mitigating opioid-related adverse effects have been insufficiently studied. Sumatriptan, a 5-HT1D receptor agonist that regulates vasoconstriction has been shown to augment pain following craniotomy for microvascular decompression and chronic post-craniotomy headache. Herein, we evaluate the efficacy of subcutaneous sumatriptan to reduce or augment pain following craniotomy.

Methods: This single academic center, retrospective cohort study of 106 consecutive adult patients undergoing craniotomy between 7/2015 and 8/2021. Patients were divided between a control and sumatriptan cohort contingent upon administration a single 6mg subcutaneous injection of sumatriptan within 1-hour of surgery completion and prior to opioid administration. Opioid consumption at 6, 12 and 24-hours postoperative and admission total, inpatient length of stay (LOS) and 30-day representation for pain were evaluated. Craniotomy for trauma or patients with cerebrovascular pathology were excluded.

Results: Fifteen and ninety-one patients were included in for analysis in the sumatriptan and control cohort, respectively. Baselined differences in indication for craniotomy (p=0.004) and prior surgery (p=0.002) existed. A nonsignificant decrease in MEU consumption was observed at all postoperative timepoints favoring the sumatriptan cohort (p>0.05). At 6-hours post-surgery, pain score favored the control group, but similar at all other timepoints. LOS (4.0 vs 2.2 days) was greater in the sumatriptan cohort (p=0.009). Evaluation in the emergency department within 30-days of discharge was equivalent at 6 and 3 in the control vs. sumatriptan cohort (p>0.05)

Conclusion: Sumatriptan can be used in the postoperative period to decrease a patient’s reliance on opioid medications for acceptable pain management. While there was no significant difference in MEUs, patients in the sumatriptan group used less opioids at 6 and 12 hours and overall compared to the control group.
476: PHANOR L. PEROT, JR: South Carolina’s Father of Neurosurgery

Zachary S. Hubbard MD MPH (, ) Fraser Henderson, MD; Zachary Hubbard, MD; Sunil Patel, MD; David Semenoff, MD; Alejandro Spiotta, MD

Introduction: Phanor Leonidas Perot, Jr. MD PhD (1928 – 2011) was a gifted educator and pioneer of academic neurosurgery in South Carolina.

Methods: The Dr. Phanor L. Perot, Jr., MD, PhD Collection at the Waring Historical Library at the Medical University of South Carolina were reviewed by the authors for the first time.

Results: As a neurosurgical resident and then as a junior faculty member at the Montreal Neurological Institute, Perot advanced the understandings of both epilepsy and spinal cord injury under Wilder Penfield, William Cone and Theodore Rasmussen. In 1968 he moved to Charleston to lead neurosurgery. From time spent with master physicians like Isadore Ravdin and Wilder Penfield Perot himself became “the ultimate teacher”. His research spanned from epilepsy to torticollis to spinal trauma, focusing most on the basic pathophysiology of cord damage elucidated through somatosensory evoked potentials and distinguished by generous grant funding. By the time he stepped down as Chairman in 1997, the division had become a department and he had served as president of the Academy of Neurological Surgeons and the Society of Neurological Surgeons. Perot taught prolifically at the bedside and considered the neurosurgical training at MUSC his greatest achievement. Although Dr. Perot never fully retired, he also enjoyed active hobbies of fly-fishing, traveling, and hunting, until his death on February 2, 2011.

Conclusion: Phanor Perot influenced many and has earned his place in history as the Father of Neurosurgery in South Carolina.
477: The History of Closed Skeletal Traction in the Management of Cervical Facet Dislocations

Timothy Chryssikos MD, PhD (Baltimore, Maryland)

Introduction: The role and technique of closed skeletal traction (CST) in the management of cervical facet dislocation (CFD) have changed since the first half of the twentieth century.

Methods: Review of primary and secondary literature pertaining to the theory, method, and outcome of CST for CFD.

Results: Over the last 90 years there have been dramatic changes in the role of CST in the management of CFD. Beginning in the 1930s CST was undertaken as a primary intervention, often carried out in patients over the course of several weeks, and guided by the underlying theory that the healing of soft tissues rather than the achievement of bony fusion is responsible for maintaining proper vertebral alignment. Over the next several decades, an unacceptable rate of failure with post-reduction immobilization led to a reassignment of CST as one among several initial approaches to the dislocated cervical facet, with definitive treatment ultimately requiring internal fixation, a trend further solidified by technological improvements in internal anterior and posterior fixation methods during the latter half of the twentieth century. Where it is still attempted, CST tends to be carried out over relatively brief periods using markedly heavier weights. With the widespread adoption of MRI in the 1990s, concern with the herniated disc led to questioning of the safety and utility of CST. Although these concerns have largely dissipated with experience, increasingly fewer residents appear to be trained in CST methods. Other changes and innovations in CST methods are discussed alongside these changes.

Conclusion: CST has witnessed several major changes since the first half of the twentieth century, most notably its underlying theory and role in the management of CFD, and it has evolved alongside innovations in surgical technique, imaging, and critical care. CST has a long and storied history in the management of CFD, which may still be ongoing.
478: “Life and Death 2” The First Neurosurgical Computer Simulation

Ishan Bhatia (Morgantown, West Virginia)

Introduction: Simulation methods and technology for neurosurgery has been increasing in popularity for several years as methods of improving resident and student education as well as patient care. In 1990 a sophisticated, computer based simulator was designed and released commercially as a video game entitled “Life and Death 2: The Brain.” The objective of this work was to record the history of this early, computerized neurosurgical simulator for posterity.

Methods: Programmers and designers involved in the work were identified by review of the game’s credits and contacted electronically. Structured interviews were carried out to record the design, production, and commercial release of the game. In parallel, neurosurgeons of varying experience were introduced to the game and then interviewed to rate the simulation quality.

Results: Data from and first-hand accounts from the video game designers were obtained and recorded in a narrative history of the work. Impressions and recordings of neurosurgeons playing the game were recorded as well to place it in the context of modern neurosurgery.

Conclusion: “Life and Death 2: The Brain” represents an important event in the history of neurosurgery. Both as a very early and sophisticated simulation and also as an important demonstration of neurosurgery’s relationship to the popular culture through recent history.
479: The Operating Table - Past, Present and Future

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Introduction: The operating table is the central piece of furniture in the neurosurgeon’s operating room. Modern neurosurgical procedures require a variety of tables, attachments, and instruments to achieve success.

Methods: We review historical documents including catalogs, articles and books to describe the evolution of the operating table. We review other advances in the instrumentation and apparatuses utilized in the modern operating theater and determine how the operating table may be developed in conjunction and incorporating advances.

Results: The 19th and 20th century witnessed the development of the operating table from any household wooden surface to a specifically built elegant, durable, adaptable, and metal table designed with antisepsis, versatility, and functionality in mind. Modern neurosurgical operating tables vary in shape in size to serve specific function including tables for angiography, craniotomy, and spine surgery. In the last 30 years, modular tables have been developed to allow for increased versatility and customization of each case. With advances in neurosurgical tools and techniques the future operating table will be paramount in incorporating advancements into surgical procedures. The bed of the future may contain artificial intelligence to assist in surgical decision making, robotic arms for navigation guidance, and voice activated control to create efficient workflow.

Conclusion: The operating table has advanced greatly from the days of household wooden surfaces, however remains relatively simple in its current design. The future will hold significant advances to improve a surgeon's efficiency and safety.
480: Building and Implementing an Institutional Registry for a Data-driven National Neurosurgical Practice: Experience from a Multi-site Medical Center

Mohamad Bydon MD, FAANS (Rochester, Minnesota) Abdul Karim Ghaith, MD; Bernard Bendok, MD; Aaron Biedermann, NA; Mohamad Bydon, MD; Allie Canoy Illies, NA; Anshit Goyal, MBBS; Fredric Meyer, MD; Travis Paul, NA; Alfredo Quinones-Hinojosa, MD; Robert Spinner, MD

Introduction: In an era when healthcare “value” remains a much-emphasized concept, measuring and reporting the quality of neurosurgical care and costs remains a challenge for large multi-site health systems. In this article, we seek to highlight our experience in launching an electronic health record (EHR)-linked data-driven neurosurgical practice initiative to measure and improve neurosurgical quality and safety as well as improve payor contract negotiations across a large national multi-site academic medical center.

Methods: In May 2018, the Mayo Clinic commenced a partnership with Epic Systems Corporation in a $1.2 billion deal to replace its already existing in-house Electronic Health Records (EHR) system. The Department of Neurosurgery also highlighted its need for an EHR-linked patient registry aiming to capture quality outcomes such as postoperative readmissions, complications, returns to the operating room, mortality, length of hospital stay and discharge disposition for every patient undergoing a neurosurgical procedure anywhere across the 6 Mayo Clinic sites with active neurosurgery services.

Results: The current version of the neurosurgery dashboard summarizes outcomes of nearly 30,000 procedures that have been recorded in the Epic Neurosurgery Registry from its inception. It allows the user to visualize the chosen performance metrics by date, site of procedure, procedure category and individual surgeon. The dashboard is now identified as an important feedback mechanism for department chairs at each site and has facilitated multi-site discussions about their respective ongoing operative performances through monthly generated outcomes and RVU reports. The data are also being used to support research projects led by interested clinician-investigators through requests for applications (RFAs).

Conclusion: Health systems with the ability to exhibit clinical quality and cost-effectiveness will have an advantage in today’s competitive market environment. Registries and dashboards may represent a viable tool to stipulate quality of care to purchasers of healthcare services and allow internal assessment of key performance indicators.
481: Factors Associated with Pregnancy and Perinatal Outcomes in Female Neurosurgeons: A Cross-sectional Study

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Introduction: Neurosurgery is male dominated with women representing 12% of residents and 5% of practicing neurosurgeons. The conflicting demands of training and childbirth are significant deterrents to women entering the field. The aim of this study, was to examine pregnancy incidence and timing, perinatal complications, and the perceived career impact of motherhood in female neurosurgeons.

Methods: An anonymous survey sent to 643 training, practicing, and retired female neurosurgeons from the United States. The survey included multiple-choice and free-text questions examining the incidence of pregnancy, maternal age, influencing factors, support systems, and perinatal complications.

Results: Among 260 respondents, 50.8% (132/260) reported pregnancies, with an average age at first pregnancy (32.1 years, IQR 30.0 – 35.3) that was significantly higher than the national average (26.3 years). In all, 40.1% (53/132) of respondents reported perinatal complications in at least one of their pregnancies. Only a minority of respondents, 25% (33/132), noted designated program maternity allowances. The main source of childcare was provided in the form of nanny or au pair, 47.4% (55/116). The most significant challenges associated with being a mother and neurosurgeon were reported as issues with work/life balance, “mommy guilt,” and sleep deprivation. A majority, 70.1 % (82/116), reported fear of backlash from co-residents, partners, and staff, as well as hindered career advancement.

Conclusion: Female neurosurgeons face a set of challenges surrounding family planning different from male practitioners. Higher perinatal and fetal complications, backlash from colleagues, and demanding workload remain significant issues for respondents. Progress requires institutional support and mentorship for women to create a more diverse field of practitioners.
482: Affective Disorders Are Associated with Longer Hospitalization and Hospital Charges in Patients Undergoing Elective Lumbar Spinal Fusion

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Introduction: Affective disorders, including depression and anxiety disorders, were found to correlate with certain outcome measures of patients undergoing a variety of surgical procedures. However, this correlation has been under-investigated in the spine literature. The objective of this study was to examine the association between affective disorders and outcome measures in patients undergoing elective lumbar spinal fusion.

Methods: A retrospective cohort study was conducted using the National Inpatient Sample database. Patients who underwent lumbar fusions between 2011-2018 were stratified into two groups: (1) with affective disorder and (2) without affective disorder. Propensity score matching was utilized to minimize effect of confounding variables.

Results: A total of 255,875 cases of lumbar fusions met the inclusion criteria. 25,843 (10.1%) patients carried the diagnosis of affective disorder and were significantly more likely to be non-white (45.1% vs. 19.9%) and of older age group (59.2 vs. 49.9 years) as compared to patients without affective disorders. Patients with affective disorders had longer hospital stay (6.1 vs. 3.1 days), (P <0.001) as well as increased hospital charges (88,819$ vs.78,650), (P <0.001). No difference was observed in the rates of postoperative complications or short-term mortality between the 2 groups.

Conclusion: Our analysis found that affective disorders were significantly associated with increased length of hospital stay as well as increased total hospital charges in patients undergoing elective lumbar spinal fusion. Future studies are encouraged to further investigate the feasibility of perioperative screening for affective disorders and address them accordingly.
483: From Their Eyes: What Constitutes Effective Formative Feedback for Neurosurgery Residents

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Introduction: Formative feedback is an acknowledged means of fostering improvement. Within neurosurgical resident education, the defining characteristics of quality feedback from the perspective of the resident have yet to be fully elucidated. The Surgical Autonomy Program is an intra-operative assessment tool based on Vygotsky’s theory of a learner’s Zone of Proximal Development (ZPD). The SAP allows the assessment of a resident’s operative performance and document written feedback. The goal of this study is to identify factors that influence neurosurgery residents’ perception of quality regarding written formative feedback from the operating room using the SAP.

Methods: SAP data from 2019-2021 at two neurosurgery training programs were reviewed. The quality of feedback was determined by the residents at the time of their operative evaluation. Using a constant comparative technique, the written feedback was coded based on emerging themes and compared to its feedback level.

Results: There were 2968 SAP entries evaluated. The median time to evaluation completion was 28 hours (Q1 16.1 - Q3 53.6). When ZPD was fully used, the residents reported high quality feedback 91.4% of the time compared to 58.6% when it was not used. Qualitative analysis of the written feedback revealed 6 independent themes: Blank, Non-Specific, Specifics, Next Steps, Key Points, and Autonomy. Any written feedback in the Specifics, Key Points, and Autonomy categories were associated with higher level feedback than leaving the space Blank (p<0.05) or writing Non-Specific comments (p<0.05). Combining categories of feedback into a written evaluation were significantly (p<0.05) better than using just a single category.

Conclusion: Use of ZPD resulted in high quality feedback. Providing comments that discuss the resident’s specific performance in the case, key learning points, or their autonomy results in higher quality feedback than not writing anything or something non-specific. Combining categories of feedback results in the highest quality of written feedback.
Association of Medicaid Expansion Under the Affordable Care Act with Receipt of Meningioma Treatment

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Introduction: The Affordable Care Act (ACA) was designed to increase the number of insured Americans to improve access to care. We examined the impact of Medicaid Expansion (ME) on changes in insurance coverage and receipt of treatment in patients with meningioma.

Methods: The National Cancer Database (NCDB) was queried for patients with a diagnosis of meningioma aged 40-65 from 2011 to 2017. The periods from 2011 to 2013 and from 2014 to 2017 were defined as pre- and post-ACA implementation, respectively. Patients were categorized as living in a Medicaid expansion state (ME) or not (NME). A difference-in-difference (DID) analysis was performed to compare the impact of ME in insurance coverage and receipt of surgery, radiation therapy, and care at an academic hospital.

Results: A total of 53,087 patients met inclusion criteria of which 40.4% and 59.6% lived in NME and ME states, respectively. The cohort mean age was 54 years, 74.5% were female, 52.1% underwent surgery, and 10.6% received radiotherapy. After ACA implementation, uninsured rates in meningioma patients decreased in both NME (11.9% to 9.4%, p <0.001) and ME states (5.5% to 2.7%, p <0.001). Medicaid coverage increased in ME (12% to 17%, p <0.001) but not in NME states (8.3% to 8.1%, p 0.58). After adjusting for other factors, only Medicaid coverage increased significantly after ACA implementation (5.7%, p <0.001). Largest gains in Medicaid were observed for Hispanic, low-income, and low education groups. No differences were observed in receipt of surgery, receipt of radiotherapy, or treatment at academic hospitals after ME.

Conclusion: Among patients with meningioma, ACA implementation was associated with a significant increase in Medicaid coverage. While changes in insurance coverage were observed, ME did not impact receipt of meningioma treatment. Further research is warranted to evaluate the impact of the ACA on access and outcomes in neuro-oncological care.
485: Influence of Healthcare Disparities on Outcomes for Spinal Metastasis Patients

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Introduction: The objective of this analysis was to compare sociodemographic characteristics and outcomes between cohorts of patients receiving separation surgery for spinal metastases at two neighboring institutions, one private and one public, affiliated with a major academic medical center in a large metropolitan area.

Methods: Patients who received separation surgery for spinal metastases between 2013 and 2021 were included in this analysis. Sociodemographic factors, treatment characteristics, and outcomes were compared between those treated at a private hospital and those treated at a neighboring public hospital using Rao-Scott chi square tests.

Results: Compared to those treated at our private hospital, patients treated at our public hospital were more often younger (p=0.005), of Black or Hispanic race (70% vs. 14.9%, p<0.001), and insured via Medicaid or Emergency Medicaid (48.6% vs. 3.2%, p<0.001). They more frequently presented with ESCC grade 3 compression (81.6% vs. 49.2%), potentially unstable or unstable lesions as denoted by SINS >7 (64.1% vs. 37.7%), and increased neurologic impairment as denoted by ASIA Impairment Scale scores of A, B, or C (35% vs. 7.9%). Local progression was less frequently observed in patients treated at our public hospital (28.2% vs. 54.7%, p=0.001), although this is likely due to poorer clinical and radiographic follow-up amongst this cohort. Median survival was significantly lower in patients treated at our public hospital (Median [Range]: 81 [11-1,873] days vs. 264 [0-3,092] days, p<0.001), although this is also likely confounded by lower rates of follow-up.

Conclusion: This study highlights substantial disparities amongst patients treated for spinal metastases at neighboring institutions affiliated with a major academic medical center. Further work is needed to identify reasons for these disparities and create avenues by which to mitigate them.
486: Legal Considerations of the Neurosurgical Physician and Physician Assistant Team

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Introduction: The physician-physician assistant (PA) team increases access to care, but both parties must understand the laws and regulations of the agency relationship between the parties to avoid liability. This review of case law, Federal and State law (and the impact on the agency relationship), complaints filed, and settlements will educate the stakeholders on sources of liability and potential mitigation strategies.

Methods: The research consisted of a review of common law, federal complaints and self-disclosures, settlements, and legal reviews found in the LexisNexis database, press releases of the Department of Justice and Office of Inspector General, and Google searches.

Results: Case law demonstrates that physician liability can arise from the physician-PA agency. Physician liability can arise when physicians do not fulfill the statutory supervision requirements or function under a legal agreement when required by law or regulation or when the PA practices out of the physician's control. The interaction of PAs and physicians employed by different entities can create further physician liability under the Anti-Kickback Statute. When the same legal entity does not employ both parties, PAs rendering services for physicians' patients has resulted in allegations of violating the Anti-Kickback Statute and False Claims Act when claims are submitted to Medicare and Medicaid. As a result, physicians have faced Civil Monetary Penalties, criminal penalties, and medical board sanctions.

Conclusion: Health care law and regulations governing PA practice and supervision along with health care fraud continue to evolve. The successful physician-PA team must remain vigilant of the changes to reduce liability to avoid criminal and civil penalties. Creating an environment promoting clarification and knowledge-sharing, without fear of retaliation, increases dialogue within the agency, reducing errors and mitigates liability. Modernization of the law requires further studies to evaluate the liability of both parties of the agency.
487: Predicting Resilience and Burnout in Neurosurgery Trainees and Neurosurgeons Globally: Need for a Culture Shift

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Introduction: Neurosurgery trainees and staff are at risk of burnout due to highly stressful work environments and long hours. Although some are highly resilient to burnout, we know very little about why this is, how to predict who will be resilient and who will burnout, and whether these factors differ across nations.

Methods: A 95-item international survey designed using a physician wellness framework and validated measures of burnout was sent to neurosurgical trainees and staff between June and November 2021. Univariate analyses (Chi-squared test and Fisher’s exact test) were carried out to analyze associations between burnout and age, gender, years after graduating from medical school, number of years working as staff neurosurgeon, academic level, type of practice, relationship status, having children, age of having first child and countries.

Results: A total of 368 neurosurgical staff and trainees (66% neurosurgeons, 5% fellows, and 29% residents) responded to the validated burnout scale. Median age was 35-44 years in neurosurgeons and fellows and 25-34 years in residents. Male and female were 70% and 28%, respectively. Prevalence of burnout was 35.3%, and significantly differed in neurosurgeons, fellows, and residents (p = 0.022). Burnout was found in 44% of Associate Professors (N = 27) compared to 24% of Assistant or Full Professors (N = 46). Being single was more predictive of burnout (OR = 1.84, 95% CI: 1.09-3.10, p = 0.019) than being married or in a relationship. There was no difference in burnout based on the remaining variables.

Conclusion: We identified protective and risk factors for resilience and burnout in neurosurgical trainees and staff that were similar across countries and in private and academic practice. There is an immediate need to address those factors including neurosurgeon staff culture at the organizational and institutional level to improve practices that protect against burnout and build resilience.
488: Supplementary Insurance to Medicare: A Significant Factor in Discharge Disposition After Lumbar Spine Fusion in New York

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Introduction: Lumbar fusion surgery is largely an elective procedure performed primarily for degenerative pathology, but also for tumor, fractures, and infections. It has been shown that utilization of government insurance is a risk factor for nonhome discharge after spine surgery. Without a clear reason for this association, we conducted this study to attempt to further clarify why government insurance is an independent risk factor for non-home discharge after lumbar fusion.

Methods: We performed a retrospective analysis of data abstracted from the SPARCS database from 2015, 2016, and 2017. Patients were identified who were holders of Medicare and who underwent elective lumbar spine fusion. Patients were divided into three groups based on whether they held supplementary insurance. Length of stay and discharge disposition were assessed.

Results: 14,208 cases are included in the analysis. On both univariate and multivariate analysis, risk factors for non-home discharge include increased age (p<0.001), female sex (p<0.001), increased APR-DRG severity of illness (p<0.001), and payer group. Payer Group C—those patients with private insurance as primary payer and Medicare as secondary payer are more likely to be discharged home (p<0.001).

Conclusion: After lumbar fusion, among Medicare patients with secondary insurance, those with private insurance as the primary payer are more likely to be discharged home than those with Medicare as primary payer. This information helps to better identify those patients who will likely need rehabilitation post-discharge and can aid to streamline the discharge process.
489: A Qualitative Study of Fear and Unintended Consequences Emerging from Restrictive Opioid Prescribing Policies

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Introduction: The opioid crisis has driven significant societal harm, and one of the most common reasons for opioid prescriptions is back pain. In an effort to reduce opioid-related harms, SB 273 was signed in 2018, and aimed to restrict opioid prescribing in West Virginia, with similar laws enacted in over 60 other states and locations. This study aims to better understand the impact of the legislation on patients and providers with particular attention paid to unintended consequences of the legislation.

Methods: One-time, 30-60 minute, semi-structured interviews were conducted with purposively-sampled 20 general practitioners and specialists practicing throughout West Virginia during the implementation period of the law. Interviews focused on experience with opioid prescribing, influences of prescribing, impacts of SB 273, and impact on patient care. Content analysis was performed by generating a code book and organizing information into themes, with particular attention to how themes related to each other. Theme saturation was achieved. This information was triangulated with previously published quantitative analysis of prescribing trends associated with SB 273.

Results: Four themes emerged, 1. Fear of disciplinary action, 2. Exacerbation of opioid prescribing fear due to restrictive legislation, 3. Resulting care shifts and treatment gaps, and 4. Conversion to illicit substances. The clinicians recognized the harms of inappropriate prescribing and how this could affect their patients. Decreases in opioid prescribing were already occurring prior to the law implementation. Disciplinary actions against opioid prescribers and restrictive opioid prescribing policies contributed to prescriber fear and shifts in care that led to forced tapering and opioid under-prescribing. Providers felt that taking on patients who legitimately required opioids could jeopardize their career.

Conclusion: A wholistic and patient-centered approach should be taken by legislative and disciplinary bodies to ensure patients are not abandoned when disciplinary actions are taken against prescribers or new legislation is passed.

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Introduction: Adult spinal ependymoma presents a rare benign tumor entity. Due to its incidence peak in the fourth decade of life, it mostly affects patients during a professionally and physically active time of life.

Methods: We performed a retrospective monocentric study, including all patients operated upon for spinal ependymoma between January 2009 and September 2020. We prospectively collected data on professional reintegration, physical activities and quality-of-life parameters using EQ-5D and SF-36. Issues encountered in returning to work and physical activities were assessed using existing spinal-cord-specific questionnaires and free-text questions.

Results: In total, 65 of 114 patients operated on for spinal ependymomas agreed to participate. Most patients suffered from only mild pre- and postoperative impairment on the modified McCormick scale, but 67% confirmed difficulties performing physical activities in which they previously engaged due to pain, coordination problems and fear of injuries. We observed a shift from full- to part-time employment and patients unable to work, independently from tumor dignity and neurological function.

Conclusion: Despite its benign nature and mild formal neurological deficits occurring in patients suffering from spinal ependymoma, the studied population described severe difficulties returning to their preoperative physical activity and profession. Clinical scores such as the McCormick grade and muscle strength may not reflect the entire self-perceived impairment appropriately.
491: Characteristics of Transfer Patients Who Undergo Craniotomy

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Introduction: Patients are commonly transferred to tertiary hospitals for neurosurgical consultation due to lack of neurosurgical coverage or referral for management of a complex case. Using data from the National Inpatient Sample (NIS) database, we assess a cohort of patients who were transferred to another hospital and underwent a craniotomy during that hospitalization.

Methods: Data was extracted from the 2018 NIS database. We included all patients who underwent a craniotomy procedure during a specific hospitalization. One group was directly admitted to the hospital either for elective surgery or through the emergency department. The other group was made up of patients who were transferred into the hospital from a different acute care hospital. Demographic, length of stay, mortality, and payer data were assessed.

Results: The cohort is made up of 16,364 patients, with 13,006 as direct admits, and 3,358 as transfers from an acute care hospital. In multivariate analysis, patients in the third (p=0.001) and fourth income quartiles (p<0.001) are less likely to be transfer patients when compared to direct admit patients. In multivariate analysis, there are a more transfer than direct admit patients with Medicaid (p=0.037), no insurance (p=0.009), and “other” payer arrangements (p<0.001). The mean total charge for the hospitalization of the direct admit patients was $190,849 compared to $236,352 for the transfer patients. The patients who were transferred had a higher mortality rate compared to the direct admits (p=0.001) and a longer length of stay (p<0.001).

Conclusion: A cohort of transferred patients who undergo craniotomy have many differences when compared to patients directly admitted to the hospital. The transfer patients are more likely to have Medicaid or no insurance. Their care is associated with a higher cost. They have increased mortality and a longer hospital LOS. It is important to study this aspect of neurosurgery to optimize the efficiency of transfers.
492: Role of Early Postoperative CT Scan in Elective Cranial Surgeries

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Introduction: The practice of routine early postoperative CT scan after cranial surgeries is being increasingly questioned. The financial implications, health hazards and resource constraints of an unnecessary scan dictate that the patients who would be most benefited from a routine postoperative CT scans need to be identified.

Methods: All patients undergoing elective cranial surgeries in our department from June 2019 to February 2021 were included in this prospective study. Postoperative clinical status and the findings of neurological examination were noted. CT scan done within 24 hours post-surgery was analysed for presence of any significant findings. Interventions and surgical reintervention done on the basis of clinical findings and CT findings were noted.

Results: A total of 153 patients were included in the study. More than half the interventions made based on clinical findings were in patients with unexpected clinical deficits. Radiographically significant changes were present in 40 of the 153 scans. Patients with unexpected clinical findings and those who were sedated or comatose were more likely to have significant CT findings. 27 patients required an intervention based on CT findings, while 7 of these were reoperated. CT was a strong predictor of need for medical and surgical intervention in patients who could not be reliably assessed by clinical examination.

Conclusion: Our study corroborates the findings from past retrospective studies that close neurological monitoring and identification of unexpected focal deficits can predict the need for intervention in the postoperative period. Routine CT scans can be selectively performed where clinical examination is unreliable.
493: Improving Education on Cost-effective Care in Neurosurgery: A Personalized, Web-based Intervention for Residents

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Introduction: While training residents in the socioeconomics aspects of neurosurgery has become a priority for residency programs across the country, programs dependent on in-person participation are difficult to implement given resident schedules and the COVID-19 pandemic. The goal of this study was to assess the efficacy of a web-based, socioeconomic educational program for neurosurgery residents.

Methods: Coding and billing data from 13 neurosurgical procedures were organized into 5 interactive modules sent to residents weekly. Residents also completed a 20-question pre- and post-intervention examination based on 4 distinct educational domains as described by the Accreditation Council for Graduate Medical Education (ACGME)’s Neurological Surgery Milestones: Billing code information, Procedure-specific concepts, Material costs, and Operating room procedures.

Results: The pre-intervention survey was completed by 23/27 residents (85.2%) with a mean score of 9.55. The post-intervention survey was completed by 17/27 residents (63.0%) with a mean score of 9.97. Overall, there was no statistically significant difference between correct pre- vs. post-responses assessing residents’ knowledge of billing codes (3.96 vs 4.41, p=0.33), procedure protocol (3.09 vs 3.53, p=0.11), material (0.95 vs 0.647, p=0.75), or operating room protocols (1.55 vs 1.06, p=0.61). However, respondents’ accuracy for code-related question #1 (“What is a CPT code?”) and procedure-specific questions #8 (“For a supratentorial craniotomy for subdural hematoma evacuation, what is the average length of the procedure?”) and #9 (“For a supratentorial craniotomy for tumor resection, what is the average physician charge?”) increased significantly following the intervention (p=0.0040, p=0.016 and p=0.0060, respectively). Importantly, these questions were among the most replicated during the 5-week intervention.

Conclusion: Our program demonstrates that increased access to billing and coding data can serve as a decentralized, virtual model of education for the socioeconomics of neurosurgery. Additionally, our experience demonstrates the potential of self-driven learning modalities that can easily be integrated into existing resident workflows.
494: Surgical Start Time Impacts Length of Stay for Elective Neurosurgical Procedures

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Introduction: Staffing storages and resource diversion can be major obstacles in the routine delivery of elective surgical care. Efforts to minimize hospital length of stay (LOS) have been implemented in many systems, but definitive strategies to accomplish such have remained elusive. Surgical scheduling of elective neurosurgical procedures based on optimizing start time has the potential to reduce LOS.

Methods: Retrospective data from a quaternary care academic institution were analyzed from elective adult neurosurgical cases performed from 2017 through 2019. Emergent or urgent add-on cases were excluded. Variables included primary procedure, age, diabetes status, American Society of Anesthesiologists (ASA) class, and surgical start time. Analysis of the median LOS following surgery was performed using Mann-Whitney tests and Cox hazards model. Matched-cohort analysis of mean total hospitalization costs was performed using the Student's t-test.

Results: 1640 elective neurosurgical cases were analyzed in which 213 patients had surgical start times after 3 PM. The median LOS for the after 3 PM group was 1 day longer than the before 3 PM start time cohort (3.0 vs 2.0, p < 0.05). Case-matched cost analysis for frequently performed neurosurgical cases with an after 3 PM start time failed to demonstrate a significant difference in total hospital charges.

Conclusion: Optimization of surgical services scheduling to increase the proportion of elective surgical cases started before 3 PM has the potential to decrease post-surgical LOS for adult patients undergoing Neurosurgical procedures.
496: Novel Bipolar Electric Field Therapy for the Treatment of Glioblastoma: Preliminary in-vitro and in-vivo Results

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Introduction: Despite aggressive neurosurgical resection and chemoradiation, the patient survival is extended only to a median of 14 months in patients with glioblastomas. Intermediate frequency (100-300 kHz), low intensity (1-3V/cm) Tumor Treating Fields (TTFields) has emerged as a treatment modality for primary and recurrent glioblastomas. Our study explores neuromodulation through Deep Brain Stimulation (DBS) as a glioblastoma therapeutic platform.

Methods: In-vitro studies utilizing standard Deep Brain Stimulation (DBS) leads and the novel bipolar electrodes using murine and patient derived glioblastoma lines; in-vivo studies in C57BL/6 mice model with intracranial implantation of the novel electrodes were performed.

Results: In-vitro experiments showed complete glioblastoma eradication between the two leads of a DBS as well as a novel electrode design upon sinusoidal waveform stimulation. Thermometric measurement revealed no evidence of hyperthermia upon electrode stimulation. Such eradication was also observed for brain metastasis (lung cancer) lines but not seen for cultured human astrocytes. In-vivo results in C57BL/6 mice using GL261-Luc cells demonstrated >50% decrease in the photon emission from the intracranially implanted tumor using IVIS Optical imaging, after 14 days of continuous bipolar electric field therapy. Such treatment did not induce seizures. The mice treated with electric field therapy outlived the control mice without any treatment by 4 days. No significant difference in survival was noted between the mice when only the electrodes were implanted but no therapy was delivered.

Conclusion: We report a novel bipolar electric field model that has a potential to serve as a supplemental therapy in multi-drug resistant GBM. This warrants further studies to assess efficacy and morbidity.
497: ACOT-7 Knockdown Regulates IRE1α and Prolongs Survival in Preclinical Breast Cancer Brain Metastases

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Introduction: The brain microenvironment poses a significant challenge for metastatic cancer cells committed to reside within its parenchyma. Nevertheless, genetic aberrations help metastatic cancer cells adapt to arising stresses. In this work, we aimed to identify genes that are responsible for colonization of breast cancer brain metastases (BCBM).

Methods: We conducted an in silico analysis of NKI Breast Cancer data to identify genes that correlate negatively with survival. We then utilized paired breast cancer/brain metastases models of CN34/CN34-Br and BT474/BT474-Br cell lines for in vitro and in vivo experiments. Knockdown (KD) studies were conducted to understand the role of selected genes in brain metastasis. To further elucidate the functional implication of identified genes, quantitative RT-PCR, clonogenic assays, whole-proteome analysis and FA oxidation assay were conducted. Western blots were done to support findings. Intracranial injections of BCBM cells in murine models were used to elucidate survival impact.

Results: ACOT-7 was found to be overexpressed in brain metastases when compared to primary breast tumors (p=0.021). In patients with BCBM, ACOT-7 overexpression was identified to be negatively correlated with patient survival (p<0.0001). In vitro, ACOT-7 KD cells showed decreased clonogenic growth in comparison to controls (p<0.0001). Whole proteome analysis of ACOT-7 KD BCBM cells demonstrated an increase in the pool of protein processing markers (p<0.0001). Subsequently, significant increases in basal oxygen consumption rate were observed (p<0.001), indicating that ACOT-7 regulates oxidative phosphorylation. Alterations in IRE1α suggested potential involvement of endoplasmic reticulum stress/unfolded protein response in the process. In vivo, mice with intracranial injection of ACOT-7 KD cells exhibited better survival rates compared to control (p<0.01), with a rise in median survival by ~60%.

Conclusion: ACOT-7 overexpression in BCBM and its critical role in metastatic colonization and poor patient outcomes make it a promising target for future therapeutic interventions.
498: Determining Surgically Relevant Structural Connectivity Inter-individual Biotypes Using Simulated Brain Surgery

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Introduction: Network based approaches of the brain connectome can allow neurosurgeons to preoperatively predict a patient’s sensitivity to brain surgery before critical functions are altered. We aim to create a theoretical brain surgery model to examine if there are specific epicenters in the brain which when removed constitute the worst cognitive outcomes, and if these areas are different between individuals.

Methods: We simulated neurosurgery on structural graphs generated from DTI-neuroimaging of 80 healthy adults and using a validated parcellation scheme. Realistic surgeries in 8 major cortices were performed with serial deletions of 1-10 parcellations in combination per lobe, in which the parcellations had to be anatomically adjacent to each other, rather than in distant or opposite hemispheric lobes. The impact of each surgery, or deleted node, on an individual was measured by changes in global efficiency (GE: inverse of shortest distance between two nodes on a structural graph), which is a proxy for patient cognitive functioning.

Results: Specific epicenters were identified that constituted the largest decrease in GE when removed as compared to just removing more brain parcellations together, suggesting a location specific pattern to worse injuries. Identified epicenters were only partially explained as eloquent regions (35-75%). The worst combinations of 7 or 8 deleted parcellations always included the components of previous worst deletion combinations. Although epicenters were largely consistent between individuals, unique “connectotypes” in a subset of individuals were identified in which unexpected, spatially different epicenters were present in each lobe.

Conclusion: There are unique epicenters in structural connectivity that can directly predict the sensitivity to neurosurgery. Theoretical brain surgery provides a more insightful approach to neurosurgery by demonstrating the risks of small surgical decisions that generally do not alter the surgery but can differentially harm patients with different connectotypes if inter-individual structural connectivity differences are not considered.
499: BOLD Asynchrony Is a Contrast-independent Biomarker of High-grade Glioma in Patients on Bevacizumab

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Introduction: Radiographic monitoring of high-grade glioma (HGG) is typically accomplished using contrast-enhanced T1-weighted MRI. Bevacizumab (BEV) is an adjunctive therapy for HGG that can cause "pseudo-response", a loss of contrast enhancement (CE) despite persistent tumor, which hampers monitoring. The purpose of this study was to determine whether temporal dynamic in blood oxygen level-dependent (BOLD) functional MRI (fMRI) could serve as an alternative to CE in the presence of pseudo-response.

Methods: We identified 21 HGG patients monitored before and after BEV treatment between 2010 and 2020 (median age = 62, range = 29-77, 62% male) for this retrospective cohort study. Serial T1-weighted images were used to define regions of stable CE and resolved CE. Using an fMRI scan collected during BEV treatment, we measured the dynamics of the BOLD signal in CE regions with the dynamics of BOLD signal in the contralateral, non-enhancing control hemisphere, yielding a measure termed BOLD asynchrony (BA). BA was compared between stable and resolved CE regions, and correlated with progression-free survival (PFS), overall survival (OS), and spatial recurrence. Student t-tests and linear regression were used for statistical comparison.

Results: BA remained elevated in regions that showed BEV-related elimination of CE (resolved CE mean=0.69, std=0.31, p < .0001) compared with the contralateral hemisphere (contral mean=2.53, std=0.29). BA in these regions of resolved CE was correlated with prolonged PFS (r-squared=0.271, p=0.016) and OS (r-squared=0.312, p=0.009). Areas where tumor eventually recurred showed higher BA (mean=1.42, std=0.37, p=0.03) than areas without subsequent recurrence (mean=0.63, std=0.34).

Conclusion: In HGG patients treated with BEV, BOLD asynchrony persists in areas that lost contrast enhancement, is inversely correlated with prolonged PFS and OS, and is associated with tumor recurrence. These data suggest that BOLD asynchrony reflects non-enhancing tumor burden in the recurrent setting, and that BOLD fMRI has potential for tracking progression in HGG patients on Bevacizumab.
**500: Transcriptomic Landscape of Diffuse Infiltrating Gliomas Identifies Immune Subgroups in IDH Wildtype and Mutant Patients**

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**Introduction:** Gliomas are the most common primary malignant brain tumors with no durable treatment. Although immunotherapy has shown efficacy in many solid tumors, efficacy in glioma has been limited. Development of effective immunotherapy for gliomas require better understanding of the tumor microenvironment (TME). In this study, we performed high-dimensional profiling of the immune components of the TME and peripheral blood in matched samples using single-cell RNA-sequencing (scRNAseq), spectral cytometry, and multi-spectral imaging to generate a comprehensive immune atlas of glioma. Furthermore, we used our atlas in combination with available TCGA data to identify distinct subsets of patients based on immune signatures.

**Methods:** The study was approved by institutional IRB. 20 patients provided consent for collection and analysis of tumor and peripheral blood. Fresh tumor samples and paired peripheral blood samples were collected at time of surgery. Tumor infiltrating leukocytes (TILs) were sorted from homogenized tumor samples. ScRNAseq was performed using 10X Genomics chemistry. Spectral cytometry was performed using Cytek Aurora. Multi-spectral imaging was performed using Akoya VECTRA. TCGA dataset was stratified using CIBERSORT.

**Results:** IDH wildtype (IDHwt) and mutant (IDHmut) tumors exhibited vastly different TIL immune landscapes. IDHmut TIL was dominated by myeloid cell infiltration with reduced T and B cells compared with IDHwt. Gene expression analysis of myeloid cells from IDHwt and IDHmut TILs revealed higher expression of pro-inflammatory cytokines such as TNF-a and IL-6, suggesting that these myeloid cells play a role in shaping anti-tumor immunity. Using our scRNAseq data, we also stratified glioma patients into four distinct subgroups based on their immune infiltration.

**Conclusion:** We were able to generate an uniquely comprehensive immune atlas of glioma patients and identified dramatic differences in TIL between IDHwt and IDHmut patients, ultimately laying a groundwork for genotype-specific immunotherapy in glioma. Furthermore, novel stratification of patients by their immune infiltration will allow for more personalized immunotherapy beyond genotype alone.
501: MRI Radiogenomics of Pediatric Medulloblastoma: A Multi-center Study

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Introduction: Radiogenomics of pediatric medulloblastoma (MB) offer an opportunity for MB risk stratification, which may aid therapeutic decision-making, family counseling, and selection of patient groups suitable for targeted genetic analysis.

Methods: The authors retrospectively identified consecutive pediatric patients with newly diagnosed MB on MRI at 12 pediatric sites spanning July 1997 to May 2020. A total of 1800 features were extracted from T2- and contrast-enhanced T1-weighted, preoperative MRI scans. A two-stage sequential classifier was designed—one that first identifies non-wingless (WNT) and non-sonic hedgehog (SHH) MB and then differentiates therapeutically relevant WNT from SHH. The authors then developed a classifier that distinguishes high-risk Group 3 from Group 4 MB. The best-performing model for each binary classifier from six candidate classifiers was selected using a reduced feature set, and performance measured on a holdout test set with the micro-averaged F1 score. Model accuracy score was compared to No Information Rate using the Wald statistic.

Results: The multinational study cohort comprised 263 patients (mean age at diagnosis, 87 +/- 60 months; 166 males). A two-stage classifier outperformed a single stage multi-class classifier. The combined, sequential classifier achieved a micro-averaged F1-score of 0.88 and a binary F1-score of 0.95 specifically for WNT. A Group 3 versus Group 4 classifier achieved an area under the receiver operating characteristic curve of 0.98. Of the Image Biomarker Standardization Initiative features, texture and First Order-features were most contributory. As measured by expression of the endothelial marker, ERG, vascular density was greater in Group 4 relative to Group 3 (p = 0.03, Wilcoxon rank-sum).

Conclusion: MRI-based machine learning decision-path can be used to reliably predict the four clinically relevant molecular pediatric MB subgroups.
502: Identification of Targetable Glioblastoma Specific Antigens Using a B-cell-based Vaccine

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Introduction: The immunosuppressive environment created by glioblastomas (GBMs), an aggressive brain tumor with a dismal prognosis, suggests a role for immunotherapy. We have developed a B-cell based vaccine (BVax) which has demonstrated a survival benefit in preclinical murine models when combined with radiation therapy and temozolomide, the current standard of care treatment for GBM. BVax shows superiority to previous cellular vaccines including dendritic cell vaccines. In this study, BVax-derived antibodies are used to identify targetable GBM specific antigens.

Methods: BVax-derived antibodies are generated by treating GBM tumor bearing B-cell knockout mice with BVax. Immunoprecipitation-mass spectrometry was performed using BVax-derived antibodies and GBM lysate. Results were validated using computational analysis from B-cell receptor sequencing and single cell RNA sequencing.

Results: BVax demonstrates a plasmablast phenotype that specifically localizes to the brain in preclinical murine models of GBM. Treatment of GBM bearing mice with BVax-derived antibodies, without the parent BVax cells, led to a survival benefit. Immunoprecipitation-mass spectrometry analysis identified GBM specific antigens that are uniquely recognized by BVax, 5 localized to the membrane and 31 localized to the cytosol. These results were validated by B-cell receptor sequencing and single cell RNA sequencing analysis.

Conclusion: Humoral immunity plays a role in the therapeutic efficacy of BVax. BVax travels from the peripheral blood to the brain, where it is activated into plasmablasts and produces anti-tumoral antibodies which confer a survival benefit. Locally produced BVax-derived antibodies avoid limitations from the blood brain barrier. Identification of GBM specific antigens that are uniquely recognized by BVax-derived antibodies provide potential additional therapeutic targets for GBM. These antigens are currently being tested to determine the biological relevance for the therapeutic efficacy of BVax. Future work will utilize these targets as the foundation for next generation BVax therapies such as chimeric antigen receptor B cells.
503: Genetic Manipulation of CD97 Inhibits Patient-derived Glioblastoma Stem Cell Invasion in Vivo

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Introduction: Glioblastoma (GBM), the most common malignant brain tumor in adults, is difficult to treat due to rapid growth of cells, and aggressive invasion. It’s currently unknown what causes GBM to be so invasive. CD97 is an adhesion GPCR involved in invasion and metastasis in multiple cancer types, but is relatively unstudied in glioblastoma. Recently, we found that by genetically manipulating CD97 levels in the patient-derived glioma stem cells (pdGSC)s, CD97 knockdown decreases invasion in vitro in patient derived GBM cells, and CD97 overexpression increases invasion in pdGSCs cells. However, the effect of CD97 manipulation on glioma invasion in vivo is unknown.

Methods: We created multiple genetic CD97 constructs. We made a CD97 overexpression construct, as well as an overexpression control construct, a knockdown construct which has decreased expression due to shRNA against CD97, as well as a knockdown control construct, a non-cleavable N-terminus fragment (NTF) construct which is unable to be activated, and a construct which has a deleted NTF (dNTF) which is thus constitutively activated. We transduced pdGSCs with lentiviruses containing our CD97 constructs and selected them with puromycin. We then stereotactically injected them into the right frontal lobe of mice brains, then sacrificed the mice and sectioned their brains to analyze for invasion.

Results: Interestingly, the dNTF construct which is constitutively active, shows very strikingly well circumscribed margins with mostly dead cells—minimal local parenchymal invasion. Also interestingly, in our non-cleavable NTF construct which is constitutively inactive, there was absolutely no corpus callosum invasion.

Conclusion: In conclusion, CD97 level correlates with pdGSC invasion both in vitro and in vivo. Deletion of CD97 NTF may reduce or eliminate local invasion, and stabilization of NTF from dissociation may reduce or eliminate corpus callosum invasion. The hypothesis that pharmacologic manipulation of the CD97 NTF may inhibit GBM invasion warrants further investigation.
504: Circulating Tumor-Leukocyte Hybrid Cells: A Novel, Sensitive, and Specific Biomarker for Glioma in Peripheral Blood

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Introduction: Non-invasive biofluid-based markers show increasing potential in glioma diagnosis, classification, and disease monitoring. Though promising in other cancers, circulating tumor cells (CTCs) are rare in glioma patients. In contrast, circulating tumor-leukocyte "hybrid" cells (CHCs) are more readily detectable than CTCs in many cancer types, correlate with survival, and exhibit key molecular properties of the primary tumor. In this study, we examine whether CHCs are sensitive to disease status and exhibit a conserved mutational profile in glioma.

Methods: Pre-operative peripheral blood samples were collected from 13 adult patients with presumed or recurrent glioma and 4 patients with non-glioma pathology. Isolated mononuclear cells were stained with cancer-specific anti-GFAP and leukocyte-specific anti-CD45 antibodies. Semi-manual quantification of putative CHCs (GFAP+/CD45+) and CTCs (GFAP+/CD45-) was blinded to clinical status. CTC and CHC number were normalized to density per 50,000 cells and compared between patient groups. To investigate hybrid cell phenotype, cells isolated from a patient with H3 K27M mutation were also stained with anti-H3 K27M antibody.

Results: CTCs and CHCs were identified in 4 (30.8%) and 13 (100%) of 13 glioma patients, respectively, and CHCs were detected at greater density per 50,000 cells (p=0.015). CHC number discriminated primary glioma from non-glioma pathology (p=0.023), though rare GFAP+/CD45+ cells were also detected in patients with inflammatory pathologies. CHCs from a patient with primary diffuse midline glioma also stained positively for an H3 K27M mutation found in genetic analysis of the primary tumor.

Conclusion: CHCs provided greater sensitivity as a biomarker for glioma than CTCs in this pilot cohort and discriminated glial tumors from non-glial pathology. Further investigation is required to ensure specificity of CHCs as a reliable marker for glioma, however the display of a conserved H3 K27M mutation in CHCs is promising. Ongoing studies seek to further molecular classification of this cell population with IDH R132H.
506: Radiogenomics and Radiomics of Skull Base Chordoma: Machine Learning-based Classification of Genetic Signatures and Clinical Outcomes by Multiparametric MRI

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Introduction: Evidence supports that skull base chordoma (SBC) is a heterogenous disease spanning a spectrum of biological behavior. Homozygous 9p21(p16/CDKN2A) and 1p36 deletions have been shown to account for some of this variability, and can be used to guide management. In this study, we aimed to establish whether specific MRI-based radiomics signatures could be used as a non-invasive biomarker predicting clinical outcomes, and whether they correlate with these genetic aberrations.

Methods: We evaluated radiomics signatures in a cohort of 252 primary and recurrent SBC pre-operative MRI scans. The lesions were segmented using 3D slicer v4.10.2 to create a volume of interest for radiomics texture analysis from T1 post-contrast and T2 MRI sequences. We extracted 800 features from each volume of interest: 10 histogram-based features, 195 second-order texture features, and 195 volume-dependent features. Unsupervised analysis through consensus clustering techniques was performed to identify distinct groups based on radiomics texture features. The identified cluster groups were then correlated with progression free survival after surgery (PFSS), as well as the cell percentages with homozygous 9p21 deletions and 1p36 deletions on Fluorescent In Situ Hybridization.

Results: Tumors were grouped into 4 radiomics-based clusters. These clusters had distinct PFSS curves on Kaplan-Meier graphs (p value < 0.0001), suggesting a strong correlation with clinical outcomes. In addition, significant differences were observed in the percentages of 1p36 (p value<0.00072) and homozygous 9p21 deletions (p value=0.026) suggesting a strong association with the tumor’s genetics.

Conclusion: We identified MRI-based radiomics signatures that are strongly correlated with clinical outcomes and genetic markers commonly used to guide management in SBC. These radiomics signatures may prove to be a non-invasive, cost and time effective means of pre-operative individualization of care for patients with SBC.
507: Integrated Computational Analyses Reveal Novel Insights into the Stromal Microenvironment of Shh-subtype Medulloblastoma

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Introduction: Medulloblastoma is the most common malignant brain tumour of childhood. While our understanding of this disease has progressed substantially in recent years, the role of tumour microenvironment remains unclear. Given the increasing role of microenvironment-targeted therapeutics in other cancers, this study was aimed at further exploring its role in medulloblastoma.

Methods: Multiple computational techniques were used to analyze bulk and single cell RNA sequencing data from primary samples derived from all four molecular subgroups of medulloblastoma. Gene expression is used to infer stromal subpopulations, and network-based approaches are used to identify potential therapeutic targets.

Results: Bulk data was obtained from 763 medulloblastoma samples and single cell data from an additional 7241 cells from 23 tumours. Independent bulk (285 tumours) and single cell (32868 cells from 29 tumours) validation cohorts were used to verify results. The SHH subgroup was found to be enriched in stromal activity, including the epithelial-to-mesenchymal transition, while group 3 is comparatively stroma-suppressed. Several receptor and ligand candidates underlying this difference in microenvironment are identified and correlate with the metastatic potential of SHH medulloblastoma. Additionally, a biologically meaningful gradient from "stroma-active" to "stroma-suppressed" cells is detected within individual SHH tumours, which may play an important role in the development of targeted therapy.

Conclusion: This study helps elucidate the role of the stromal microenvironment in SHH-subgroup medulloblastoma using an array of computational techniques. We suggest numerous treatment vulnerabilities which can be further explored using in vitro and in vivo methods.
509: Expression of Thrombin-cleaved Osteopontin and Integrin α9 and β1 Signaling Pathway Molecules in Chronic Subdural Hematomas

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Introduction: Chronic subdural hematoma (CSDH) is considered to be an inflammatory and angiogenic disease. Osteopontin is an extracellular matrix protein. Osteopontin is cleaved by thrombin, resulting in N-half osteopontin, which is more prominent in integrin signal transduction. Integrin β1 plays an important role in endothelial cell adhesion, migration, survival during angiogenesis. We examined the expression of N-half osteopontin in the CSDH fluid and the expression of integrin α9 and β1 and the downstream components of the angiogenic signaling pathways in the outer membrane of CSDHs.

Methods: Twenty samples of CSDH fluid and 8 samples of CSDH outer membrane were included. The concentrations of N-half osteopontin in the CSDH fluid were measured using ELISA kits. The expression of integrin α9 and β1, vinculin, talin-1, focal adhesion kinase (FAK), paxillin, α-actin, Src and β-actin was examined by western blot analysis. The expression of integrin α9 and β1, FAK and paxillin was also examined by immunohistochemistry. We investigated whether CSDH fluid could activate FAK in cultured endothelial cells in vitro.

Results: The concentration of N-half osteopontin in CSDH fluid was significantly higher than that in the serum. Western blot analysis revealed above-mentioned molecules in almost all cases. In addition, integrin α9 and β1, FAK and paxillin were localized in the endothelial cells of vessels within the CSDH outer membrane. FAK was significantly phosphorylated immediately after treatment with CSDH fluid in cultured endothelial cells.

Conclusion: Our data suggest that significantly high concentrations of N-half osteopontin in CSDH fluid might play an important role in angiogenesis in endothelial cells through integrins α9 and β1. The N-half osteopontin and integrin signaling pathway might be a useful therapeutic target for treating the growth of refractory CSDH.
510: Improving Trauma Readiness in the Military Neurosurgical Community - Early Experience from the Army Military Civilian Trauma Team Training (AMCT3) Program

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Introduction: As military engagements overseas wane, the military neurosurgical community struggles with case volume and maintaining trauma readiness. The AMCT3 Program was founded in 2018 with the goal of embedding military specialists at high volume civilian trauma centers for improved case volumes and trauma readiness.

Methods: A military neurosurgeon was embedded at a civilian trauma center in October of 2019. Over 18 months, metrics to include operative volume, consult volume, and hospital billing patterns were collected. In addition, six military treatment facilities with neurosurgical services were surveyed for similar annual clinical metrics.

Results: 865 initial consult encounters were completed. From this clinical volume, 201 operative cases occurred (an annual rate of 134 cases per year). This included 63 cranial trauma cases, 39 oncologic cranial procedures, 28 miscellaneous cranial procedures (burr holes and CSF diversion procedures), 52 instrumented spinal procedures, and 19 non-instrumented spinal procedures. In comparison, military neurosurgeons completed 84 operative cases per year. Of note, the only level one trauma center in the military completed 63 cranial trauma cases in the 2019 calendar year amongst its staff altogether. Financial data was available for 15 months of the embedded surgeon’s tenure in which the hospital billed 3.34 million dollars for the surgeon’s services.

Conclusion: With an increasing focus on trauma readiness in the military medical community, military civilian partnerships represent a mutually beneficial arrangement. Further study into expansion opportunities for multiple specialties should occur in order to widen the benefits this collaboration could confer.
512: MRI-based Treatment Response Assessment Maps, Trams, for Depicting Short/long-term Subtle BBB Disruption in Traumatic Brain Injury

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Introduction: BBB disruption (BBBd) is suggested as a possible mechanism by which secondary TBI leads to cognitive decline and early dementia. Here we used TRAMs calculated from delayed-contrast MRI to depict long-term subtle BBBd in moderate TBI mice and validated the results by studying blood vessels coverage by astrocytes end-feet (BVCA).

Methods: 75 closed-head injury mice were followed by TRAMs 1/7/14/30/60/98/133/180/240/450/540 days. BBBd was calculated from TRAMs as the delayed signal intensity increase versus control mice. BVCA was calculated by staining for astrocytes and vessels.

Results: Significant BBBd was depicted in the injury site in all mice post-TBI. TRAMs BBBd volumes were x2.5 larger than enhancing volumes on T1-Gd (p<0.02) up to day 133 and found long after no enhancement was detected on T1-Gd.
By day 30 BBBd volume at the injury site (frontal cortex) dropped sharply by x3.666±0.004 and the disruption intensity dropped from 20.6±1.5% to 10.4±1.5%. BBBd remained constant up to day 540. Significant correlation (r²=0.78, p<0.02) was found between BBBd and BVCA. Surprisingly significant BBBd (4.8±1.0%) was found in the contralateral posterior cortex up to day 540.
The ipsilateral ventricle volume increased sharply up to day 30 (x5.455±0.001 of aging controls) and by another x1.429±0.001 by day 540.
Significant/Subtle disruption was found in the ventricles of aging/control mice. TBI ipsilateral ventricle disruption increased up to 15.5%±2.4% above that of controls and remained disrupted, while the contralateral ventricle disruption was initially significantly higher than controls but converged with aging controls at day 540.

Conclusion: TRAMs enables depiction of subtle BBBd, with significantly higher sensitivity than T1-Gd. Long-term abnormal BBBd was depicted not only in the injury site but also in both ventricles and distant cortex regions.
513: Technical Nuances and Complications of Endoscopic-assisted Ventricular Catheter Placement in Ventriculoperitoneal Shunt Insertion: A Single Center Experience

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Introduction: Ventriculoperitoneal shunt (VPS) failures most commonly occur within the first 30 days and the documented failure rates are 17.7% for primary shunts and 25.6% for revisions in adults. Multiple adjuncts to aid in the procedure have been proposed including ultrasound, navigation, and endoscope. Current literature states there is insufficient evidence to recommend the use of endoscope for routine ventricular catheter placement with some studies even demonstrating that it may be more detrimental than beneficial.

Methods: A retrospective study of EA VPS performed at a single institution by a single surgeon in a 5-year period. Shunt failure was defined as any VPS requiring revision after initial placement, whether primary (first-ever VPS) or secondary (revisions after initial placement). All EA VPS were performed using neuroendoscopy and peel-away endoscopic sheath. Distal portion was completed with general surgery assistance and laparoscopy.

Results: A total of 113 EA VPS were performed out of which 105 had at least a 30 day follow-up. Mean age was 52.6 and mean follow up was 513 days. Majority of the shunts placed were primary 86.7% and 13.3% were revisions. The 30-day failure rates were (5.6%) for primary shunts and (13%) for secondary shunts. In both primary and secondary shunts, there were no cases of proximal catheter obstruction. The etiology of failures low pressure hydrocephalus (LPH), distal obstruction, and mass lesion.

Conclusion: The 30-day failure rates demonstrated here are significantly lower than the documented rates in literature. Furthermore despite being described as the most common cause of failure, there were no cases of proximal catheter obstruction. If external/anatomical causes of shunt failure such as tumor burden or LPH are excluded, the failure rates are even lower. Considering these findings as well as the theoretical advantages, further research efforts are necessary to elucidate the true benefits of endoscope-assistance in VPS operations.
514: Cerebral Cortical Functional Connectivity Following Mild, Repetitive Traumatic Brain Injury in the Mouse

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Introduction: Mild traumatic brain injury (mTBI) often results in brief loss of consciousness, impaired attention and concentration, memory problems, impulsivity, and headache without associated structural pathology on CT imaging. Effects of repeated mTBI are cumulative and can lead to chronic traumatic encephalopathy, suggestive of global alterations in cortical networks.

Methods: Using a transparent, morphological conformant polymer skull, we performed Ca2+ imaging to evaluate how mTBI alters patterns of dorsal cerebral cortical activity. Transgenic mice (Thy1-GCaMP6f) were subjected to single injury directly to the motor cortex, for 3 consecutive days. Sham mice underwent the same treatment without cortical impacts. On mice head-fixed to a mobile disk we performed mesoscopic Ca2+ imaging of the dorsal cerebral cortex during spontaneous behaviors. To assess for changes in cortical function, we used spatial independent component analysis to segment the Ca2+ imaging data into independent components (ICs) in sham and mTBI mice starting 2 weeks prior and up to 7 weeks post-injury. Correlations between IC time courses determined cerebral functional connectivity (FC).

Results: Histopathological examination of the brain following mTBI demonstrated transient ipsilateral elevation of GFAP (marker for reactive astrocytosis) and Iba1 (marker for microglial activation) post-injury with recovery 6 weeks post-injury. Similarly, morphological analysis demonstrated transient microglial activation following mTBI. Motor and cognitive effects performed using rotarod and Barnes maze, respectively, did not demonstrate deficits following TBI. We observed significant widespread, bilateral changes in FC between ICs following impact that persisted for up to 7 weeks, far exceeding the changes observed in sham controls.

Conclusion: These demonstrate that our mTBI model produces a transient neuroinflammatory response, no identifiable alterations in cognitive or motor behavior but widespread, and chronic alterations in FC. The findings recapitulate salient features of human mTBI thus providing a means to study disease mechanisms and possible therapeutic interventions for traumatic brain injury.
515: Patterns of Intracranial Pressure Monitoring in Patients with Severe Traumatic Brain Injury: A TRACK-TBI Study

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Introduction: Intracranial pressure (ICP) monitoring provides important information for the management of severe traumatic brain injured (TBI) patients but its practice remains varied. We used data from TRACK-TBI, a prospective, multi-institutional database to study the pattern of ICP monitoring in 13 trauma centers in US.

Methods: We retrospectively reviewed all patients with Glasgow Coma Score (GCS) 3-8 in the TRACK-TBI study to see whether an ICP monitor was placed. Their clinical and radiographic data were analyzed.

Results: 221 patients (61%) had ICP monitor placed while 140 (39%) did not. There was no significant difference in terms of age, sex, race, or injury cause between the two groups. There was significant site-to-site variability in the proportion of patients monitored (median 56%, range 0-100%). There was no significant difference between the admission GCS (4.4 vs 4.2) between the unmonitored versus the monitored group. The monitored group had a larger mean midline shift (3.9mm vs 2.9mm) and were more likely to have cisternal effacement and a higher Rotterdam score. Patients with blood alcohol levels higher than 80mg/dL were less likely to get an ICP monitor, although there was no difference in terms of toxicology screen results. Although the initial GCS of the two groups were similar, unmonitored patients saw a greater improvement of their GCS during the first 3 days and were more likely to achieve a GOS-E of 7 or 8 at 6 months.

Conclusion: Although the initial GCS was similar between the monitored and unmonitored group, there was significant site-to-site variability regarding decisions to place monitors. Decisions for monitoring occurred more often in patients with worse radiographic injury and in whom there was a less subsequent clinical improvement, reflecting more severe injury. Further research will be needed to further refine the group that will most likely benefit from ICP monitoring.

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Introduction: The North American Clinical Trials Network for Spinal Cord Injury (NACTN) is a consortium of tertiary medical centers that includes a prospective SCI registry. Since NACTN began in 2004, there appears a benefit from early surgical decompression and stabilization. The NACTN registry data was analyzed to evaluate the effect of early surgery on patient outcome.

Methods: NACTN patients were divided into early and late surgery (before and after 24 hours from injury). Participants were further categorized based on arrival time to the NACTN hospital. Associations of participants' descriptors within surgery groups were performed followed by associations with hospital arrival time. The null hypothesis was that degree of injury based on AIS grade would not influence surgical timing.

Results: 688 NACTN patients were included for analysis. 279 (41%) had early surgery while 371 (54%) had late surgery. 38 (6%) patients did not have surgery and were excluded. From 2005-2018, there was a significant trend (p<0.05) towards early surgery. Early surgery patients were younger (p<0.05), more likely to be involved in a MVA (p<0.05) and had a worse initial AIS grade (P<0.05), a lower motor score (p<0.05), and decreased sensory scores (p<0.05).

Of the 643 patients with arrival data available, 83 (12.9%) arrived more than 24 hours after injury. Of 560 patients who arrived within 24 hours of injury, 278 (49.6%) had surgery within 24 hours while 282 (50.4%) had surgery after 24 hours. Early surgery was applied to 45 % of AIS A-C, and 20% of AIS D patients.

Conclusion: Despite early arrival, half the patients did not have surgery within 24 hours, and factors within the hospital provided much of the delay. Surgical care decisions regarding AIS D incomplete SCI patients and their urgency for surgical intervention may play a role in the outcomes of this study and require further investigation.
517: Antiplatelet, Anticoagulant, or Endovascular Treatment for Stroke Prevention in Blunt Cerebrovascular Injury: A Retrospective Cohort Study with Systematic Review and Meta-analysis

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Introduction: Ischemic stroke occurs following trauma-related blunt cerebrovascular injury (BCVI) in up to 20% of cases. Preventative treatment includes antiplatelets, anticoagulants, and/or endovascular treatment (ET) to decrease the risk of ischemic stroke, but the optimal choice remains unclear. The objective of this study was to compare the ischemic stroke rate between these three treatments.

Methods: Following PRISMA guidelines, we queried the OVID Medline, Embase, Web of Science, and Cochrane Library databases from September 2019 to inception to identify studies reporting treatment-stratified outcomes in BCVI patients. Meta-analysis was performed to compare ischemic stroke rates between the treatment groups, using odds ratios. Retrospective review of our institutional experience with BCVI treatment was performed and added to the meta-analysis.

Results: Retrospective review at our tertiary trauma center found a total of 149 patients with 269 BCVI over a five-year period, with an incidence rate of 5.3% out of all trauma patients. There were three ischemic strokes in 40 patients treated with antiplatelets, zero strokes in 23 patients treated with anticoagulation, and 15 strokes in 86 patients who were untreated or had delayed treatment due to perceived risk of hemorrhage from other injuries. Analysis of seven comparative studies of antiplatelets (n=334) versus anticoagulation (n=325) found no significant difference in ischemic stroke rate (OR 1.27, 95% CI 0.40-3.99), but a decrease in rates of hemorrhagic complications (OR 0.38, 95% CI 0.15-1.00). Analysis of seven comparative studies of antithrombotics (n=805) versus ET (n=235) also found no significant difference in stroke rate (OR 0.71, 95% CI 0.35-1.42).

Conclusion: Based on meta-analysis, antiplatelets and anticoagulants were similarly effective in reducing ischemic stroke risk in BCVI, but antiplatelets were better tolerated in this population of trauma patients. The addition of endovascular treatment did not further reduce stroke risk compared to antithrombotics alone.

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518: Association Between Physiologic Frailty and Discharge Outcomes After Admission for Non-operative Traumatic Brain Injury

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Introduction: Frailty, the decline of physiologic reserve with age, is associated with adverse outcomes in traumatically injured patients. No prior study, however, has assessed the relationship between physiologic frailty and outcomes after TBI in elderly adults.

Methods: The records of all patients aged 70 or older admitted to the neurosurgical service of a single institution for non-operative TBI between January 2020 and July 2021 were retrospectively reviewed. Only patients for whom the FRAIL score, a simple metric that assesses functional independence, activity tolerance, weight loss, and comorbidities, could be generated were included. The primary outcome was adverse discharge disposition (either in-hospital expiration or discharge to skilled nursing facility (SNF), hospice, or home with hospice).

Results: 143 patients (mean age 83yo) were included. 69% of patients were on antiplatelet agents or anticoagulants at time of admission. 87% of patients arrived with Glasgow Coma Score (GCS) 13-15 and 89% were admitted from home. The mean length of stay was 4 days, 8% had an in-hospital complication, and 54% had an unfavorable discharge destination. 52% of patients attended follow-up within 3 months. The rate of readmission within 30 days was 14%. Patients were characterized as nonfrail (FRAIL score 0/5, n=21, 15%), prefrail (1-2/5, n=78, 55%), or frail (FRAIL 3-5/5, n=44, 31%). On univariate analysis, there was a significant difference in unfavorable discharge destination between frailty categories (nonfrail 19%, prefrail 58%, frail 66%, p=0.001). In multivariate linear regression, frail status (aOR 5.70, p = 0.02) but not prefrail status (aOR 2.81, p = 0.15) remained associated with unfavorable discharge. Frailty was not associated with increased readmission rate, LOS, or rate of complications.

Conclusion: Frailty is associated with unfavorable discharge destination independently of patient age and GCS. The rates of complications, readmission, and follow-up in this population are low.
519: Delayed Intracranial Hemorrhage of Mild Traumatic Brain Injury Patients Under Antithrombotics on Routine Repeat CT Scan: A Systematic Review and Meta-analysis

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Introduction: Background: Patients under antithrombotics experiencing mild traumatic brain injury (mTBI) may benefit from a routine repeat CT scan to detect delayed intracranial hemorrhage (dICH).

Methods: Objectives: The primary outcome was the incidence of dICH on routine repeat CT scans of mTBI patients under antithrombotics within an intra-hospital observation period of up to 48 hours. The secondary outcomes were potential risk factors, readmissions, neurosurgical interventions, and mortality.

Methods: A systematic review and a meta-analysis of single proportions were performed according to the PRISMA and PRESS guidelines. The risk of bias was assessed using Newcastle-Ottawa Scale.

Results: Eighteen studies with 4613 patients were included. Pooled incidence of dICH was 2% [95% CI 1-2%] with similar rates between different antithrombotic regimens, even in combination. Of the 67 patients with dICH reported (1.45%), eleven required surgery (0.24%), while six died (0.13%). Loss of consciousness was a risk factor of dICH (risk ratio 3.04 [95%CI 0.96; 9.58]). A total of 48 patients were reported for readmission without associated death or surgical intervention.

Conclusion: The contribution of this routine repeat CT scan should be questioned due to limited clinical significance of dICH and unsubstantiated clinical benefit of its early or systematic detection.
520: Hemispherotomy for Post-traumatic Epilepsy

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Introduction: Hemispherotomy is a highly effective treatment for some forms of drug-resistant hemispheric epilepsies such as hemispheric malformations, MCA stroke, Sturge-Weber, and Rasmussen’s Encephalitis. Post-traumatic epilepsy has been reported to occur in 2-5% of traumatic brain injury (TBI). Unlike these classical indications for hemispherotomy, the effects of TBI are rarely unilateral, and TBI has not been evaluated as an indication for hemispherotomy. Here we report the results of four cases of hemispherotomy for drug-resistant post-traumatic epilepsy in children.

Methods: Patients were prospectively consented and enrolled in an IRB-approved study monitoring outcomes of epilepsy surgery at Children’s Hospital of Philadelphia. TBI was defined as an acquired brain injury due to external forces. The standard International League Against Epilepsy definition of drug-resistant epilepsy was used. All patients had undergone craniectomy and cranioplasty as a result of injury, followed by lateral approach hemispherotomy years later. Outcomes were assessed at routine follow-up.

Results: Four patients with drug-resistant epilepsy underwent hemispherotomy for post-traumatic epilepsy. All patients were male with mean age of 9.3 years (range 5-12). Two precipitating traumas were non-accidental and two were vehicular. All patients were completely seizure-free throughout the follow-up period (mean 12.3 months, range 3-30 months). No patient experienced any surgical complication, shunt placement or revision, or any reoperation. One patient is off all anti-seizure medications (ASM) while three patients are weaning off their last ASM. Three patients experienced significant, rapid cognitive improvement after surgery, and one remained at pre-operative baseline.

Conclusion: Here we demonstrate the use of hemispherotomy to treat drug-resistant, hemispheric post-traumatic epilepsy in four children with excellent epilepsy and cognitive outcomes, and no major complications.
521: Surgical Decision Making in Brachial Plexus Birth injuries: a Three Year Retrospective Review of 34 Patients

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Introduction: Brachial plexus birth injuries range from transient to profound impairment. Decision making can be divided into two parameters; when to operate and extent of repair. We present 34 patients who had total of 36 operations (brachial plexus and/or Oberlin transfers) and what guided the decisions.

Methods: Patients with partial injuries (isolated biceps dysfunction) were considered for Oberlin transfer alone, while the more extensive injuries were best managed with brachial plexus repair. Decisions for surgery were made by 4 months of age when possible and the ages were 4 months to 14 months at time of surgery. Two patients had Oberlin transfers only and the rest had brachial plexus repairs; 2 of these required an Oberlin transfer as a second operation for failed biceps recovery at 10 months post op.

Results: All patients's pre-operative and post-operative improvement was graded with the Mallet scale. The 2 patients with Oberlin transfer only improved the fastest. The earliest improvement in upper/middle trunk group was 5 months post op. The patients with all three trunk injuries (ex. flail arm) had the slowest and most incomplete recovery.

Conclusion: Decision making in brachial plexus birth injuries can be in two parameters. First, the necessity to operate based on close monthly physical exams and second, extent of repair based on outcome goals. The second decision can be assisted by intra-operative findings (including nerve stimulation).
522: LITT Therapy for SEGA: Establishing Its Role in Standard of Care

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Introduction: Subependymal giant cell astrocytoma (SEGA) is the most common CNS tumor in patients with tuberous sclerosis (TS). Although these are benign, their proximity to the foramen of Monroe frequently causes obstructive hydrocephalus, a potentially fatal pathology. Historically, open surgical resection was the treatment mainstay; however, this can cause significant morbidity. The development of mTOR inhibitors changed the treatment landscape, but limitations exist for their use. Laser interstitial thermal therapy (LITT) is an emerging modality that has shown promise in treatment of a variety of intracranial lesions. No series has directly compared these modalities in SEGAs. We present a series of 12 patients treated with a combination of these modalities, comparing efficacy at SEGA control and discussing their relative merits and shortcomings.

Methods: We retrospectively collected data from 12 patients with SEGAs treated at our institution from 2010-2021, including tumor volume pre-/post-intervention, to determine tumor control. Paired t-test was used to determine statistical significance in tumor control.

Results: Three patients each underwent LITT and resection, five had only mTOR treatment, and one patient had all three modalities. There was no statistically significant difference in tumor control between the three modalities (LITT vs. resection: p=0.29, LITT vs mTOR: p=0.84; mTOR vs resection: p=0.30). Only one patient in our series required permanent CSF diversion, one had recurrence, and five discontinued mTOR inhibitor due to cost or side effects.

Conclusion: Our study indicates that LITT is potentially as effective for tumor control in SEGA treatment compared to the standard of care. This modality is less invasive than open resection and may be an alternative surgical option for those whom mTOR inhibitor use is not an option. We recommend an updated paradigm for SEGA treatment which includes LITT in select cases, and argue that centers specializing in SEGA treatment have LITT capability to offer to their patients.
523: Microsurgical Treatment of Pediatric Arteriovenous Malformations: A Large Single Center Case Series

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Introduction: Arteriovenous malformations (AVMs) in the pediatric population carry a lifetime risk of hemorrhage, seizures, neurological deficits, and headaches. Given the long life-expectancy of children, a surgical cure is preferred if it can be accomplished with low morbidity. The scarcity, variety in presentation, and variety of anatomical factors for AVMs can make decision making more difficult. Optimal patient counseling and treatment strategies require full understanding of surgical options and outcomes. Unfortunately, there are few large series detailing the microsurgical outcomes of pediatric AVMs.

Methods: All pediatric patients who had angiographically confirmed diagnosis of cerebral AVM over a 15-year period at a single institution were retrospectively reviewed. Demographics, clinical data, and anatomical features were analyzed. Outcomes for patients undergoing microsurgical treatment were also analyzed.

Results: 61 patients with cerebral AVM were identified. 41 underwent microsurgical treatment. Spetzler-Martin grade was I, II, or III for 40 of 41 patients. 19 underwent adjunctive pre-operative embolization. Complete obliteration rate was 95%. One patient with a small deep residual was treated with radiosurgery, and later achieved complete obliteration. Another patient with small deep residual is being managed with close observation. 3 patients had delayed recurrences that were treated with repeat surgery. Post-operative deficits occurred in 6 patients, 2 with hemianopsia and 4 with motor deficits. All were patients with AVMs in eloquent cortex. 4 of these 6 patients had significant improvement at last follow up. 4 patients had new onset of seizures post-operatively. mRS score at last follow up was 0-2 for 38 patients, a 3 for two patients, and 4 for one patient. Average follow up was 2.8 years.

Conclusion: Microsurgical resection of pediatric AVMs has high rates of obliteration with good outcomes in select patients. Continued long term follow is recommended due to potential for recurrence. Location in eloquent cortex is a strong predictor for post-operative deficit.
Comparison of Surgical Interventions for Early-onset Scoliosis: A Systematic Review and Meta-analysis

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Introduction: In the management of early-onset scoliosis, several growth-preserving techniques are employed, based on the principles of growth guidance or distraction. Our aim is to compare the effectiveness of traditional growing rods (TGR), magnetically-controlled growing rods (MCGR), Shilla growth-guidance techniques, and vertically expandable titanium ribs (VEPTR) interventions in their ability to correct early-onset scoliosis (EOS), as well as their complication and reoperation rates.

Methods: A systematic review of the literature was performed to identify studies reporting outcomes of growth-preserving surgical interventions for early-onset scoliosis. Outcomes of interest included the correction of Cobb angle, T1-S1 distance, complication rate - defined as cases with either device-related complications, medical complications, or infections - and reoperation rate.

Results: A total of 90 studies were included in this analysis, which included 46 TGR, 25 MCGR, 13 VEPTR, and 6 Shilla. A total of 1,119 patients were included, with a mean age of 6.88 (+/- 1.244) and an average follow-up of 47 months. At final follow-up, TGRs were found to have the highest percent reduction in the Cobb angle (42.86; 95% CI [38.82-47.31], followed by MCGR (38.47. 95% CI [33.74-43.85]) and Shilla growth guidance technique (38.29; 95% CI [26.53-55.26]), and, finally, VEPTR (22.14; 95% CI [17.37-28.21]). The T1-S1 percent improvement was the highest for the TGR (21%), followed by VEPTR (18%), then the Shilla growth guidance technique (17%), and finally the MCGR (15%). The Shilla growth guidance technique had the highest per-patient complication rate (58%), followed by TGR (53%), then VEPTR (49%), and finally MCGR (41%). No statistical significance was demonstrated between the groups in the terms of T1-S1 correction and complication rate.

Conclusion: TGR remains a reliable option in the management of EOS. VEPRT is significantly inferior to the rest of the options in decreasing Cobb angle. The rest of the modalities have similar effectiveness and complication profiles.
525: Clinical Outcomes for Pediatric Hydrocephalic Patients Treated with ETV+CPC: A Systematic Review and Meta-analysis

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Introduction: Endoscopic third ventriculostomy and choroid plexus cauterization (ETV+CPC) is a novel procedure for infant hydrocephalus developed to mitigate the risks associated with permanent implanted shunt hardware. This systematic review and meta-analysis summarizes the literature surrounding ETV+CPC intraoperative abandonment rate, peri-operative mortality rate, cerebrospinal fluid infection rate, and failure rate.

Methods: The review was performed using seven different databases in accordance with PRISMA guidelines, including articles from inception to October 2019. Studies included controlled trials, cohort studies, and case-control studies of patients with hydrocephalus less than 18 years of age treated with ETV+CPC. Pooled estimates were calculated using DerSimonian and Laird random effects modelling and significance of subgroup analyses were tested using meta-regression. The quality of pooled outcomes was assessed using the GRADE approach.

Results: After screening and reviewing 12,321 citations, sixteen articles met inclusion criteria. The pooled estimate for ETV+CPC failure rate was 0.44 (95%CI[0.37,0.51]). Subgroup analysis showed a statistically significant difference in failure rate by geographic income level, with low and middle income countries having a lower failure rate (0.33 (95%CI:[0.28,0.38])), compared to high income countries (0.53 (95%CI:[0.46,0.60]);p-value <0.01). The pooled estimate for perioperative mortality rate (n=7 studies) was 0.001 (95%CI:[0.00,0.004]), intraoperative abandonment rate (n=5 studies) was 0.04 (95%CI:[0.01,0.08]), and postoperative CSF infection rate (n=5 studies) was 0.0004 (95%CI:[0.00,0.003]). All pooled outcomes were of low quality evidence.

Conclusion: This systematic review and meta-analysis provides the most comprehensive pooled estimate for ETV+CPC failure rate to date (44%), demonstrates a statistically significant difference by geographic income level, and provides the first reported pooled estimates of ETV+CPC perioperative mortality (0.1%), intraoperative abandonment (4%), and CSF infection (0.04%). These results can help determine which children may benefit most from ETV+CPC. The low quality of evidence suggests the need for further high quality research to improve our understanding of these outcomes and their relevant explanatory variables.
526: Spinal Dysraphism in Epispadias-exstrophy Complex

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Introduction: Cloacal and bladder exstrophy belong to a spectrum of diseases, epispadias-exstrophy complex (EEC), that are thought to occur due to complications of gastrulation and neurulation. The neurological manifestations of this spectrum of diseases have been reported 1-6 however the prevalence and scope of neurological disease is not well known. In this project, we report the largest series of exstrophy patients (n=90) with spinal dysraphism.

Methods: A prospectively maintained IRB-approved database of exstrophy patients was queried for spinal dysraphism in addition to hydrocephalus and Chiari malformation.

Results: Analysis revealed 6.4% (90/1401) of patients with exstrophy had coexisting spinal dysraphism. Within the cohort, 40 were male and 50 were female. Spinal dysraphism was most prevalent in patients with cloacal exstrophy at 78.1% (75/96) followed by cloacal variant (25.6%, 11/43), classic bladder variant (0.75%, 2/266) and lastly classic bladder exstrophy (0.2%, 2/996). Within spinal dysraphism, lipoma-based closed defects (27.7%, 25/90) and tethered cord (27.7%, 25/90) were most common. Hydrocephalus and chiari malformation occurred in 32% (29/90) and 30% (27/90) of patients. Of the 29 patients with hydrocephalus, 6 (20.7%) underwent shunt placement. Neurosurgery did not have a negative effect on bowel/bladder function and neurosurgical complication rate for spinal dysraphism was low at 15.5% (14/90).

Conclusion: In this study, we report the largest series of patients with EEC and coexisting spinal dysraphism (n = 90). Spinal dysraphism occurred in 6.4% of all patients with EEC and was most common in the subset of patients with cloacal exstrophy (78%). Lipoma-based closed defects (27.7%, 25/90) and tethered cord (27.7%, 25/90) were most common and the rates of hydrocephalus and Chiari were 32% and 30%. These data indicate that the neurosurgical burden of EEC patients is significant however the complication rate is low.
527: The Role of Vagus Nerve Stimulation in Genetic Etiologies of Drug Resistant Epilepsy: A Meta-analysis

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Introduction: Drug-resistant epilepsy (DRE) affects many children. Vagus nerve stimulation (VNS) can provide better seizure control. Its role in children with genetic etiologies of epilepsy is not well-described. We systematically reviewed the literature to examine the effectiveness of VNS in this cohort.

Methods: A systematic review was performed investigating the impact of VNS on seizure outcomes in children with genetic etiologies of epilepsy using four databases. Primary outcomes included seizure freedom, >=90%, and >=50% seizure reduction rate. Secondary outcomes were seizure severity and quality of life (QoL), including cognitive, functional, and behavioral, outcomes. Random-effects meta-analysis was performed.

Results: 125 articles resulted, 47 of which were included. 216 non-duplicate patients were analyzed. Most common diagnoses were Dravet Syndrome (DS) (42.6%, 92/216) and Tuberous Sclerosis Complex (TSC) (29.2%, 63/216). Seizure freedom was not reported in any patient with DS; the pooled proportion with >=50% seizure reduction was 39% (95% CI: 21%-58%). Secondary outcomes of VNS in DS demonstrated variability on cognition but a benefit in seizure duration and status epilepticus. In TSC, the pooled seizure freedom rate was 41% (95% CI: 12%-71%), >=90% seizure reduction rate 30% (95% CI: 8%-56%), and >=50% reduction rate 71% (95% CI: 48%-91%). For secondary outcomes of VNS in TSC, several studies reported decreased seizure severity, and improved QoL outcomes. There was limited evidence regarding use of VNS in other genetic etiologies of epilepsy. Those studied included mitochondrial disease, Rett, Doose, Landau-Kleffner, Aicardi, Angelman, Ring Chromosome 20, and Lissencephaly; they had variable responses in a limited number of cases.

Conclusion: We conducted a systematic review of VNS outcomes in children with genetic etiologies of DRE. Among the most studied, TSC had substantial seizure reduction and improvements in QoL, DS had less robust seizure reduction. Increased testing, diagnosis, and long-term follow-up studies are necessary to better characterize VNS response in these children.
Feasibility of Low Field-strength Magnetic Resonance Imaging in the Pediatric Neurosurgery Clinic

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Introduction: Pediatric patients undergoing magnetic resonance imaging (MRI) of the brain often experience anxiety and difficulty holding still. Many patients receive general anesthesia or limited, “quick brain” MRI protocols. These methods isolate children and expose them to the risks of a high field strength environment. A portable, low-field-strength MRI (lfMRI) may be well suited for pediatric patients. We assessed the feasibility of lfMRI in pediatric patients in the outpatient setting.

Methods: We evaluated an FDA-cleared, portable, 0.064T MRI unit in a neurosurgery outpatient clinic. We included all patients receiving lfMRI. Feasibility data were recorded.

Results: Ten patients received lfMRI with ages ranging from 9 months to 27 years; there was one patient over age 18. The indications for imaging included ventricular evaluation (n=5), evaluation of reported intracranial mass (n=1), Chiari malformation (n=2), evaluation of craniocervical junction instability (n=1) and follow-up from traumatic brain injury (n=1). Parents remained with the patient throughout the scan. Mean scan time was 11.2 minutes, ranging from 9-15 minutes. Images were available immediately for physician review. All images were adjudicated as evaluable, although in larger patients the cervical region was not completely imaged.

Conclusion: LfMRI is feasible for use in the pediatric outpatient clinic setting and is well suited for ventricular size assessments. Diagnostic information is provided to outpatient providers and families in real-time through PACS or portable devices. There was no disruption in clinic workflow. We established an MR-safe environment in a standard outpatient clinic room. Adequate images, including flexion views, were obtained in all patients. Additional considerations for implementation include safety in patients with programmable devices, machine size, and interpretation of images. Changes in coil design could improve posterior fossa and craniocervical junction imaging. We plan to compare image quality and patient-centered outcomes between low-field strength and limited acquisition of high-field strength MRI in pediatric patients.
529: Effects of Extended Operative Time on Surgical and Hospital Outcomes After Posterior Spinal Fusion for Adolescent Idiopathic Scoliosis

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Introduction: Extended operative time (EOT) has been associated with increased complication rates and longer of hospital stays (LOS). The aim of this study was to determine risk factors and the impact of EOT in adolescent idiopathic scoliosis (AIS) patients undergoing posterior spinal fusion (PSF).

Methods: A retrospective cohort study was performed using the American College of Surgeons National Surgical Quality Improvement Program-Pediatric (NSQIP-P) database from 2016 through 2018. All pediatric patients (age 10 - <18 years) with AIS undergoing PSF were identified. Patients were then categorized by operative time: Non-Extended Operative Time (Non-EOT) and Extended Operative Time (EOT) - those with an operative time > 309 minutes or > 75th percentile for the overall patient population. A multivariate regression analyses were used to determine risk-factors for EOT and impact on LOS.

Results: A total of 4,632 patients were identified, of which 1,136 (24.5%) had an EOT. Age and comorbidities were similar between the cohorts. The EOT cohort had more 13+ levels fused (EOT:38.9% vs. Non-EOT:17.8%, p<0.001) with a greater proportion (78.8% vs. 64.9%) and total amount of blood transfused (EOT: 420.6±361.4 mL vs. Non-EOT: 244.5±217.2 mL, p<0.001). Compared to the Non-EOT cohort, the EOT cohort had slightly higher rates of complications (EOT:2.9% vs. Non-EOT:1.0%, p<0.001), longer hospital stays (EOT: 4.0±1.2 days vs. Non-EOT: 3.6±1.1 days, p<0.001), and unplanned 30-day readmissions (EOT:4.2% vs. Non-EOT:2.2%, p=0.006). On multivariate analysis, Asian race, ASA classification 2 and 3, starting anesthesia time, levels fused and total blood transfused were found to be a significant independent risk factor for EOT, with 13+ levels fused being the greatest predictor [aOR: 4.9, 95% CI:(2.67,8.98),p<0.001]. Additionally, EOT was found to be a significant predictor on multivariate analysis for longer hospital stays [RR: 0.26, 95% CI: (0.16,0.36), p<0.0001].

Conclusion: Our study demonstrated that extended operative time may be associated with slightly increased complications and longer LOS.
530: Pediatric Stereotactic Image-guided C1-2 Transarticular Screw Placement

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Introduction: Atlantoaxial instability is a common pediatric pathology which often requires neurosurgical intervention. C1-2 transarticular screw placement has been shown to be a safe and effective option for treatment of instability in this population. Upper cervical spine anatomy is unique, and requires careful technique to avoid neurologic or vascular injury during screw placement. One technique which can aid in screw placement, but is not commonly utilized in children, is the use of stereotactic image guidance. We examined our series of pediatric patients with spinal instability treated with stereotactic image-guided C1-2 transarticular screws.

Methods: A single-center, retrospective study was conducted at our institution examining pediatric patients from 2020-2021, undergoing C1-2 transarticular screw placement. All screws were placed using stereotactic image guidance based on intraoperative 360 degree fluoroscopy. Demographic, clinical, radiographic, and outcome data were examined. Primary outcomes included radiographic signs of fusion and resolution of cervical instability.

Results: Six patients were identified who underwent C1-2 transarticular screw placement with stereotactic image-guidance. Three patients (50%) were male and three were female. The median age was 10 years (SD=4.31 range=2-15). Three patients (50%) had instability related to congenital anomalies, two (33%) related to trauma, and one related to tumor (17%). All patients underwent surgery for C1-2 transarticular screw placement. Ten total screws were placed. Two trajectories were avoided due to concern for aberrant vertebral artery anatomy. No patients experienced postoperative complications. On postoperative imaging all screws were placed in satisfactory positions, and no patient had evidence of spinal instability.

Conclusion: We present our series of children who underwent C1-2 transarticular screw placement with stereotactic image-guidance. All patients had favorable clinical and radiographic outcomes without complications. We use this series to highlight the role of stereotactic image-guidance to augment understanding of variant anatomy and detail the technique for C1-2 transarticular screw placement in pediatric patients.
531: Impact of Transfer Status on Discharge Disposition and Adverse Events Among Pediatric Patients Undergoing Malignant Brain Tumor Resection

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Introduction: Interhospital transfer (IHT) to obtain higher level of care for pediatric patients requiring neurosurgical interventions is common. Specifically, pediatric patients with malignant brain tumors may benefit from subspecialty care and resources available at pediatric centers. We aimed to assess the impact of IHT in pediatric neurosurgical patients to identify areas of improvement in treatment of this patient population.

Methods: We retrospectively evaluated pediatric patients (<19 years old) undergoing resection of primary malignant brain tumor using data from the Nationwide Readmissions Database (NRD) for 2010-2018. We evaluated association of IHT with specific patient/hospital characteristics on overall patient outcomes. Patient and hospital data for each index admission provided by NRD was analyzed by univariate and multivariable analyses.

Results: Among 2,279 non-elective admissions for malignant brain tumors in pediatric patients, 132 patients (5.8%) underwent interhospital transfer for higher level of care. There is an increased likelihood of transfer when a patient is younger (<7 years old, p=0.006) or the disease process is more severe, as characterized by higher pediatric Complex Chronic Conditions (CCC, p=0.0004) and increased APR-DRG mortality index (p=0.002). Patients who are transferred (OR 1.87, 95% CI 1.04-3.35, p=0.037) and patients who are treated at pediatric centers (OR 6.89, 95% CI 4.23-11.22, p<0.0001) are more likely to have a routine discharge home. Patients who are transferred were not associated with increased likelihood of mortality(p=0.12) or major complication(p=0.99).

Conclusion: IHT in malignant brain tumor occurs primarily among younger patients with disease burden that is likely to be more complex and with higher acuity. Further study is warranted to confirm whether transfer to a pediatric center truly improves patient outcomes and decreased adverse events in this complex population.
532: Somatic Loss of PBRM-1 as a Candidate Driver Event in Pediatric Pineoblastoma

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Introduction: Pineoblastomas comprise a heterogeneous and aggressive pediatric neuroectodermal tumor subtype. Because of their rarity, there is limited insight into the molecular mechanisms underlying their development.

Methods: A global clustering scheme was developed to better understand subgroups of this disease. We examined the somatic genomic profile of a pineoblastoma tumor in order to delineate the mechanisms driving tumor formation.

Results: Whole exome sequencing (WES) revealed a somatic genetic profile consistent with loss of Protein polybromo-1 (PBRM-1) together with various copy number variations (CNV) previously reported in literature.

Conclusion: PBRM-1 has been reported to prevent genomic instability. Our investigation suggests that its loss could be acting as the driver for tumor formation and genomic instability in pineoblastomas.
**533: First-in-human Use of Novel Platinum-nanorod (PtNR) Multi-thousand Channel High Density Grid During Craniotomies for Pathologic Brain Resections**

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**Introduction:** A novel high-density, thin film, multi-thousand channel grid was developed and tested in animals and used in humans for cortical recording during craniotomies for pathologic brain resections. Objective: To report superior spatiotemporal cortical dynamics revealed by first-in-human use of platinum-nanorod based multithousand channel high density grids.

**Methods:** Two grids with the following densities: 100 electrodes/cm² on 1024 3.2x3.2 cm grid and 32 electrodes/cm² on 2048 8x8 cm grid for cortical recording in 20 patients during pathologic brain resection, along with conventional clinical grids for functional and seizure mapping. Results of post-hoc analysis of recordings during SSEP, grasp motion, movement and vibrotactile stimulation of fingers, spontaneous and stimulated ictal activity are reported.

**Results:** SSEP recording revealed precise curvilinear nature of the M1-S1 functional boundary (M1-S1 FB) which differed from the anatomical central sulcus, confirmed by stimulation mapping. Correlate of grasping motion revealed dynamic high Gamma activity (HGA) across the (SMA; -100 mSec, M; 0-250 mSec and S1, >300mSec), with propagating beta waves across M1-S1 with clear beta waves suppression during motion. Movement and vibrotactile stimulation of individual fingers were associated with correlated, localized, spatially distinct HGA with each finger in M1 and S1 respectively. Finally pathological epileptiform discharges (spontaneous and induced by stimulation) were recorded and its propagation mapped across the surface area covered by the grid with significant enhancement of epileptiform discharge detection (p< .001)

**Conclusion:** PtNR high-density grids were used in humans during resective surgeries and reveal superior spatiotemporal dynamics of human cortical functions compared to currently available surface grids.
534: High Density Electrocorticography Reveals Functional Microstructure of Human Superior Temporal Gyrus

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Introduction: Brain-computer interfaces (BCI) have enormous potential, but fundamental questions hold back clinical utility. For example, speech prostheses could improve quality of life for patients with aphasia, but animal models have low utility and access to human cortex is limited. To study functional organization of human speech processing, we designed an experiment to record neural activity from cortex involved in receptive speech processing. We used custom-built, ultra-high density electrode arrays to record from speech areas in patients undergoing awake craniotomy.

Methods: During awake craniotomy, clinical functional mapping identified areas that produced evoked potentials from receptive language. Then ultra-high density, conformal electrode arrays were placed on the cortical surface. The patient listened to consonant-vowel combinations of real words, nonsense words, or noise-vocoded (inarticulate) words for 5 to 10 minutes.

Results: Patients' microrecordings showed modulation of neural activity in response to language, with consistent robust selectivity for real words over noise. Auditory stimuli produced robust cortical responses and phase-amplitude coupling in slower (2-8Hz) and faster frequencies (70-190Hz). With electrodes in a linear array (128 channels, two rows, 50μm pitch), boundary regions and approximate spatial dimensions were identified. Two-dimensional response characteristics were then studied using a larger electrode (1024 channels, 16x64 electrode array, 200μm pitch). Spatial and temporal modulation of neural activity in the gamma-band occurred in grouped segments as small as 1-2mm.

Conclusion: Spatial, temporal, and frequency characteristics of receptive-speech processing was studied in awake patients. These results will aid in the development of speech-prostheses and BCI by guiding organization of electrodes.
535: Impact of Subthalamic Nucleus Stimulation on Urinary Dysfunction and Constipation in Parkinson’s Disease

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Introduction: The effect of subthalamic nucleus deep brain stimulation (STN DBS) on urinary dysfunction and constipation in Parkinson’s disease (PD), like other non-motor symptoms, is mixed. This study aims to identify potential surgical and non-surgical variables predicting these two forms of autonomic dysfunction.

Methods: We retrospectively evaluated 74 patients who underwent STN DBS for PD. Global Cerebral Atrophy (GCA) scale was estimated on preoperative 3-T MRI. Active electrode contact was localized relative to the STN midpoint in Talairach space. The Movement Disorder Society Unified Parkinson Disease Rating Scale (MDS-UPDRS) Part-I items 10 and 11 were applied preoperatively and 6-12 months postoperatively to assess urinary dysfunction and constipation, respectively. A multiple linear regression model was used to investigate the impact of GCA and active electrode contact location on urinary dysfunction and constipation follow-up score controlling for age, baseline score, motor improvement percent change, and levodopa-equivalent dose changes.

Results: Among 74 patients, 23 improved, 28 deteriorated, and 23 remained unchanged for urinary dysfunction; 25 improved, 15 deteriorated, and 34 remained unchanged for constipation. GCA score, anterior active electrode contacts in the left hemisphere, and age significantly predicted urinary dysfunction follow-up score (R² = 0.36, P<0.001). Increasing GCA and age were associated with worsening urinary problems; anterior active contact locations were associated with improved urinary symptoms. Baseline constipation score, anterior active electrode contacts in both hemispheres, and motor improvement were significant predictors for constipation follow-up score (R² =0.31, P<0.001). Higher baseline constipation score was associated with worsening constipation; anterior active contact locations and motor improvement were associated with improvement in constipation.

Conclusion: Anterior active contact locations are associated with improvement in constipation and urinary function in PD patients after STN DBS. PD patients with greater GCA scores before surgery were more likely to experience urinary deterioration after DBS.
536: Distinct Perceptive Pathways Selected with Bursting and Tonic Patterns of Thalamic Electrical Stimulation

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Introduction: Novel patterns in electrical stimulation of the brain or spinal cord hold tremendous promise in improving treatments for movement disorders and pain syndromes. However, there are a paucity of experimental studies in humans that compare the differing clinical effect of stimulation patterns and provide insight into the underlying mechanisms. In this work, we performed electrical macrostimulation with uniform pulse train (tonic) and bursting stimulation patterns of somatosensory thalamus (ST) where the terminal effect, evoked sensations or percepts, are readily reported by patients and easily related to anatomic thalamocortical pathways via the well-known thalamic somatotopy. We hypothesized that stimulation patterns would evoke different percepts in either location or quality.

Methods: During awake deep-brain stimulation surgeries in 15 human subjects, we electrically stimulated the sensory thalamus with tonic and bursting patterns. Stimulation amplitudes at the threshold of perception and percept location/quality were compared.

Results: The resulting tonic and burst percepts were located in widely separate, non-overlapping body regions (i.e., face vs. hand) in a majority of patients. The effect was not simply due to the difference in average pulse density between patterns but also the temporal irregularity inherent in bursting patterns (p < 0.001). The quality of burst percepts also consistently differed from that of tonic waveforms (p = 0.013, Fisher’s exact test). Thus, temporal differences in patterned stimulation is found to select for distinct perceptive pathways that likely correspond to distinctive anatomic pathways.

Conclusion: Selecting for specific functional pathways via stimulation patterns may lead to improved clinical efficacy in movement disorders and pain syndromes as well as improvements in side-effect avoidance, intraoperative localization, and sensory prosthetics.
537: Safety and Effectiveness of the Assessment and Treatment of Idiopathic Normal Pressure Hydrocephalus in 424 Patients in the Adult Hydrocephalus Clinical Research Network

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Introduction: Idiopathic Normal Pressure Hydrocephalus (iNPH) is a disorder of the elderly (age >60 years) with progressive worsening of gait and balance, cognition, and urinary control. Symptoms are not specific to iNPH, and patients typically require additional assessments using criteria recommended by the International iNPH guidelines (e.g., large volume CSF removal by lumbar puncture (LP) or by an external lumbar drain (ELD)) before considering treatment with a CSF-shunt. The objective is to describe the processes and outcomes of prospectively enrolled patients at 5 sites of the Adult Hydrocephalus Clinical Research Network (AHCRN) who underwent evaluation and treatment for suspected-iNPH, with 1-year postoperative follow-up.

Methods: AHCRN registry data from a 50-month interval includes entry criteria; demographics; comorbidities; examination findings using standard AHCRN gait and neuropsychology assessments; shunt procedures, complications of CSF drainage, and complications within 30 days of surgery.

Results: 547 patients were referred for assessment of suspected-iNPH. After initial examination, 123 patients (21.6%) did not meet clinical criteria to proceed with further iNPH-related testing. 424 patients (74.4%; mean age 76.7 ± 6.0 years; males=269) underwent either an LP or ELD and 193/424 (45.6%) underwent insertion of a ventriculoperitoneal shunt. By 8-12 months after shunt surgery, gait velocity was 0.96 ± 0.35 m/s, or 54% faster than pre-CSF drainage. Mean MoCA scores increased from 21.0 ± 5.0 (median=22.0) at baseline to 22.6 ± 5.5 (median=24) 12-months post-surgery. Gait and cognitive improvements were clinically significant. No deaths were associated with CSF drainage or shunt surgery. 8% of shunt-surgery patients experienced minor complications. The 30-day reoperation rate was 4.1%.

Conclusion: This AHCRN study, undertaken at 5 adult hydrocephalus centers, demonstrated that testing of patients with suspected-iNPH, using the CSF drainage criteria described by the International iNPH Guidelines, successfully identified those who could undergo CSF-shunt surgery with a high rate of improvement and a low rate of complications.
Introduction: Corpus callosotomy is a palliative procedure used to treat catastrophic, generalized non-localizing medically refractory epilepsy. Controversy exists between the use of partial vs. complete callosotomy (CCC) procedures for this patient population. We present our ten year, single institution experience with single step, complete corpus callosotomy in the treatment of this challenging epilepsy population.

Methods: An IRB approved retrospective observational study was performed in patients aged 6 months to 49 years who underwent clinically indicated, single step, CCC at Advent Health Orlando, from September 2011 through August 2021.

Results: One hundred sixteen patients (57% male) met eligibility criteria. Ninety patients were pediatric and 26 were adults. All patients had generalized seizures which were poorly lateralized both by clinical semiology and electroencephalography. CCC was performed by a single surgeon (JB) and the extent of callosotomy was confirmed by MRI. There were 2 surgical infections, 2 intracranial hemorrhages and 3 CSF wound leaks. One bone flap was removed for infection, one ICH required burr hole drainage, and one CSF would leak required ventriculo-peritoneal shunt. Postoperatively 56% of subjects achieved freedom from drop seizures a 44 months and 13% achieved freedom from all seizure types at 27 months. Transient supplemental motor area syndrome like deficits were seen in 57 patients. The incidence and duration of these symptoms increased with the patients' age a surgery. Pre and post-operative neuropsychological testing was obtained in 14 patients and was stable in 13 of 14 patients tested.

Conclusion: Complete corpus callosotomy is a well tolerated treatment for this patient population. Durable freedom from drop seizures and all seizure types can be achieved following this procedure. Transient SMA like deficits can occur post-CCC. The incidence and duration of these transient deficits increases with patient age. Our neuropsychological test data suggest that this procedure usually does not result in permanent neuropsychological decline.
539: Ambulatory Local Field Potential Recordings from the Thalamus in Epilepsy: Early Experience

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Introduction: Stimulation of the anterior (ANT) and centromedian (CM) thalamic nuclei has been shown to reduce seizures in intractable limbic and generalized epilepsy, respectively. Stimulation targets thalamo-cortical networks and results in acute widespread cortical desynchronization. Progressive reduction in seizure frequency has been observed over years of ANT stimulation. The electrophysiology of ANT and CM, and the chronic effects of ANT/CM stimulation on cortical activity, are not well characterized.

Methods: Two patients received bilateral deep brain stimulation (DBS) systems capable of recording ambulatory local field potentials (LFP). One patient underwent ANT DBS for multifocal epilepsy; the other underwent CM DBS for primary generalized epilepsy. Broadband LFP was recorded after implantation and at outpatient appointments up to 9 months after surgery. Peaks in the alpha band were identified and used for ambulatory narrow-band (+/-2.5 Hz) LFP.

Results: Peaks in LFP power were observed at 6-11 Hz (ANT) and 10-15 Hz (CM). Circadian variation was observed in median power-in-band (PIB) and PIB extreme outlier events. Activity consistent with interictal discharges was identified on outpatient recordings. LFP line length correlated with PIB in CM (R^2 0.12-0.14, P<0.0001) but not ANT. Ambulatory 10-minute epochs with 90-120 s of stimulation had 10-12% greater PIB than epochs with 60-90 s of stimulation (P<0.001). In ANT, PIB was higher with stimulation on at 0.5-1.5 mA compared to stimulation off (0.029-0.042 uV^2/Hz, P=0.001), and higher after versus before stimulation at 1.5 mA (0.020 uV^2/Hz, P=0.047) but not at 0.5 mA or 1.0 mA.

Conclusion: Interictal activity was identified in ambulatory recordings from ANT and CM. Spectral analysis of thalamic recordings revealed physiologic and potentially pathologic trends which might aid in the development of biomarkers to guide thalamic stimulation for epilepsy. Long-term thalamic LFP with markers of cortical activity are needed to understand the significance of these findings.
540: Stereotactic Magnetic Resonance Guided Laser Ablation of Periventricular Nodular Heterotopia

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Introduction: PVNH is the most common form of neuronal heterotopia and often results in pharmaco-resistant epilepsy. Advances in minimally invasive approaches to localize and treat such epilepsy have provided novel strategies for managing nodular heterotopia-related epilepsy. Here we report our experience with PVNH-associated epilepsy managed using robotic guided stereo-electroencephalography and laser interstitial thermal therapy (LITT).

Methods: We used a prospectively maintained database of epilepsy patients to identify all patients with PVNH associated epilepsy that were managed over a 10-year interval using SEEG and laser ablation. Details regarding epilepsy, the neurophysiology, management, complications, and outcomes at the last follow-up were compiled.

Results: A total of 32 patients were identified. Median/average follow-up after the intervention was 18/28.8 months (range: 2 – 79). The average age at the time of surgery was 29.7 years (range: 16-50). The average age at epilepsy onset was 14.25 (range: 1-26). The average time between seizure onset and time of intervention was 15.4 years (range: 1-42). During the follow-up period, only two patients (6.25%) did not exhibit worthwhile improvement (Engel class IV). Eight patients (36%) initially underwent seizure focus resection of a non-PVNH site with no worthwhile improvement in seizures (Engel IV) prior to PVNH ablation.

Conclusion: MRI-guided LITT for PVNH-associated epilepsy is a feasible, safe, and efficacious intervention. When PVNH is present, ablation should be considered as a first-line treatment for the improvement of epilepsy. Patients should be carefully selected, particularly to determine the role of PVNH in the epileptogenic network.
541: Convection Enhanced Delivery of Autologous Cerebrospinal Fluid Improves Basal Ganglia Visualization During MRI-guided Deep Brain Stimulation Surgery

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Introduction: To determine the safety and feasibility of convection enhanced delivery (CED) of autologous cerebrospinal fluid (CSF) for improving intraoperative magnetic resonance imaging (MRI) of the basal ganglia during stereotactic neurosurgery.

Methods: This pilot study was conducted in four patients with Parkinson’s disease (PD) who underwent MRI-guided deep brain stimulation (DBS) of the globus pallidus internus (GPI). CSF was obtained via lumbar puncture after general anesthesia and prior to incision. A frameless stereotaxy system was installed, and an infusion catheter was inserted to the GPI using intraoperative MRI. Infusion of autologous CSF was performed at a convective rate of 5 µL/minute with a maximum volume of infusion (Vi) of 500 microliters. T2-weighted MRI scans were obtained every 15 minutes up to a maximum of 105 minutes in order to calculate the volume of distribution (Vd). Safety was assessed with adverse event monitoring, and clinical outcomes were measured with changes in unmedicated UPDRS part III and PDQ-39 scores from baseline to six months postoperatively.

Results: All four infusions were safe and without adverse events. The mean unmedicated UPDRS part III and PDQ-39 scores improved by 24% and 26%, respectively. The Vd:Vi ratio ranged from 2.2 – 2.8 and peaked 45 minutes from the onset of infusion, which is when the GPI could be fully visualized on T2-weighted MRI. Two patients underwent refinement of the stereotactic targeting based on infusion-enhanced images.

Conclusion: The convective administration of autologous CSF to deep brain structures appears safe and feasible for enhancing intraoperative MRI during stereotactic procedures. Infusion-enhanced imaging with target-specific infusates could be developed to visualize neurochemical circuits or cellular regions that currently are not seen with anatomic/structural MRI.
542: Caudate Beta Power During Working Memory Is Increased in Parkinson’s Disease Patients

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Introduction: Cognitive impairment (CI) is the most frequent nonmotor symptom in Parkinson’s Disease (PD) and is associated with deficits in executive functions including working memory. Previous work has shown that caudate beta power is important in learning and working memory. Decreased dopamine in motor cortico-striato-thalamo-cortical (CSTC) circuits results in increased beta power and PD motor symptoms. Analogous changes in cognitive CSTC circuits involving the caudate may contribute to PD CI. A better understanding of anatomic structures and neurophysiologic changes associated with working memory deficits is needed to develop novel treatment strategies for PD CI.

Methods: Five patients who underwent DBS surgery for PT or ET in 2021 at Vanderbilt University Medical Center and had trajectories through the caudate were consented and included in our IRB-approved study. Intraoperative, bilateral, simultaneous local field potential recordings were obtained from 17 total caudate channels during a 2-back verbal memory task with performance feedback. Signals were sampled at 1000Hz, Butterworth band pass filtered, and de-meaned. Average Z-scored beta power following feedback was compared between PD and ET patients using a paired t-test. Data processing and statistical analyses were performed in MATLAB.

Results: There was a significant increase in average caudate beta (15-30Hz) power during the 500ms feedback period following correct trials. This increase was significantly greater in PD compared to ET patients.

Conclusion: Changes in beta power between PD and ET patients may reflect underlying dopaminergic dysfunction in cognitive CSTC circuit structures such as the caudate. Structures within this circuit may be implicated in PD memory impairment and may serve as potential targets for neuromodulation to improve working memory.
543: Short-latency Myogenic Evoked Potentials in Human Subjects from Cerebellar Dentate Nucleus Deep Brain Stimulation

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Introduction: Cerebellar dentate nucleus (DN) stimulation is a potential site of therapeutic neuromodulation. Here, we report in a small cohort of human subjects evidence for myogenic evoked potentials in response to DN electrical stimulation.

Methods: Patients with upper extremity weakness from prior stroke underwent surgical implantation of a DN DBS system as part of the EDEN trial. In two of these subjects the DN was stimulated at a low frequency in order to elicit evoked potentials (EP). Electromyography (EMG) was recorded from the upper extremities. The signal was bandpassed (10-1000 Hz), rectified, and a moving RMS of the power was generated. Stimulus-locked sweeps of the data were averaged to generate an EP. The experiment was performed with the upper extremities in a resting state and during motor block-tracking task.

Results: Single pulses of DN electrical stimulation evoked robust responses in upper extremity muscles ipsilateral to stimulation during the motor task. In some trials, evoked potentials could be elicited in the resting state. The resultant potential was short latency consisting of both muscle activation (P1, 32.5 ms latency; P2, 105.4 ms) and stimulus-induced suppression of EMG activity below baseline (N1, 58.2 latency). Individual sweeps of EMG activity were then sorted by baseline power, and EPs were regenerated according to this metric. During periods of relatively greater EMG power, P1 and P2 were 2.8 and 1.3 times larger, respectively.

Conclusion: DN stimulation results in bidirectional modulation of EMG power in a way that is gated by the underlying muscle state, with greater evoked EMG power during baseline muscle contraction. These short-latency peaks in EMG power are not likely explained by the dentatothalamocortical pathway. This an early demonstration of DN stimulation evoked myogenic potentials in humans, and more experiments are needed to understand the mechanism and clinic-physiological relevance of this EP paradigm.
544: Presence of Massa Intermedia; Implications on Neurocognitive Performance in a Geriatric Population

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Introduction: Massa intermedia (MI) is an inconsistent connection between the two thalami in humans, being absent in approximately 8% of brains. Its role is poorly understood. Recent diffusion weighted MR based tractography studies suggest MI is a midline commissure with widespread connectivity to cortical and subcortical regions. In this study, we aimed to identify neuropsychometric differences in brains with, and without MI.

Methods: All subjects were selected from the Rush Memory and Aging Project. This is a large longitudinally studied cohort with all subjects having previously undergone high resolution T1 MRI studies as well as neuropsychological evaluations with over 100 metrics. Slices containing the third ventricle were investigated for presence or absence of MI. If present, longest superoinferior and anteroposterior dimensions were measured. Neuropsychometric results were compared in subjects with, and without MI.

Results: 620 subjects were included in the study with mean age of 78.22(SD=7.56) years. 76.3% of the cohort were female participants. MI was present in 494 (79.7%) of the participants. Mean MI size was 5.48(2.67) and 3.58(2.3) mm in anteroposterior and superoinferior dimensions respectively. Females had a significantly higher prevalence and larger MI size (Chi Square test p<0.001, Mann Whitney U test p<0.001 respectively). Episodic memory and global cognition were significantly higher in those with MI (Mann Whitney U test p<0.001 and =0.048 respectively). Tremor score was lower in those with MI (p=0.044).

Conclusion: Subjects with MI demonstrated better performance in both cognitive and motor domains. This study further supports the role of MI in normal neurocognitive functions.
546: Prediction Model for Neurogenic Bladder Recovery One Year After Traumatic Spinal Cord Injury

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Introduction: Neurogenic bladder is a common complication after spinal cord injury (SCI) that carries substantial medical and psychological burdens on the inflicted individual. The objective of this study is to build a model to predict bladder recovery one year after traumatic spinal cord injury.

Methods: We queried the National Spinal Cord Injury Model Systems database for patients with traumatic SCI who had neurogenic bladder at the time of injury. The primary outcome of interest was the complete recovery of bladder function at one year. We developed a predictive model and translated it to a calculator that can identify the likelihood of achieving complete bladder recovery.

Results: We identified a total of 2,515 patients with abnormal bladder function at baseline who had an annual follow-up. A total of 417 patients (16.6%) recovered bladder function in one year. Predictors of complete bladder recovery included the following baseline parameters: sacral sensation, American Spinal Injury Association (ASIA) impairment score, bowel function at baseline, voluntary sphincter contraction, anal sensation, S1 motor scores, and the number of days in the rehabilitation facility. The model performed with a discriminative capacity of 90.5%.

Conclusion: We developed a prediction model for the probability of complete bladder recovery one year after spinal cord injury. The model performed with a high discriminative capacity and was successfully translated into an online calculator. Bladder function is a critical consideration in spinal cord injury recovery. This prediction model demonstrates potential utility in the counseling, research allocation, and management of individuals with SCI.
547: Lateral Mass Screws versus Pedicle Screws at C7 - Reoperation Rates for Adjacent Segment Disease (Operative ASD) and Nonunions (Operative Nonunions) in Posterior Cervical Fusions Stopping at C7

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Introduction: The two commonly used fixation techniques at the C7 level in posterior cervical fusions (PCFs) that stop at C7 are lateral mass screws (LMS) and cervical pedicle screws (CPS). The superiority of one method over the other is unknown. Hence the objective of our study is to determine if there a difference in reoperation rates for symptomatic adjacent segment disease (operative ASD) or symptomatic nonunions (operative nonunions) in PCFs using LMS versus CPS at C7.

Methods: A retrospective analysis from our spine registry (Kaiser Permanente) identified a cohort of patients with cervical degenerative disc disease who underwent primary PCFs stopping at C7 with either LMS or CPS at C7. LMS were used at all rostral levels in both groups. Demographic and operative data were extracted from the registry and operative ASD and operative nonunions were adjudicated via chart review. Patients were followed until validated operative ASD or nonunion, membership termination, death, or end of study (03/31/2021). Descriptive statistics and adjusted logistic regression models were calculated for operative ASDs and operative nonunions.

Results: We found 274 patients with PCFs stopping at C7 with either LMS (n=150) or CPS (n=124) at C7 with average follow-up time of 7.1 (±0.31) years and average time to operative ASD of 4.6 (±0.31) years and to operative nonunion of 1.6 (±0.3) years. There were 7 operative ASDs (LMS=5, CPS=2) and 4 operative nonunions (LMS=1, CPS=3) with no statistical difference between LMS versus CPS for either operative ASDs (OR: 0.72 95% CI=0.09-5.58, P=0.755) or operative nonunions (OR: 4.61 95% CI=0.74-28.67, P=0.101).

Conclusion: A large cohort of patients with PCFs stopping at C7 with an average follow-up of > 7 years found no statistical difference in reoperation rates for symptomatic ASD (operative ASD) or symptomatic nonunions (operative nonunion) using either LMS or CPS at C7.
Introduction: Degenerative disc disease (DDD) is one of the leading causes of chronic debilitating low back pain. DDD is characterized by changes in cellular characteristics resulting in loss of extracellular matrix (ECM) water holding capacity of the nucleus pulposus (NP). DDD can lead to translation of physiological loads from the anterior 2/3 of the spinal column to the posterior 1/3, resulting in increased stress on the facets and ligamentum flavum causing facet hypertrophy and canal stenosis. Novel stem cell regenerative therapies could restore the anterior column load via NP regeneration.

Methods: A hydrogel scaffold was created composed of self-assembling polyethylene glycol (PEG) functionalized with acrylate and thiol end groups. The scaffold was impregnated with NP cells differentiated from human umbilical cord mesenchymal stem cells (MSCs) or undifferentiated MSCs. Impregnated NP-scaffolds were implanted into an ex vivo rabbit model of DDD and the viability and function of NP cells was analyzed.

Results: The NP-scaffolds limited leakage and retained the cells in the NP region of the degenerated disc. Both the NP-scaffold and the overall disc environment promoted differentiation of the MSCs into cell types capable of producing ECM products, including sulfated glycoaminoglycans, at higher levels compared to undifferentiated MSCs injected into the intervertebral disc. NP-scaffold cells also expressed chondrogenic markers, like SOX9, COL2, and ACAN, as well as NP markers FOXF1, K19, and vimentin at higher levels as determined by real-time polymerase chain reaction (PCR) and immunostaining.

Conclusion: This study demonstrated that a hydrogel scaffold impregnated with differentiated NP cells derived from human umbilical cord stem cells was much more effective at disc regeneration than undifferentiated MSCs alone. This method can lead to novel therapies for the treatment of DDD.
549: Optimal Realignment Outweighs Increased Perioperative Risk in ASD Surgery

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Introduction: An increased risk of perioperative complications comes with increasing complexity. However, some patients persevere through short-term complications and manage to still achieve optimal, long-term outcomes. We sought to demonstrate the superiority in long-term outcomes of achieving optimal realignment despite the increased risk of transient perioperative complications.

Methods: Operative ASD patients with baseline (BL) & 1-year (1Y) data were included. Patients were stratified based on meeting 1Y optimal outcome. Optimal outcome: improvement in all three age-aligned SRS-Schwab modifiers, proportioned (P) in GAP, and a 2Y-ODI score of less than 25. Multivariate analysis was used to determine significance for complications. Published methods converted ODI to SF-6D. Cost was calculated using the PearlDiver database and CMS.gov definitions.

Results: 469 ASD patients included. 63% of patients underwent a posterior approach, 37% combined. 52% underwent decompression, 66% underwent an osteotomy. BL radiographics: SVA:63.3±70.7 mm, PI-LL:14.4±21.2, PT:23.49±11.1. Patients grouped as follows: 105 “optimal” (O), 364 “not optimal” (NO). Comparison revealed differences in age, BMI, and FI. NO group had less levels fused and osteotomies, but significantly higher EBL and decompressions. Controlling for age and frailty, the O group had more perioperative complications (58.1% vs NO: 52.8%), significantly more GI complications (p=.027) and overall medical complications (10.5% vs NO: 8.5%). NO group had more reoperations (p=.004), major complications (p=.024), instrumentation failures (p=.079), and higher rate of PJK/PJF. Groups were significantly different in utility gained, 2-year QALYs, and overall cost (O: $74,371.08 vs. NO: $87,945.87, p=.008).

Conclusion: Despite undergoing more invasive procedures and sustaining more perioperative complications, patients meeting optimal outcome experienced less major/mechanical complications, fewer reoperations, and lower rates of PJK/PJF. Accordingly, a higher, transient perioperative complication profile should not preclude surgical correction in ASD patients who demonstrate baseline characteristics suggestive of successful long-term outcomes.
550: Lumbar Motion Is Maintained with Paraspinous Tension Band for Degenerative Spondylolisthesis: Results from 24-month FDA Study

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Introduction: Durable outcome for degenerative spondylolisthesis (DS) usually requires decompression and fusion. Fusion, however, places greater stress at adjacent levels with increased incidence of adjacent segment disease. A novel interspinous tension band is proposed for segmental stabilization after decompression for DS, as an alternative to fusion. An FDA IDE study (NCT03115983) compares decompression and transforaminal interbody instrumented fusion (control group) to decompression and stabilization with the tension band (treatment group) for symptomatic DS.

Methods: Prospectively enrolled IDE study subjects with 24 months postoperative radiographic follow-up were included in this analysis. X-rays obtained during the follow-up period for both the treatment (n=75) and control (n=52) groups were reviewed by an independent Core Laboratory for flexion/extension range of motion (ROM) and translation at the index, supradjacent and subjacent levels.

Results: For the treatment group, pre-op to 24-month post-operative ROM was reduced 33% (p<0.01) and translation was reduced 29% (p<0.01). The control group as expected showed a significantly greater decrease in ROM (68%, p<0.01) and translation (77%, p<0.01) at the index level. Both treatment and control groups did not have statistically significant change at supradjacent and subjacent levels. At 24 months, considering the ranges of motion at the index and adjacent segments, adjacent segments accounted for 73% of motion in the treatment group and 87% in the control group.

Conclusion: Unlike fusion, paraspinous tension band for DS maintained both stability and the anatomic range of motion and translation at the index levels out to 24 months. Thus, less incidence of adjacent segment disease may be expected with DS treated with paraspinous tension as opposed to fusion. These results should be confirmed with a longer follow-up including clinical outcomes in propensity score-matched patients.
551: Verteporfin-loaded Microparticles for Treatment and Radio-sensitization of Spinal Metastatic Disease

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Introduction: Spinal metastatic disease has unique genetic drivers differing from the tumor of origin, therefore there is a need for novel targeted therapies to combat these tumors.

Methods: We assessed the efficacy of verteporfin (VP) in vitro using cyquant assays, colony formation assays (CFA), real-time PCR, western blots, and transwell migration assays in two spinal metastatic cell lines (LG6-lung to spine metastasis, RBC3-breast to spine metastasis), obtained from primary patient derived tissue. We used verteporfin-loaded microparticles (VP-MP) in vivo to assess its ability to inhibit tumorigenicity in a subcutaneous xenograft model using 64 mice.

Results: VP led to a dose dependent decrease in clonogenicity, migration, and cell proliferation via inhibition of yes associated protein (YAP) and YAP downstream effectors, Cyclin D1, CTGF, TOP2A, ANDRD1, MCL-1, FOSL2, KIF14, and KIF23. VP significantly inhibits LG6 and RBC3 clonogenicity at 0.5uM for LG6 (p=0.0248) and RBC3 (p=0.0006), with an IC50 of 3.26uM and 5.39uM, respectively. VP results in a decrease in cell migration at 3uM (p=<0.0001) and 5uM (p=<0.0001). Radiation after VP pretreatment led to significantly decreased clonogenicity in LG6 with 0.1 uM of VP (p=<0.0001) and RBC3 with 0.25uM of VP (p=0.0123). Linear regression curves show radiation and VP have a significantly greater cell killing capacity than VP alone for LG6 (p=<0.0001) and RBC3 (p=<0.0001). YAP knockdown results in significantly diminished protein expression of cyclin D1 (p=0.0031), decreased gene expression of CTGF (p=0.0006) and ANKRD1 (p=0.0082), and decreased cell migration (p=<0.0001). Both systemic intraperitoneal VP (p=0.0481) and VP-MP (p=<0.0001) resulted in significantly diminished in vivo tumor growth when compared to vehicle and vehicle microparticles.

Conclusion: Targeted therapy with VP mediated inhibition of the YAP regulatory axis leads to diminished clonogenicity, migration, cell proliferation, and increased radiosensitization of spinal metastatic tumor cells in vitro. Both VP and VP-MP significantly diminish tumor growth in vivo.
552: Determining Timeframe of Maximum Clinical Improvement in Surgical Decompression for Cervical Spondylotic Myelopathy When Stratified by Preoperative Myelopathy Severity

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Introduction: While surgical decompression is an important treatment modality for cervical spondylotic myelopathy (CSM), it remains unclear if severity of preoperative myelopathy status affects potential benefit from surgical intervention, and when maximum postoperative improvement is expected.

Methods: This was a retrospective analysis of prospectively collected patient reported outcomes (PROs). 1,151 patients with CSM were enrolled in the Quality Outcomes Database at 14 U.S. hospitals. Baseline demographics and pre- and postoperative PROs at baseline, 3- and 12-months were collected. These included the modified Japanese Orthopedic Association (mJOA) score, Neck Disability Index (NDI), Quality Adjusted Life Years from the EQ-5D (QALYs), and visual analog scale from the EQ-5D (Eq-VAS). Preoperative myelopathy severity was defined using established criteria from the AOSpine study group: mild (mJOA = 15-17), moderate (mJOA = 12-14), or severe (mJOA < 12).

Results: For NDI, Eq-VAS, and QALY, patients in all myelopathy cohorts achieved significant, maximal improvement at 3-months, without further improvement at 12-months. For mJOA, moderate and severe myelopathy groups demonstrated significant, maximal improvement at 3-months, without further improvement at 12-months. The mild myelopathy group did not demonstrate significant change in mJOA, but did maintain and achieve higher PRO scores overall when compared to more advanced myelopathy cohorts.

Conclusion: Patients with moderate and severe myelopathy experience maximal improvement in their pain, disability, and quality of life following cervical decompression by 3-months postoperatively. Patients with mild myelopathy improve in all PROs at 3-months except mJOA score, evaluation of which may be constrained by both ceiling effect of mJOA score and/or the 12-month time limitation of this study. Interestingly, the mild myelopathy cohort was theoretically able to maintain baseline higher functional status from operative intervention when compared to more advanced myelopathy states. The data presented here will aid surgeons in patient selection, preoperative counseling, and expected postoperative time courses.
The Comparison of Deep Learning and Classical Machine Learning Algorithms to Predict Post-operative Outcomes for Anterior Cervical Discectomy and Fusion Procedures with State-of-the-art Performance

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Introduction: Anterior cervical discectomy and fusion (ACDF) is among the most common surgical interventions to treat cervical spine disorders. Due to its popularity, it is critical to predict unfavorable post-operative outcomes to optimize surgical decision-making and pre-operative planning. In the present study, several machine learning algorithms were applied to a large, national ACDF database to predict 90-day post-operative complications, 90-day readmission, and 2-year reoperation.

Methods: The Thomson Reuters MarketScan Commercial Claims and Encounters Database and Medicare Supplement were queried from 2007-2016 to identify adult patients who underwent an ACDF procedure (N=178,816). Traditional machine learning algorithms: logistic regression, SVM (radial basis function), SVM (polynomial), were compared with deep neural networks (DNN). We generated 217 DNNs with randomly built architectures and trained them on the 90-day complication task to approximate an upper bound. Lastly, we investigated meaningful input variables by considering the gradient of the DNN predictions with respect to each input variable for the prediction of 90-day post-operative complications in ACDF.

Results: DNN achieved AUCs of 0.823, 0.713, and 0.671 for 90-day post-operative complications, 90-day readmission, and 2-year reoperation, respectively. Logistic regression achieved AUCs of 0.820, 0.712, and 0.671. SVM approaches were significantly lower. The upper bound of deep learning performance was approximated as 0.832. Gradients with respect to myelopathy, metastatic cancer, and stiffness were the most positive. Gradients with respect to 1-2 level fusion, weakness, and geographic region were the most negative. Gradients for biomechanical cage use and 3+ level arthrodesis were centered around 0.

Conclusion: Using DNNs, we achieved the highest AUC to date for the prediction of post-operative complications among the ACDF population; the model may have a role in clinical prognostication after multi-center validation. The results also suggest limited added knowledge exists in interactions between the input variables used. Future work should identify novel variables that may increase predictive power.
554: 6-month Outcomes for Patients Undergoing Posterior vs Circumferential Surgical Approach for Isthmic Spondylolisthesis

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Introduction: There is no consensus on the optimal surgical approach in treating isthmic spondylolisthesis (IS). Both posterior and circumferential surgical approaches are used.

Methods: Prospective, multicenter; observational, comparative study of surgically naïve patients with IS grade I-III at a single level between L4 and S1. Subjects between 18 and 80 years of age, enrolled at one of 12 sites in North America. Followed for 2-years. Patients with significant scoliosis or cauda equina syndrome are excluded. Interim analysis compares 6-month follow-up outcomes between posterior and circumferential surgical approaches.

Results: So far, 161 patients have been enrolled (115 posterior and 46 circumferential). Majority of patients were operated at L5/S1 (74.6% posterior and 95.7% circumferential). Six-month data is available for 112/126 subjects (84 posterior and 28 circumferential). Currently, there are no differences in age, race, gender, or the baseline score values between the groups. There has been an improvement in all endpoints in both groups. While pain outcomes trend better in the circumferential group and EQ-5D scores in the posterior group, neither of these is significant. There are no differences between the posterior and circumferential groups in change in Oswestry Disability Index (ODI) (20.0 and 15.5 respectively, p = 0.2277); lumbar pain (2.6 and 3.0 respectively, p = 0.5817); buttocks and leg pain (3.1 and 3.5 respectively, p = 0.4701); EQ-5D Index (0.23 and 0.14 respectively, p = 0.098); SF-36 Physical Component Score (PCS) (10.7 and 11.3 respectively, p = 0.7347); and SF-36 Mental Component Score (MCS) (7.0 and 3.4 respectively, p = 0.1855).

Conclusion: Patients in both treatment groups have improved in quality of life, pain, and functional outcomes. The extent of improvement is clinically meaningful. There are no differences in outcomes between the posterior and circumferential surgical approaches; however, this is an ongoing study and the current sample size is insufficient to provide confirmatory evidence.
555: Preoperative Insomnia on Poor Postoperative Pain Control After Elective Spine Surgery and the Modified CAPPS Score

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Introduction: Poor pain control after spine surgery is common. The Calgary Postoperative Pain after Spine Surgery (CAPPS) score was developed to identify this subset of patients to allow for optimization of care. Insomnia is prevalent, but its impact on postoperative pain is unknown. The objectives of this study were to examine the relationship between preoperative insomnia and poor postoperative pain control and to update the CAPPS score to improve the prediction of pain.

Methods: In this prospective cohort study, poor postoperative pain control was defined as the mean numeric rating scale (NRS) for pain>4 at rest in the first 24-hours after surgery. Patients were scored using the CAPPS score which included seven prognostic factors: age<70 years, female sex, daily use of opioid medication, preoperative axial neck or low back pain>7 on NRS, patient-health questionnaire-9 depression score≥10, ≥3 motion segment surgery, and fusion surgery. A multivariable model was created to investigate the association between Insomnia Severity Index (ISI) and poor pain control after adjusting for the CAPPS score. The model was then transformed to create the Modified CAPPS score.

Results: Of 219 patients, 49.7% experienced poorly controlled pain. The prevalence of clinical insomnia (ISI≥15) was 26.9%. Preoperative ISI was independently associated with poor pain control (OR 1.09, p=0.004) after adjusting for the CAPPS score (OR 1.61, p<0.001). The model was discriminative (AUC 0.80) and calibrated (Hosmer-Lemeshow p=0.35). The Modified CAPPS score retained discrimination (AUC 0.78) and calibration (Hosmer-Lemeshow p=0.57). Low-, high-, and extreme-risk groups stratified by the Modified CAPPS score had 17.3%, 49.1%, and 80.7% predicted probability of experiencing poorly controlled pain compared to 32.0%, 64.0% and 85.1% in the original CAPPS score.

Conclusion: Preoperative insomnia is common and is a novel modifiable risk factor for poor pain control after spine surgery. Preoperative detection and optimization of insomnia may lead to improved pain outcomes.
Return to Work, Activities of Daily Living and Disability Improvement: 12-month Outcomes of an FDA IDE Trial of Decompression and Tension Band Stabilization for Degenerative Spondylolisthesis

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Introduction: Degenerative spondylolisthesis (DS) symptoms may be relieved with surgical decompression, however the addition of instrumented fusion is usually considered essential to achieve durable results. A novel interspinous tension band is proposed for segmental stabilization after decompression for DS, as an alternative to lumbar fusion. An ongoing FDA IDE study (NCT03115983) is comparing decompression and stabilization with the tension band (D+TB) to decompression and instrumented fusion (D+F) for symptomatic DS.

Methods: Prospectively enrolled subjects ≥12 months postoperative were included. Study records were queried for work status preoperatively and at 12 months, as well as time to return to work (RTW), activities of daily living (ADL) and change in disability (Oswestry Disability Index; ODI) at 12 months vs preop.

Results: 246 subjects (140 D+TB, 106 D+F) ≥12m postoperative were included in this analysis. Preoperatively, 50% of D+TB and 39% of D+F subjects were working, while 7% D+TB and 12% D+F were not working due to their spinal condition. At 12 months, 45% of D+TB and 34% of D+F subjects were working, while 2% D+TB and 13% D+F were not working due to their spinal condition, with a significant reduction for the D+TB group (p=0.04). Mean±SD RTW time for D+TB/D+F subjects was 5.3±6.6/13.6±11.7 weeks, while return to ADL time was 5.4±6.4/13.8±18.8 weeks (both p<0.01). Mean±SD reduction in disability at 12 months from baseline was 38.3±18.2 for the D+TB group and 33.0±21.8 for the D+F group (p=0.06) with effect sizes of -2.1 and -1.5, respectively.

Conclusion: These results indicate a significant advantage of faster recovery for the D+TB group allowing faster RTW and ADL compared to D+F, with similar improvements in disability after one year for patients treated with decompression and stabilization for symptomatic DS. These results should be confirmed with longer-term follow-up of propensity score-selected subjects to demonstrate whether this advantage and long-term outcomes are durable.
557: Assessing Pre-operative Functional Decline in Lumbar Fusion and Lumbar Decompression Patients Through Smartphone-based Accelerometry

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Introduction: Treatment of degenerative lumbar spinal pathologies typically escalates to surgical intervention when symptoms begin to significantly impair functional activity. Currently, surgeons rely on subjective patient assessment to estimate decline in patient wellness and quality of life as well as track their recovery. In this paper, we use smartphone-based accelerometer data to provide an objective, continuous measurement of physical activity that can aid in characterizing pre-operative functional decline.

Methods: One year of pre-operative activity data (steps-per-day) from 16 endoscopic lumbar fusion (LF) and 14 lumbar decompression (LD) patients was retrospectively extracted from patient smartphones. A data-driven algorithm was constructed to identify and characterize functional decline preceding surgical intervention. Estimated onset of functional decline was compared to clinical notes in patients who presented with acute decline (< 6 months of symptoms), chronic decline (≥ 6 months of symptoms), or acute-on-chronic decline (< 6 months of novel, worsening symptoms in addition to ≥ 6 months of chronic symptoms).

Results: LD patient data classified acute and chronic decline with 100% accuracy and acute-on-chronic decline with 75% accuracy when validated against the patient’s clinical history. Acute decline onset was predicted 4.8 ± 6.5 weeks before the reported onset of symptoms in clinical documentation. LF patient data classified acute and acute-on-chronic decline with 100% accuracy and chronic decline with 7.14% accuracy. Acute decline onset was predicted 23.9 ± 26.9 weeks after reported symptom onset.

Conclusion: Accelerometer data predicted acute decline more accurately in LD than in LF patients, likely due to the limited length of pre-operative activity data and our algorithm’s low threshold for detecting acute reduction in activity. This preliminary study highlights the potential of using smartphone-based accelerometer data to detect patients’ symptom onset and decline in functional status easily, effectively, and accurately to enable earlier surgical intervention.