Monday's Abstracts

Paper 1 *(DOI: 10.3171/2014.1.PEDSpaper1)*
Origins of the ASPN, the American Board of Pediatric Neurosurgery, and the Specialty of Pediatric Neurosurgery: A Behind the Scenes Look

Marion Walker, M.D.

Introduction: The origins of pediatric neurosurgery as a distinct subspecialty began in earnest in the early 1970s. A desire to recognize pediatric neurosurgery led to the organization of the American Society of Pediatric Neurosurgeons (ASPN), a pediatric neurosurgery journal, the American Board of Pediatric Neurosurgery (ABPNS), and the development of fellowship training programs. This presentation looks at original documents saved from this period to portray a candid and behind the scenes look at the struggles to create the subspecialty we now enjoy.

Methods: Original documents from the era of the early origins of pediatric neurosurgery were reviewed. These documents include original bylaws of the ASPN, letters exchanged between early pediatric neurosurgery leaders and the American Board of Neurosurgery (ABNS), the RRC, and significant adult neurosurgery leaders. Original bylaws of the ABPNS and the Accreditation Council for Pediatric Neurosurgical Fellowships (ACPNF) were reviewed.

Results: Pediatric neurosurgery has been well established as a subspecialty of neurosurgery thanks to the untiring efforts of our early leadership. Creation of the ABPNS and the ACPNF has resulted in establishment of appropriate training and certification of pediatric neurosurgeons.

Conclusions: Pediatric neurosurgery is now a well recognized subspecialty of neurosurgery. Many pediatric hospitals require ABPNS certification to obtain full privileges.

Paper 2 *(DOI: 10.3171/2014.1.PEDSpaper2)*
Bibliometrics for Pediatric Neurosurgeons in North America

Paul Klimo Jr., M.D., MPH, Garrett T. Venable, B.Sc., Nickalus Khan, M.D., Frederick A. Boop, M.D.

Introduction: Bibliometrics is defined as the study of statistical and mathematical methods used to quantitatively analyze scientific literature. The application of bibliometrics in neurosurgery is growing. The authors calculate a number of publication productivity measures for nearly all pediatric neurosurgeons in North America.

Methods: A bibliometric profile consisting of the h-index, g-index, m-quotient, contemporary (hc) h-index, and e-index was calculated for 284 pediatric neurosurgeons. Descriptive statistics were calculated for the group as a whole; comparisons were based on academic rank (chairman, professor, associate, assistant & instructor) and gender. Departments that had an accredited fellowship program were ranked based on several productivity metrics. Calculations were carried out in August/September 2013.

Results: There were 245 male and 39 female pediatric neurosurgeons. The median h-index, g-index, m-quotient, hc-index, and e-index are 12, 22, 8, and 21, respectively, with positively skewed distributions. All indices demonstrated a positive relationship with increasing academic rank. When comparing gender, all productivity metrics were statistically higher in males, including the e-index, which measures excess citations. Based on the cumulative h-index, the top 5 programs for publication productivity are: Harvard, University of Toronto, Northwestern University, University of Washington (Seattle) and Washington University (St. Louis). Further analysis is currently underway for both gender and programs.

Conclusion: This study represents the most detailed publication analysis of pediatric neurosurgeons and their programs to date. The results for the metrics presented should be viewed as academic benchmarks for comparison purposes. Departmental metrics should be made readily available to prospective fellow candidates to assist them when choosing which programs to apply to.

Paper 3 *(DOI: 10.3171/2014.1.PEDSpaper3)*
Should American Pediatric Neurosurgery Embrace Infolded Fellowships?

Frederick A. Boop, M.D.

Organized pediatric neurosurgery has been at the forefront of the sub-specialization movement for twenty years. The development of the ABPNS, the ACPNF and a re-certification process have served neurosurgery as the model for other areas of subspecialization. At present, though not an ABMS recognized subspecialty Board, the ABPNS credential has become recognized by both third party payers and by children's hospital credentialing committees nationally.

Recently the ABNS and the Society of Neurological Surgeons have voiced strong support for infolded subspecialty fellowship training in neurosurgery as part of the mandatory 7 year residency. NCAST, the credentialing committee for subspecialty training, has deferred to each Joint Section regarding the decision to accept infolded fellowships or not. This author will review the current status of the physician workforce shortage, GME funding issues, including HR 1852-The Children's Hospital GME Support Re-authorization Act of 2011, offer an assessment of the current pediatric neurosurgery workforce and will discuss the implications of infolded pediatric neurosurgery fellowship training vs post-residency training as it currently exists.

Paper 4 *(DOI: 10.3171/2014.1.PEDSpaper4)*
Impact of Surgeon Experience on Outcomes of Craniopharyngioma Resection in Children: A Single Surgeon Experience of 116 Surgeries

Jeffrey H. Wisoff, M.D., Tracy Ma, B.A., Omar Tanweer, M.D., Jessica Wisoff, M.A., Luigi Bassani, M.D., Robert E. Elliott, M.D.

Introduction: Preliminary evidence suggests a correlation between surgeon experience and improved oncological and functional outcomes in children with craniopharyngiomas.

Methods: We retrospectively analyzed the records of 99 consecutive children (40 females/59 males; mean age: 9.7 years) who underwent a total of 116 attempted radical resections by a single surgeon. Functional status before and after surgery was assessed using the Craniopharyngioma Clinical Status Scale (CCSS). Dividing the cases into quartiles of 29 surgeries, regression analysis was used to assess the impact of surgeon experience on extent of resection and complications.

Results: All primary tumors were completely removed and the mean rate of complete resection for recurrent tumors was 60.8%. Preoperative COS scores predicted postoperative outcome better than clinical characteristics like patient age, sex, tumor size, location or presence of hydrocephalus. Controlling for differences between groups, multivariate regression analysis revealed increasing surgeon experience to be correlated with less deterioration in neurological, hypothalamic and cognitive functioning at latest follow-up. There was no impact on pituitary or visual outcomes. Likelihood of recurrence appeared to decrease over time.

Conclusions: The surgical philosophy of attempted radical resection did not change during the 25-year experience as evidenced by the stable extent of resection over time. Preoperative CCSS scores predicted outcome more highly than clinical or imaging characteristics. However, increasing surgeon experience with craniopharyngioma resection correlated with improved neurological, hypothalamic and cognitive outcomes. Such data support the notion of early referral of children with craniopharyngiomas to centers with high volume.

Paper 5 *(DOI: 10.3171/2014.1.PEDSpaper5)*
Natural History of Subependymal Giant-Cell Astrocytomas in Childhood: A Radiographic Survey

Kurtis Auguste, M.D.

Introduction: Subependymal giant cell astrocytomas (SEGAs) are tumors commonly found in the lateral ventricles of children with Tuberous Sclerosis. Though frequently quiescent or slow-growing, a small percentage of these lesions can progress and their location can impact the outflow of cerebrospinal fluid. This study analyzed a series of SEGAs with the goal of identifying potential characteristics which may predict progression or need for surgical resection.

Methods: We conducted a retrospective review of medical records and serial brain magnetic resonance images (MRIs) in 52 Tuberous Sclerosis patients less than 18 years of age who carried a diagnosis of SEGA. We measured SEGA dimensions at each interval time point and documented the patient's clinical status, including signs or symptoms of obstructive hydrocephalus. We also documented tumors which progressed and studied the patients who went on to surgical resection. To calculate volume, the formula ½ AxBxC was used where the A and B measurements were gathered in the axial plane and either the sagittal or coronal plane was used for C depending on the orientation of the mass.

Results: A total of 52 SEGA patients were identified, 29 of which had serial MRIs and were included in this study. There were 16 male and 13 female patients. Mean age at first MRI scan was 116 months or 9.7 years (range: 6 months to 17years). The average number of MRIs per patient was 4.8 and the average interval in between scans was 12.3 months (range 1 to 84 months). 17.2% (4/29) of these lesions showed significant progression over time. 10.3% (2/29) of patients required surgical resection of their SEGAs due to rapid increase in size and obstructive hydrocephalus. The lesions which were most likely to progress and become surgical were more often attached anterior to the foramen of Munro. Of the lesions that required surgery, each demonstrated sudden, rapid increases in size after many years of static behavior. There did not appear to be a critical tumor volume predictive of warranting surgery.

Conclusions: The majority of patients with SEGAs harbor lesions that remain static and do not progress. A small percentage progress and half of those lesions required surgery. An anterior attachment of the lesion may predispose these tumors to a need for intervention. SEGAs requiring surgery increased rapidly after many years without change suggesting a possible genetic 'trigger' for growth. Because of this potential, regular interval imaging during childhood should remain standard of care.

Paper 6 *(DOI: 10.3171/2014.1.PEDSpaper6)*
Effect of ReOperation(s) on Recurrent Glioblastoma in Pediatric Patients

Rupal Parikh, B.S., Tong Yang, M.D., Stephania DaSilva, B.A., Floyd H. Gilles, M.D., Jonathan L. Finlay, M.D., J. Gordon McComb, M.D., Mark D. Krieger, M.D.

Introduction: Glioblastoma carries a poor prognosis in pediatric patients. Debate exists as to the efficacy of second surgery at the time of progression or recurrence. This study aims to evaluate the effect of repeat surgery for recurrent glioblastoma.

Methods: An IRB-approved retrospective analysis was performed on all children treated for pathologically confirmed glioblastoma at a single institution between 1986 and 2013.

Results: 45 children (21 female) were identified. The median age at time of presentation was 9 (range 0–20) years. Median duration of follow-up was 14 (range 0–232) months. Patients who underwent gross total resection (GTR, 16/45) had a median OS and PFS of 87 (range 43–131) and 42 (range 0.0–108) months, respectively, whereas patients who underwent subtotal resection (STR) or biopsy (Bx) had a median OS and PFS of 16 (range 11–22) and 4 (range 2–6) months, respectively ($p = 0.03$, and $p = 0.023$, respectively). 36 patients had radiographically confirmed progression or recurrence within the study period with a median time to recurrence of 4 months. 19/36 patients had re-operations: 12 patients had 2 resections, 4 patients had 3 resections, 2 patients had 2 resections, and 1 patient had 7 resections. Patients who underwent reoperation upon recurrence had a median survival from time of recurrence of 14 (range 1–28) months and patients who did not undergo reoperation upon recurrence had a median survival from date of recurrence of 10 (range 1–19) months, ($p = 0.014$). In multivariate analysis, accounting for age, gender, tumor location, EOR, chemotherapy, and radiation, re-operation upon recurrence was found to be significantly associated with increased survival from date of recurrence ($p = 0.017$, $n = 33$).

Conclusions: EOR is significantly associated with increased OS and PFS. Re-resection upon recurrence of glioblastoma is associated with increased overall survival. Age at time of primary resection and gender were not found to be significant prognostic factors in patients with recurrent glioblastoma.

Paper 7 *(DOI: 10.3171/2014.1.PEDSpaper7)*
Combined Anterior and Posterior Approach Vertebroplasty for an 11 Year Old Patient with an Axis Osteoblastoma: A Three-Year Follow-Up

Mauricio Munoz Martinez, M.D.

Introduction: Awkward placed primary bone tumors can be challenging due to anatomical relationships. Achieving permanent results without adding further instability can be difficult being curettage and embolization the surgical choices. This is a three-year follow up after a 360º vertebroplasty on an 11 years old patient with a C2 osteoblastoma. An 11 y/o girl showed at our E.R with painful torticollis, significant myelopathic findings and irregular breathing pattern. CT bone scan and MRI showed a C2 tumor causing a 360º compression of the upper medulla.

Methods: Posterior dural decompression was performed upon arrival reporting benign osteoblastoma. Through an open anterior cervical approach and using biplanar fluoroscopy, a 14 G needle was introduced at C5 level and advanced to the tip of the odontoid. A vertebroplasty of odontoid with PMM and $BaSo_4$ was carried out. A third procedure delivered cement to the posterior arches. VAS pain scale, neck CT and an inclinometer were used during follow up.

Results: Total motor recovery and functional painless head rotation, flexion and extension was recovered after surgery. After 36 months follow up there is no tumor relapse nor neck deformity despite the child's normal growth. Posterior fixation wasn't needed.

Conclusion: Although transoral odontoid vertebroplasty has been described to be an effective procedure in adults. Anterior cervical approaches are much rare and no cases are reported in pediatrics. By delivering PMM inside the anterior and posterior elements of C2 through a combined approach, the tumor is embolized and the craniocervical junction remains stable.

Paper 8 *(DOI: 10.3171/2014.1.PEDSpaper8)*
MR Imaging for Distribution Assessments in Children Undergoing Direct Drug Delivery in the Brain Stem

Kyung Peck, Zhiping Zhou, Ranjodh Singh, Mark M. Souweidane, M.D.

Introduction: Methodologies for measuring drug distribution during treatment with convection-enhanced delivery (CED) are not established. Standard MR sequences without contrast administration would provide a noninvasive and safe platform for monitoring distribution during CED. The purpose of this study is to introduce a method to measure volume of distribution using non-linear regres-

sion (NLR) analysis that employs real-time infusion volume as a model parameter.

Methods: MR imaging was used to monitor changes in the brain stem during CED treatment for diffuse intrinsic pontine glioma (DIPG). T2-weighted imaging was performed before and during infusions at different intervals to determine the relationship between volume of distribution (Vd) and the volume of infusion (Vi). A NLR analysis employing real-time infusion volumes measured at each infusion time point and T2 signal intensity was performed to measure Vd_{NLR}, and determined a localized mask. These measurements were compared to Vd_{SAS} obtained from semi-automated segmentation (SAS).

Results: In all cases dynamic changes were seen in the Vd during infusion. The Vd/Vi ratio appears to be linear. The results show that R^2 (a measure of the goodness of fit) obtained from Vd_{NLR} /Vi is higher than that obtained from Vd_{SAS} /Vi for all cases.

Conclusions: Standard, non-contrast MR imaging can be used to assess important parameters during CED treatment for children with DIPG. A NLR method using real-time infusion volume can be used to localize voxels sensitive to the changes over time and generate a mask more sensitive to the signal intensity increase. This methodology can be implemented into ongoing and future clinical trials that employ CED in the brain stem.

Paper 9 *(DOI: 10.3171/2014.1.PEDSpaper9)*

Late Recurrence of Dysembryoplastic Neuroepithelial Tumors

Mark Fedor, M.D.

Introduction: Dysembryoplastic neuroepithelial tumors (DNETs) are considered benign WHO Grade I lesions. Patients commonly present with seizures. Surgical resection is presumed to be curative with very few recurrences described in the literature. However, with long term MRI follow-up, the appearance of new ring-enhancing areas many years after the original surgery is being increasingly reported.

Methods: Case report with literature review of "recurrent dysembryoplastic neuroepithelial tumor."

Results: We present an 11 year old boy who underwent resection of a left temporal DNET at 2 years of age. He was followed with serial MRI scans which were all stable until 9 years later when a new ring enhancing area was found at the edge of the resection cavity. He underwent another operation for removal of this region. Pathology found it to be DNET as before. There are 15 other cases in the literature which report DNET recurrence. Many describe this type of new contrast enhancement on MRI. However, transformation to a higher-grade tumor was rare and associated with previous radiation therapy.

Conclusion: Our case agrees with the previously described reports of DNET recurrence. Although the appearance of a new ring enhancing lesion seems worrisome radiographically, malignant transformation is extremely rare in the absence of radiation therapy. Interestingly however, MRI imaging does reveal a more dynamic natural history to DNETs and argues for continued long-term follow-up.

Tuesday's Abstracts

Paper 10 *(DOI: 10.3171/2014.1.PEDSpaper10)*

Development of an Synthetic Simulator for Neuroendoscopy – Validation and Performance Assessment. Will you have to "Fly" it to Maintain Competence?

James Drake, M.D., Gerben Breimer, Faizal Haji, Vivek Bodani, Thomas Looi

Introduction: Neuroendoscopic procedures are ideal for simulation as they are technically demanding with significant risk. We have constructed a realistic low cost, reusable brain simulator for Endoscopic Third Ventriculostomy (ETV) and evaluated it for fidelity. We have also developed a procedural checklist and global rating scale (GRS) to standardize training and evaluation.

Methods: A brain silicone replica including choroid plexus, veins, mamillary bodies, infundibular recess, basilar artery and synthetic skull was immersed in water. Standard neuro-endoscopic equipment was used. A thinned out third ventricle floor dissects appropriately and is quickly replaceable. Fidelity was scored by 16 neurosurgical trainees (PGY 1-6) and 9 pediatric and adult neurosurgeons. A procedural checklist was created including Setup, Exposure, Navigation, Ventriculostomy, and Closure, Errors and GRS. Twenty international experts were invited to participate in an electronic Delphi survey, to establish content validity.

Results: The simulator is portable, robust, and sets up in minutes. Over 95 % of participants agreed or strongly agreed that the simulator's anatomical features, tissue properties and bleeding scenarios were realistic. Participants stated the simulator developed required hand-eye coordination and camera skills. Seventeen experts graded each ETV step, error and GRS with a rapidly emerging consensus on content.

Conclusions: A low-cost reusable silicone-based ETV simulator realistically represents the surgical procedure to trainees and neurosurgeons. It can develop the technical and cognitive skills for ETV including complications. The assessment tools will be incorporated into the teaching and evaluation process for standardization, and potentially certification.

Paper 11 *(DOI: 10.3171/2014.1.PEDSpaper11)*

"The Revolution Reservoir:" A CSF Shunt System that Prevents Proximal Obstruction by Autonomous Catheter Rotation

Matthew D. Smyth, M.D., Chester Yarbrough, M.D., Richard Marcus, Sam Stone, Michael Winek, Devon Haydon, M.D., Guy Genin, Ph.D., Eric Leuthardt, M.D.

Introduction: Proximal shunt obstruction rates remain high, accounting for the majority of CSF shunt malfunctions, and posing a significant burden to patients and limited health care resources. A shunt system that translates patient movement into catheter rotation, *in situ*, may reduce the rate of proximal obstruction caused by tissue and choroid plexus ingrowth.

Methods: A group of neurosurgeons and engineers have collaborated to create a working prototype of the device which has the capability of shunting CSF, while rotating, using kinetic motion of the subject to drive the rotational movement.

Results: Successful bench-top and large animal (swine) tests will be presented. A cost-benefit analysis will also be discussed.

Conclusion: A shunt device that incorporates active rotation of the catheter tip may reduce tissue ingrowth and shunt obstruction, and may lower the shunt malfunction rate. The introduction of a novel shunt component (compatible with existing shunt hardware) that reduces obstruction rates would revolutionize the management of hydrocephalus.

Paper 12 *(DOI: 10.3171/2014.1.PEDSpaper12)*

MRI Time-Spatial Labeling Inversion Pulse (Time-Slip) Findings to Support Possible Cerebrospinal Fluid (CSF) Olfactory Drainage in Humans

Shinya Yamada, M.D., Ph.D., Mitsue Miyazaki, Ph.D., Cheng Ouyang, Ph.D., Robert Anderson, R.T., William G. Bradley, M.D., Ph.D., J. Gordon McComb, M.D.

Introduction: The traditional concept of CSF circulation is that CSF is produced in the ventricles by the choroid plexus, exits the 4th ventricle via the foramina of Magendie & Luschka, enters the subarachnoid space to drain into the blood stream through the arachnoid granulations at the superior sagittal sinus (SSS). Previous animal experiments, including primates, have called this circulation

pathway into question. Until now there has been no way to non-invasively visualize CSF movement in the normal human subject. Using a newly developed modification of arterial spin labeling, time-SLIP, such observations are now possible.

Methods: Healthy normal volunteers underwent a non-contrast MRI of the head using the time-SLIP technique on a Toshiba 3T scanner.

Results: CSF movement was noted at the cranial base, especially in the cribriform plate region at inversion times of 1500-4500 msec after pulse labeling CSF in the region of interest. Little such movement was seen over the convexity, particularly near the SSS.

Conclusion: These observations raise the possibility that more or most CSF is draining at the cranial base in preference to the SSS.

Paper 13 *(DOI: 10.3171/2014.1.PEDSpaper13)*
Ventriculoperitoneal Shunt Infection Rates: Implementation of a Uniform Protocol and Evaluation of Outcomes

Eric R. Trumble, M.D., Matt P. Diehl, PA-c, MPAS, and James Baumgartner, M.D.

Introduction: The Patient Protection and Affordable Care Act (ACA) has provisions to take effect in 2014 that will require hospitals (and over time, most physicians, to participate in Accountable Care Organizations. Florida Hospital is the largest provider of government paid (Medicare and Medicaid) neurosurgical services in the nation. As such, Florida Hospital has begun implementation of treatment protocols for the disease processes most commonly cited as outcome parameters by the federal government (Centers for Medicare & Medicaid Services). Implementation of these protocols were initiated as part of EMR and CPOE implementation via Cerner. Focus has been on general diagnoses, e.g. ventilator associated pneumonia (VAP), catheter associated infections (urinary and blood borne), and unintended return to surgery. Each sub-specialty within the hospital has been tasked to provide at least 1 protocol to follow and show outcomes within the top 25%of the nation (allowing additional Medicare funds to be reimbursed beginning in 2014). In pediatric neurosurgery, the protocol designed was for ventriculo-peritoneal shunt implants and the outcome assessed was ventriculo-peritoneal shunt infection.

Method: A single surgeon covering the third largest NICU in the United States (with greater than 1200 discharges in 2006) prospectively gathered data on all shunt implants using a standardized surgical protocol. The protocol consisted of: 1. Minimizing surgical personnel in the OR (<4 is preferred) 2. Eliminating the use of a surgical assistant 3. Minimizing surgical time (<15 minutes is preferred) 4. Using unitized anti-biotic impregnated shunts 5. Minimizing use of programmable valves 6. Performing shunts with neuro trained team 7. Performing shunt as first case of day in terminally cleaned room.

Results: The infection rate dropped from 20.6% in 2003 to 1.8% in 2006. The only infection in 2006 was in a patient with greater than 100 previous shunt operations whose skin broke down and she developed a candidal shunt infection. The ventriculoperitoneal shunt infection rate in the practice has remained <2% since 2003.

Conclusions: With stringent adherence to the strict protocol utilized in this study, less than 2% ventriculoperitoneal shunt infection rate is an attainable goal. Pediatric neurosurgeons need to be at the forefront for the creation of protocols to assist in standardization of care in an effort to minimize patient complications.

Paper 14 *(DOI: 10.3171/2014.1.PEDSpaper14)*
Surgery for Obstructive Non-Tumoral Posterior Fossa Problems

Bermans J. Iskandar, M.D.

Introduction: Safe treatment of obstructive, non-tumoral, pathologies in the cerebral aqueduct and fourth ventricle faces serious challenges owing to difficulties in maintaining fourth ventricular shunt patency, a predisposition to form complex adhesions, and risk of brainstem injury.

Methods: We present our 15-year experience in treating aqueductal and fourth ventricular obstructions that are unrelated to tumor or vascular pathology, using a multi-modality approach of microsurgical and endoscopic surgery.

Results: 95 surgical interventions were reviewed. Symptoms of bulbar and sensorimotor dysfunction were related to ventricular dilatation in some, and tethering of brainstem or cerebellar tissue in others. Pathologies included membranous and/or focal aqueductal obstruction proven or presumed to be infectious/inflammatory in origin; fourth ventricular entrapment; adhesions from chronic shunting with/without retained ventricular catheters; inability to maintain fourth ventricular shunt patency; and postoperative adhesions after tumor or Chiari surgery. A primary endoscopic approach was used in 42 cases, and microsurgery with or without endoscopic assistance in 53 cases. Clinical and radiographic goals were achieved in >90% of patients with acceptable morbidity. Challenges specific to the posterior fossa and aqueduct including adhesions and the tangible risk of brainstem injury will be described.

Conclusions: Surgery on obstructive posterior fossa and aqueductal lesions is challenging. This is especially true in the setting of complex postoperative adhesions. We describe our long-term experience with these cases using a combination endoscopic/microsurgical approach. Long-term success is likely to be maintained when CSF flow is re-established in the absence of a CSF shunt, thus improving on the typically disappointing natural history of these disorders.

Paper 15 *(DOI: 10.3171/2014.1.PEDSpaper15)*
Is Lumbar Puncture a Reliable Measure of Intracranial Pressure?

Christian B. Kaufman, M.D., Cathy C. Cartwright, R.N., Usiakimi Igbaseimokumo, M.D., Gregory W. Hornig, M.D.

Introduction: A lumbar puncture as a means of measuring intracranial pressure (ICP) is susceptible to artificial elevations. A study was carried out to investigate the reliability of lumbar puncture when compared to intracranial pressure monitor for elective evaluation of suspected intracranial hypertension.

Methods: All patients who had both a lumbar puncture and ICP monitor were reviewed over a three year period. Demographic data and indication for the ICP monitor placement including clinical features, primary diagnosis and the lumbar puncture pressures and the intracranial pressure monitor pressures were collected and analyzed for this study. ICP monitoring was performed for a minimum of 24 hours to gather longitudinal data to include various physiologic states and patient positions.

Results: There were 13 children (7 females: 6 males) aged 2–19 years (mean 10.8 years). The primary diagnosis was craniosynostosis in 8 patients, hydrocephalus in 4 patients and pseudotumor in 1 patient. All patients had headache and one child had papilledema; all had elevated CSF pressures from initial LP measurements. The mean ICP measured by lumbar puncture was 23 mmHg (range 18-33) independent of position during lumbar puncture (LP) or sedation administered for the LP. The mean ICP as measured with the ICP monitor was 7 mmHg (mean range 3-12, $p < 0.001$). The proposed surgical intervention was avoided in all the patients after confirmation by ICP monitoring.

Conclusions: This study found a significant difference in the ICP measured by lumbar puncture and ICP monitor. We feel that if the presence of elevated ICP is a factor in surgical decision making, then findings of elevated ICP per lumbar puncture should be confirmed by use of ICP monitoring in the evaluation of possible chronically raised intracranial.

Paper 16 *(DOI: 10.3171/2014.1.PEDSpaper16)*
Management of Pediatric Arteriovenous Malformations: Multimodality Approaches

Saadi Ghatan, M.D., Alexander Dash, Rahul Parikh, M.D., David S. Gordon, M.D., Alex Berenstein, M.D.

Introduction: The definition of optimal management paradigms for AVMs is imperative in children, since they carry a high cumulative lifetime risk of hemorrhage and catastrophic neurological injury. While AVMs are responsible for almost half of all spontaneous intracranial hemorrhages in children, they are also being detected with greater incidental frequency as neuroimaging becomes more commonplace, underscoring the need for rational and safe treatment guidelines.

Methods: Among over 250 pediatric AVMs, a retrospective analysis of 27 consecutive operative cases over a 10 year period (2004-2013) was undertaken at a tertiary referral center for Pediatric AVMs. VOG malformations and dural AV fistulas were excluded.

Results: AVM presentation was incidental or associated with headache and/or psychological disturbance in 12 children, while 9 others presented with seizure and 6 with hemorrhage. Eighteen patients were treated with microsurgery. In this group, there were 15 low (1-3) and 3 high grade (4,5) AVMs. Endovascular therapy was carried out in all cases, with an average of ~2 rounds of embolization, and in all cases except one, microsurgery resulted in complete obliteration of the AVM. In addition to one child with a complex AVM who had a small thalamic residual after microsurgery, another 9 children underwent SRS without or with embolization. There were 7 major but transient treatment related neurological deficits in the microsurgical group (SMA syndrome, cerebellar signs), and no evidence of AVM recurrence.

Conclusions: These data provide reassurance that multimodality intervention can mitigate the high cumulative lifetime risks facing children with AVMs, whether symptomatically or incidentally discovered.

Paper 17 *(DOI: 10.3171/2014.1.PEDSpaper17)*
Long-term Effects of Rigid Instrumentation and Fusion at the Craniovertebral Junction in Young Children

Benjamin Kennedy, Michael McDowell, Todd Hankinson, M.D., Sean Lew, M.D., Andrew Jea, M.D., Daniel Couture, M.D., Douglas Brockmeyer, M.D., and Richard C. E. Anderson, M.D. on behalf of the Pediatric Craniocervical Society

Introduction: The long-term consequences of atlantoaxial and occipitocervical fusions in young children are unknown. We present a multi-institutional study to determine the long-term effects of these surgeries on the growth and alignment of the maturing spine.

Methods: A multi-institutional retrospective chart review was conducted at five participating centers from 1995-2010. Twenty-seven patients 6 years old or younger (mean 3.4, range 1.5–6 years) who underwent OC or C1-2 rigid instrumentation and fusion with at least 3 years of clinical and radiographic follow-up were included. Preoperative, immediate postoperative, and most recent follow-up X-rays or CT scans were evaluated to assess changes in spinal growth and alignment.

Results: All patients demonstrated fusion on follow-up imaging. At a mean follow-up of 57 months, there were no cases of new sagittal malalignment, evidence of subaxial instability, or unintended subaxial fusion. The lordotic curvature of the cervical spine increased from a mean of 11 degrees postoperatively to 23 degrees at follow-up. A mean of 18% of the vertical growth of the cervical spine occurred within the fusion segment. The minimum width of the spinal canal within the fused levels grew by 0.7mm. A subgroup of 11 patients who underwent follow-up periods for longer than 60 months had similar results.

Conclusions: These longer-term follow-up results suggest that OC or C1-2 rigid instrumentation and fusion in children 6 years of age or younger does not increase risk of spinal deformity or kyphosis, subaxial instability, canal stenosis, or inhibition of growth at the instrumented levels.

Wednesday's Abstracts

Paper 18 *(DOI: 10.3171/2014.1.PEDSpaper18)*
Symptom Experience and Quality of Life in Children Following Sport-Related Head Injuries—The Concussion Research Project at Children's Hospital of Eastern Ontario

Michael Vassilyadi, M.D., Gail Macartney, Ph.D., Peter Anderson, Ph.D., Nick Barrowman, Ph.D.

Introduction: Concussion management can be challenging, particularly in children with persistent symptoms. A multidisciplinary pilot study was initiated at CHEO to determine the severity, frequency and duration of symptoms in children who have sustained a concussion while playing a sport, and their quality of life in those symptomatic greater than three months.

Methods: Symptom experience was measured using a standardized symptom inventory and the Pediatric Quality of Life Inventory (PedsQL) used. The ImPACT test was administered to screen memory, visual processing, reaction time and impulse control. Neuropsychologic consultation was arranged when necessary.

Results: There were 35 children (60% male) with a mean age of 14.9 years and 5.4 months postconcussion. Most injuries occurred in hockey, rugby or during gym or training sessions. Symptoms with the highest mean severity scores included headaches, poor concentration, dizziness and fatigue. The mean PedsQL total score was 68.5 and the ImPACT mean cognitive efficiency index was 30%. Regression analysis showed that three symptoms including depression, irritability and tinnitus explained 76% of the variance in the PedsQL scores.

Conclusion: The Concussion Research Project study at CHEO has helped optimize the assessment, management, education and follow-up of children who remain symptomatic three months following a sport related head injury. Children with persistent concussion symptoms at three months were identified to be significantly compromised with physical, cognitive and socioemotional decline. This study highlights the importance of prevention through programs such as *ThinkFirst*, and in the event of an injury the need to properly identify and manage these children.

Paper 19 *(DOI: 10.3171/2014.1.PEDSpaper19)*
Progress and Challenges in Modeling Infant Subdural Hematoma and Associated Brain Injury

Ann-Christine Duhaime, M.D., Brittany Coats, Susan Margulies, Jennifer Munoz, Declan McGuone, Colin M. Smith, Carter Dodge, Kristen Saliga, and Beth Costine

Introduction: Subdural hematoma remains a poorly understood type of brain injury early in life. In our laboratory and in those of our collaborators at two other centers, three different large animal models have been used to mimic specific features of infant subdural hematoma seen clinically. We provide an update on findings from these three models and their implications for injury mechanism and pathophysiology.

Methods: Our lab utilizes injection of intradural autologous blood combined with focal trauma, unilateral mass effect, seizures, and apnea, with the goal of modeling unilateral "big black brain" – profound damage of one hemisphere, with relative sparing of the other. Our collaborators create single, repeated, or cyclic angular rotations in the sagittal plane, modeling symmetric deceleration mechanisms. Clinical findings, serum markers, cardiac events, neuroimaging, and histopathology have been assessed.

Results: All three models demonstrate variable mixed subdu-

ral/subarachnoid hemorrhage. Recently we have been successful in reliably producing larger, primarily unilateral subdural hemorrhages by altering the order of the insults, overcoming the previously prohibitive adherence of the dural border cells to the arachnoid. Only the injection model is markedly asymmetric between hemispheres. Clinical findings, physiology, imaging, retinal findings, and neuropathology vary among models and will be described.

Conclusion: While no model to date reliably replicates all aspects of the constellation of findings seen in inflicted and accidental subdural hematoma in human children, each model offers insights into the biomechanics, pathophysiology, and associated findings in this population. These observations may have relevance to management as well as mechanism controversies in this common injury.

Paper 20 *(DOI: 10.3171/2014.1.PEDSpaper20)*
The Utility of CTA in Pediatric Cranial Trauma

Robert J. Bollo, M.D., Vijay M. Ravindra, M.D., Walavan Sivakumar, M.D., Jay Riva-Cambrin, M.D.

Introduction: Traumatic cerebrovascular injury is reported in 2% of blunt cranial trauma in adults. While CTA is frequently performed in children following cranial trauma, the incidence of vascular injury is unknown. Further, radiation exposure is associated with an increased lifetime risk of malignancy. We evaluated the utility of CTA in children with cranial trauma at a single center.

Methods: Children who underwent CTA during evaluation for traumatic cranial injury between 2003 and 2013 were retrospectively reviewed. Demographics, mechanism of injury, neurological exam, radiographic findings, and radiation dose were recorded. The primary outcome was vascular injury identified by CTA.

Results: We identified 129 patients (mean age 8.7 years range 0.3–17); 81 (63%) were male. Fifteen (11.6%) had a focal neurological deficit and 87 (67%) intracranial hemorrhage (ICH) on head CT. The most common indication for CTA was skull base fracture (67 patients, 52%). The average radiation DLP was 580 mGy-cm. Abnormality of the ICA was reported in 16 patients (12%); 81% had concurrent ICH. Six patients (4.2%) had injuries requiring treatment. Carotid stenosis was reported in nine patients, none were treated; carotid dissection was identified in five patients (two were treated); one cavernous-carotid fistula underwent embolization, and one pseudoaneurysm was identified in a patient who died. All patients requiring treatment had a focal neurologic exam or ICH. No vertebral artery injuries were identified. There were eight deaths (6.2%).

Conclusions: Our data suggest clinically significant vascular injury is rare and CTA may be reserved for patients with a focal neurologic deficit or ICH.

Paper 21 *(DOI: 10.3171/2014.1.PEDSpaper21)*
Management of Enlarging Syrinxes after Decompression for Chiari I Malformation

John S. Myseros, M.D., Tiffani DeFreitas, Robert F. Keating, M.D.

Introduction: Chiari I malformations (CMI) often present with syringomyelia (SM). Successful surgical treatment of the CMI leads to improvement in both the symptoms as well as the SHM. Persistent SM after decompression has been described, and conservative management may allow for improvement over time. We present three children, who after decompression had enlargement of their SM without further symptoms. Delayed imaging on these patients revealed decrease in the SM, to sizes smaller than those seen preoperatively.

Methods: Of 127 children less than age 18 with CMI and SH evaluated at our institution, 86 underwent decompression. There were 46 males and 40 females, ages ranging from 1.7–17.6 years. Surgically, 31.4% had bony decompression alone, while 51.2% underwent duroplasty, and 17.4% had duroplasty with fourth ventricular stent.

Results: Six of 86 patients had an increase in their SM on subsequent postoperative imaging. Three had further surgery because of either worsening scoliosis (1) or worsening pain (2). The other three were watched expectantly. These patients remained clinically stable, and subsequent imaging revealed reduction in the size of the SM. Two of these children required duroplasty, and one had bony decompression alone.

Conclusion: Although the majority of SM will improve after CMI decompression, certain patients will have postoperative imaging showing no improvement, and rarely, enlargement of the SM. In these patients, absent any progressive signs or symptoms, conservative management may be indicated. In time, the SM may diminish in size, as in these three patients, to sizes smaller than those seen preoperatively.

Paper 22 *(DOI: 10.3171/2014.1.PEDSpaper22)*
Chiari I Malformation Presenting with Acute Spinal Cord Edema

Krystal Tomei, David Shafron, Ratan Bhardwaj, David Adelson, M.D., Ruth Bristol, M.D.

Introduction: Since Chiari I malformations (CIM) involve descent of the cerebellar tonsils through the foramen magnum causing obstruction of cerebrospinal outflow and brainstem compression, patients often present with headache, lower cranial nerve dysfunction, hydrocephalus and syrinx. CIM have rarely been associated with acute spinal cord injury (SCI), most commonly with associated syringomyelia with only individual case reports of SCI in the absence of a syrinx.

Methods: We report a retrospective series of children who presented with acute SCI with CIM without syringomyelia from 7/1/10 through 7/1/13, reviewing history for trauma, acute presentation, diagnostic imaging including MRI findings, management, and recovery.

Results: Seven patients were identified with CIM and acute SCI without syringomyelia. One patient had no history of trauma. Five of seven had minor injury, such as playing in a bouncy house, or rough housing with siblings. Imaging findings included: tonsillar descent ranging from 5-16 mm, and spinal cord edema in five patients extending into high thoracic levels. Two patients recovered fully, four patients partially recovered, and one child had no recovery of function (C2 ASIA-A). No patient had syringomyelia upon presentation or even on follow up imaging post injury. Three children underwent immediate decompression, while 3 children who presented in a delayed fashion are pending decompression, and one refused surgery.

Conclusions: CIM carries a small but present risk of severe SCI with even minor trauma, even in the absence of syringomyelia. Our patients demonstrated variable and often incomplete recovery, suggesting that counseling of patients with CIM found incidentally should include the risk of SCI with minor craniocervical trauma.

Paper 23 *(DOI: 10.3171/2014.1.PEDSpaper23)*
The Impact of Flexion and Extension on Morphometric Measurements at the Craniocervical Junction in Patients with Chiari I Malformation and Normal Controls

Hugh J. L. Garton, M.D., J. Rajiv Bapuraj, Karin M. Muraszko, M.D., Cormac O. Maher, M.D.

Introduction: Cerebellar tonsil position and brainstem encroachment are frequently used in clinical decisions for Chiari I malformation (CM) patients. However, little is reported about the impact of flexion and extension on these measurements.

Methods: 20 healthy volunteers, age 21 ± 9.8 yrs and 10 CM patients, age 22 ± 14 yrs, (mean ± SD) underwent craniocervical MRI in flexion, neutral and extension. Sagittal T1 MR sequences (1.00mm slice thickness) were measured by two attending neurosurgeons to achieve consensus. Measurements were made in 22 morphometric categories. Cerebellar tonsil position (CTP) was measured in midline, right, left parasagittal planes. Ventral brainstem encroachment was assessed with the pB-C2 line of Grabb et al. Occiput–C2 (O-C2A) angle measured neck position change.

Result: In neutral position, CM pts had a CTP 13.4 ± 8 mm below FM compared with 0.8±3.5mm in controls. ($p < 0.0001$) 2 controls had CTP > 5mm below FM. From flexion to extension CM pts had O-C2A change of 14.5 ± 5.8° vs. 23.4 ± 11.8° for controls ($p = 0.03$). Mean CTP did not change from flexion to extension for either CM pts (11.9 ± 7.0 mm vs 12.3 ±7.2 mm) or controls (0.7 ± 3.4 mm vs. 0.5 ± 3.3 mm). However 3 CM pts (30%) and 1 control (5%) changed > 4 mm between positions. pB-C2 changed significantly in both CM (F: 6.8 ± 1.4 mm vs. E: 5.7 ± 7.2 mm, $p = 0.036$) and controls (F: 7.3 ±1.3 mm vs. E: 5.4 ± 2.2 mm) $p < 0.0001$.

Conclusions: Many morphometric measurements change with flexion vs. extension. Ventral brainstem encroachment, pB-C2, is significantly greater in flexion than extension in CM 1 patients and volunteers. Neck position has unpredictable but sometimes significant impact on tonsil position.

Paper 24 *(DOI: 10.3171/2014.1.PEDSpaper24)*
Chiari I, a Subcategory of Craniocerebral Disproportion: Alleviation by Supratentorial Cranial Vault Expansion

Kathryn Beauchamp, M.D., Ken R. Winston, M.D., Arianne Boylan, M.D., Nicholas Stence, M.D.

Introduction: Chiari I deformity is the neuroanatomical displacement of the cerebellar tonsils through the foramen magnum into the upper cervical spinal canal. Several neuropathologies and treatments have been proposed. This report aims to advance the comprehension of pathophysiology of Chiari I.

Methods: Patients with documented Chiari I deformity who underwent cranial vault expansion to relieve intracranial hypertension are the basis of this report.

Results: Three patients met inclusion criteria and all experienced complete resolution of their Chiari I deformities as demonstrated on postoperative magnetic resonance imaging.

Conclusions: Supratentorial cranial vault expansion has been reported by the senior author and by others for the treatment of intracranial hypertension in patients with multisutural synostosis. Resolution of Chiari I by supratentorial vault expansion can only be explained by upward translation of brain within the posterior fossa. Therefore, in our patients, Chiari I was caused by cerebellar-posterior fossa disproportion resulting from supratentorial craniocerebral disproportion. We believe that supratentorial craniocerebral disproportion should be in the differential diagnosis in patients with Chiari I deformity, particularly in patients with craniosynostosis or a history of surgery for craniosynostosis.

Paper 25 *(DOI: 10.3171/2014.1.PEDSpaper25)*
Clinical Importance of Neural Tissue Deformation in Type I Chiari Malformation

Bryn A. Martin, Nick Shaffer, Mikayla Lowenkamp, Francis Loth, John Tew, Mark Luciano, M.D., Ph.D.

Neural tissue deformation has been observed in type I Chiari malformation (CMI) patients. However, the clinical importance of deformation in CMI is not known. We assessed bulk spinal cord (SC) motion in the axial direction at the FM and C2 level for symptomatic adult CMI pre- (N = 17) and post-posterior fossa decompression surgery (N = 8) and compared motion to healthy controls (N = 6). SC velocities at the FM and C2 were obtained by standard phase-contrast MRI measurements sensitized for cerebrospinal fluid movement. Bulk tissue motion was quantified based on the integral of the average SC velocity at the FM and C2 level. In addition, cerebellar tonsillar herniation (CTH) was quantified in all subjects. Results showed that SC motion at the FM for patients pre-surgery was significantly greater than healthy controls (Median 0.41 mm, Interquartile Range (IQR) 0.32 versus median 0.23 mm, IQR 0.07, $p < 0.01$). Motion at C2 showed a similar trend between subject groups, but was on average 37% smaller than at the FM. Motion at the FM decreased significantly following surgery (Median 0.34 mm, IQR 0.16, $p = 0.03$). These preliminary results support that SC motion is elevated in CMI patients and that surgery reduces motion. Thus SC motion may provide an additional factor to help quantify CMI severity.

Paper 26 *(DOI: 10.3171/2014.1.PEDSpaper26)*
Prevalence of Spinal Cord Tethering by MRI in Infants with Sacral Dimples

Brent O'Neill, M.D., Alex Herron, Todd Hankinson, M.D., Corbett Wilkinson, M.D., Michael Handler, M.D.

Introduction: An association between sacral dimples and spinal cord tethering is well described, but the likelihood of identifying pathology with MR imaging in infants screened for sacral dimple has been rarely studied. Additionally, various guidelines for which dimples should prompt imaging have been proposed but none have been well-studied.

Methods: The radiology database at Children's Hospital Colorado was searched over a five year period for all non-contrast lumbar MRIs performed on children under one year old. Charts were reviewed. Spinal tethering was broadly defined to include fibrolipoma of the filum terminale or a conus medullaris lying at or below the L 2-3 disc space. The distance from the dimple to the tip of the coccyx was measured on all images.

Results: 317 infants were scanned for a sacral dimple. Twenty-one percent of these had tethering of which 60% underwent detethering surgery. Six patients had lipomyelomeningocele or dermal sinus, 42 had fibrolipoma of the filum terminale (8 with associated low-lying conus), and 17 had low lying conus alone. Location of dimple did not predict MRI result either by description noted in the chart or as measured on imaging.

Conclusion: MRI reveals a high rate of spinal tethering (when broadly defined) in infants with sacral dimple. No association could be identified between the level of the dimple and the likelihood of tethering.

Paper 27 *(DOI: 10.3171/2014.1.PEDSpaper27)*
Finite Element Modeling of the Pediatric Craniocervical Junction

Douglas Brockmeyer, M.D., Marcus Mazur, M.D., Benjamin Ellis, M.D.

Introduction: The biomechanics of the pediatric craniocervical junction are poorly understood, mostly due to lack of pediatric spinal cadaveric tissue available for laboratory analysis. Finite element modeling (FEM) can supply spinal biomechanical data, but ultimately FEMs need to be validated with biomechanical testing. We describe our method of producing a validated FEM of the pediatric spine, using an established adult FEM for comparison and cross-validation.

Methods: Bone and cartilage surfaces of the O-C1-C2 complex of a normal 2-year old child were segmented from CT image data using Amira software. The surfaces were imported into TrueGrid software for three-dimensional hexahedral meshing. Solid and shell elements were added to represent ligamentous structures.

FEBio software was used for FEM generation and execution of subsequent analyses. The model was validated by assigning adult material properties, then comparing the torque/rotation (moment/bending) response of the FEM to adult experimental data. Parameter studies were performed to account for the change in material properties of ligaments and cartilage that are probable in the pediatric population.

Results: The model was run using FEBio software and compared to an established FEM of the adult craniocervical junction. The behavior of the model compared favorably to the established FEM. Assignment of pediatric tissue parameters to the model did not negatively affect its performance in the normal state.

Conclusion: This is the first attempt to produce a robust, validated FEM of the pediatric craniocervical junction. Initial work has shown favorable performance of the model, and further work with focus on pathologic conditions.

Thursday's Abstracts

Paper 28 *(DOI: 10.3171/2014.1.PEDSpaper28)*
***BRAF*^{v600E} Mutations are Common in Brainstem Gangliogliomas**

Michael H. Handler, M.D., Andrew Donson, B. K. Dleinschmidt-Demasters, Lynne Bemis, Dara Aisner, Diane Birks, Jean Lefy, Amy Smith, Nicholas Foreman, and Sarah Rush

Introduction: Gangliogliomas, though WHO grade I tumors, have a worse prognosis in the brainstem. Tumors which express the *BRAF*^{V600E} mutation have been successfully treated with the agent vemurafinib. After a gratifying treatment of a brainstem ganglioglioma with the mutation, we sought to assess the incidence of the mutation in these tumors. The prognosis in incompletely resected gangliogliomas may improve with this novel targeted therapy.

Methods: Tissue was collected at two Children's Hospitals from 1995-2012. Pathological material and/or snap frozen tissue in 15 brainstem gangliomas, 11 non-brainstem gangliogliomas, and 8 brainstem juvenile pilocytic astrocytomas (JPAs) were assessed for the *BRAF*^{v600E} mutation by Sanger sequencing, VE1 immunostaining for BRAF^{v600E} and some by a novel more sensitive RNA sequencing approach. We analyzed clinical outcomes for 12/13 brainstem and 9/11 non-brainstem gangliogliomas.

Results: BRAF^{V600E} mutation was identified in 8/15 (53%)brainstem gangliogliomas compared with 5/11 (45%) of non-brainstem gangliogliomas, and 1/8 (13%) of brainstem JPAs Brainstem location was associated with a significantly shorter progression free survival (PFS) (HR = 8.81, p = 0.002) and overall survival (HR = 8.1, p = 0.038). Presence of *BRAF*^{V600E} in the brainstem gangliogliomas was associated with a significantly shorter PFS (HR = 8.5, p = 0.008) despite the small study population.

Conclusion: Our cohort confirms that brainstem location of ganglioglioma has a poorer prognosis, is resistant to conventional therapy and highlights the need to develop novel approaches. The significant percentage of *BRAF*^{v600E} mutations in gangliogliomas, particularly in brainstem, suggests that they should routinely be tested for it. Vemurafinib is effective in treating tumors which express the mutation, and may therefore improve outcome in brainstem gangliogliomas.

Paper 29 *(DOI: 10.3171/2014.1.PEDSpaper29)*
Paradoxical Activation of BRAF Protein Kinase Fusions after RAF Inhibitor Administration and Potential New Targets

Phillip B. Storm, M.D., S.S. Lang, A.J. Sievert, P.J. Madsen, and A.C. Resnick

Introduction: Pediatric low grade astrocytomas are a diverse group of tumors. We have previously shown that pediatric gliomas have BRAF mutations, specifically a BRAF V600E mutation and BRAF fusion genes. KIAA1549 was the first fusion partner identified in gliomas and recently several other partners have been found. BRAF inhibitors showed exciting results in treating V600E-dependent melanomas. We investigated the efficacy of the BRAF inhibitor PLX4720 against the BRAF fusion kinase.

Methods: Gateway cloning and site-directed mutagenesis were used to generate several Myc-tagged constructs for protein expression. Stable Myc-tagged protein expression was confirmed by Western blot analysis. The ability of the BRAF mutants to transform cells by anchorage-independent growth was determined in a soft agar assay and the relative fluorescence units (RFU) from the assay were measured.

Results: Cells expressing the KIAA1549-BRAF fusion kinase function as a homodimer that is resistant to PLX4720 and is associated with CRAF-independent paradoxical activation of MAPK signaling. Mutagenesis studies demonstrated that KIAA1549-BRAF fusion-mediated signaling is diminished with disruption of the BRAF kinase dimer interface. Additionally, the KIAA1549-BRAF fusion displays increased binding affinity to kinase suppressor of RAS (KSR), an RAF relative recently demonstrated to facilitate MEK phosphorylation by BRAF. Despite its resistance to PLX4720, the KIAA1549-BRAF fusion is responsive to a second-generation selective BRAF inhibitor that, unlike vemurafenib, does not induce activation of wild-type BRAF.

Conclusion: Our data support the development of targeted treatment paradigms for BRAF-altered pediatric astrocytomas and also demonstrate that therapies must be tailored to the specific mutational context and distinct mechanisms of action of the mutant kinase.

Paper 30 *(DOI: 10.3171/2014.1.PEDSpaper30)*
ID2/KDR Regulated Pro-malignant Myeloid Derived Suppressor Cells Drive Low Grade Glioma Transformation

Yujie Huang, Ph.D., Caitlin Hoffman, M.D., Prajwal Rajappa, M.D., Babacar Cicce, M.D., Ph.D., and Jeffrey P. Greenfield, M.D., Ph.D.

Evidence supports a crucial role for bone marrow derived cells in the tumor microenvironment as critical components regulating primary tumor growth and malignant transformation. Multiple types of BMDCs, including macrophages, T-regs, and neutrophils, contribute to immunosuppression, and proangiogenesis within the tumor microenvironment. We demonstrate a sub-population of myeloid derived suppressor cells (MDSCs) expressing KDR (VEGFR2) in the peripheral blood of both murine models and human glioma patients. The number of KDR$^+$ MDSCs is positively correlated with pathological/histological grades of tumors. The Grade III and IV patients have more KDR$^+$ MDSCs than low-grade patients. In patients with grade II astrocytomas, those with higher levels of KDR$^+$ MDSCs, have poorer progression free survival, and transform into Gr III tumors. The function of KDR$^+$ MDSCs was studied in Rosa26-cre/KDR$^{fl/fl}$ mice. The bone marrow cells from KDR-KO mice were transplanted into RCAS-tva/PDGF-BB mice. Knocking out KDR in bone marrow derived cells delays progression of low-grade tumors driven by PDGF. The median survival of tumor bearing mice was significantly increased. Isolating KDR$^+$ hematopoietic progenitor cells from tumor bearing mice bone marrow, identified TGF-β signaling and inhibitor of DNA binding protein-2 (ID2) as upstream mediators for KDR$^+$ MDSCs during glioma development. With ID2 knockout mice, we recapitulated the KDR-bone marrow knockout phenotype in tumor bearing mice. Further in vitro and in vivo assays showed TGF-β/ID2/KDR signaling axis play an important role in driving the differentiation of hematopoietic cells towards pro-angiogenic and pro-tumor phenotypes. ID2 and KDR in MDSCs promote angiogenesis and malignant transformation of gliomas.

Paper 31 *(DOI: 10.3171/2014.1.PEDSpaper31)*
Anti-CD47 Therapy Induces a Differential Anti-brain Tumor Response Among Different Macrophage Phenotypes

Michael Zhang, Sid Mitra, Achal Achrol, Sharareh Gholamin, Skender Najibi, Suzana Kahn, Abdullah Feroze, Michael Edwards, M.D., Irving Weissman, Samuel Cheshier, M.D., Ph.D.

Introduction: Anti-CD47 monoclonal antibodies used to disrupt the CD47/Sirp-α interaction in macrophages have been demonstrated to elicit an effective anti-tumor response. We hypothesize that anti-CD47 treatment could induce a differential anti-GBM response among macrophage subtypes. Macrophages have been known to polarize into M1 and M2 subtypes in response to external stimuli via classical and alternative activation pathways, leading to distinct functional activity that may have implications in solid tumor therapy.

Methods: To compare the anti-brain tumor profile of macrophage subtypes in the context of anti-CD47 therapy, we first generated monocyte-derived macrophages (M0) from human peripheral blood. Macrophages were then polarized into M1 and M2 and analyzed by flow cytometry for cell markers. The successfully polarized macrophages were then analyzed by flow cytometry for their extent of phagocytosis when co-incubated with CFSE-stained primary brain tumor cells, with and without anti-CD47. Cell populations co-presenting with CFSE and macrophage markers were considered a positive event for phagocytosis.

Results: After optimizing the polarization protocol, CD163 and CD80 were found to be good markers for M0/M2 and M1, respectively. When measuring for phagocytic activity, M0 macrophages demonstrated the highest rate over phagocytosis and over a two-fold change in phagocytosis following the addition of anti-CD47. M2 had a similar activity profile, including a large, but slightly weaker-fold response to anti-CD47. M1 macrophages exhibited minimal phagocytosis regardless of treatment. The use of different tumor lines including pediatric GBM and medulloblastoma revealed similar trends across macrophage subtypes and between treatment conditions.

Conclusion: Monoclonal antibody treatment against CD47 has potentially potent anti-tumor activity against malignant brain tumors *in vitro* depending on which type of macrophage is present. We are continuing our preclinical experiments with the goal of identifying the macrophages present in tumor samples treated with and without anti-CD47.

Paper 32 *(DOI: 10.3171/2014.1.PEDSpaper32)*
Pearls and Pitfalls of 500 Intraoperative Pediatric MRI Cases: The Cook Children's Experience

John Honeycutt, M.D., Richard Roberts, and David Donahue

Introduction: IMRI allows real-time intraoperative imaging to guide surgical intervention. The effectiveness of this technology for treatment of neurosurgical issues in the adult population has been demonstrated in empirical literature. Fortunately, the implementation of iMRI in pediatric neurosurgery has garnered attention as an advantageous alternative for certain neurosurgical issues.

Methods: Following IRB approval, the medical records of the first 500 patients who have undergone a neurosurgical procedure at Cook Children's Medical Center utilizing iMRI technology since January 2007 were reviewed.

Results: Patients ranged in age from less than one month to 24 years (mean=9.15 yrs). Diagnoses primarily included tumor (n=208, 43%), seizures (n=142, 29%), chiari malformations (n=100, 21%), and cavernous malformations (n=25, 5%). Neurosurgeons continued surgery after initial intraoperative scan more often in patients with seizures (44% of cases), tumor (43%) or Chiari malformation (39%). Of those cases 94 required a second scan and 8 required a third.

Conclusion: IMRI has become an integral part of many of our pediatric neurosurgical cases. The lead author will discuss advantages and disadvantages of using iMRI for pediatric cases.

Paper 33 *(DOI: 10.3171/2014.1.PEDSpaper33)*
Bedrest After Intrathecal Baclofen Pump Surgery

Patrick Graupman, M.D., Michael Partington, M.D., Peter Kim, M.D., Debroah Song, M.D, Christopher Najarian, M.D., Amanda Seeley, C.N.P., Alaina Laine, R.N., C.N.P, Mary Maginas, C.N.P., Teresa Schultz, C.N.P.

Introduction: In the last two decades, Intrathecal Baclofen (ITB) has been increasingly used to treat patients that have spasticity and dystonia with generally positive results. Goals of ITB treatment include improved mobility, improved comfort level, and improved ability of the patient and caregiver to perform Activities of Daily Living (ADLs). The main complications associated with ITB are infection, cerebrospinal fluid (CSF) leak and intrathecal catheter malfunction. In our hospital, patients that undergo primary ITB pump placement or catheter revisions are required to remain on flat bed rest for a period of 72 hours post-operatively in the hospital. This standard has been used with the assumption that flat positioning reduces the frequency of CSF leak and postural headache. There have been many studies on surgical techniques to best reduce the incidence of post-operative complications, such as prophylactic antibiotic therapy to prevent infection, and purse-string sutures around the catheter to reduce CSF leak. However, based on our extensive review of the literature, we have not encountered any trials evaluating if flat bed rest after ITB surgery is effective in reducing the risk of post-operative CSF leak, or demonstrating the duration of bed rest that is needed in this population. Does a period of prolonged flat bed rest following Intrathecal Baclofen Pump surgery reduce the incidence of post operative of Cerebrospinal Fluid (CSF) leak or postural headache? We hypothesize that there is no difference in risk between a 24 and 72 hour period of flat bed rest.

Method: This is a prospective, randomized, controlled clinical trial. Subjects are randomized pre-operatively into either the 72 hour bed rest group, our current standard of care, or the 24 hour bed rest group. A standardized anesthetic is used intra-operatively, and an opening pressure is obtained prior to intrathecal catheter placement or revision using the same puncture and needle that is used to introduce the intrathecal catheter. Pre-operative variables that are traced are: Primary pump placement or catheter revision, age, height, weight, presence of a functioning shunt, and presence of a spinal fusion. Intra-operative variables that are traced are: Opening Lumbar pressure (cm H_20), number of passes required with the introducer needle. Post-operative variables that are traced daily while inpatient are: Presence of postural headache, presence ballotable fluid collection at pump site or back, CSF leak out of abdominal or lumbar incision(s), presence of any of the following: Constipation (increased from pt baseline), GERD (increased from patient baseline), DVT, pneumonia, new skin breakdown, wound infection.

Results: Descriptive, inferential, and sub-group analysis will be used. We are currently in the data collection phase of our investigation. We have enrolled 49 subjects since May, 2012; 35 males and 14 females; 25 are in the 72 hour group and 24 in the 24 hour group. Thus far, the 72 hour group is trending towards having statistically significant more adverse events compared to the 24 hour group. One variable thus far that has achieved significance using Chi Square ($p = 0.003$) is that the 72 hour group has more constipation. Our plan is to continue the investigation until at least 268 total subjects are enrolled, in order to obtain power statistical significance with the numerous variables being investigated.

Conclusion: The goal of this investigation is to develop detailed evidence-based guidelines when determining bed rest duration for patients after ITB pump placement or catheter revision.

Paper 34 *(DOI: 10.3171/2014.1.PEDSpaper34)*
Patterns of Catheter Failure in Intrathecal Baclofen (ITB) Therapy: Report of a Large Series

Michael D. Partington, M.D., Emily E. Partington, B.A., Samuel Roiko, Ph.D., Linda E. Krach, M.D.

Introduction: Treatment outcomes in ITB therapy are impacted by problems with catheter function and also infection. This study was designed to examine the types of catheter failures and their temporal distribution.

Methods: Single institution, retrospective study with IRB approval. All ITB surgeries which required catheter placement or revision in a 5 year period were studied. A minimum of one year follow-up was obtained in each. All patients received a single piece catheter (Medtronic #8709). Catheter failures were classified according to mechanism of failure, and temporal patterns were studied using survival curves.

Results: During the period of study, a total of 268 catheter operations were performed. Infections in occurred in 16 cases (5.98%). Infections tended to occur early, with a median time to diagnosis of 2.5 months. Catheter malfunction occurred in 63 cases overall (23.5%), with fracture (macro or micro) causing failure in 20 cases, occlusion in 6 cases, other causes in 14 cases and no proven cause in 23. Other causes included connector failure, puncture by refill needles, spontaneous dislodgement or iatrogenic dislodgement, among others. Survival curves did not show a statistically significant difference in time to failure when analyzed by type. Overall, more than 75% of catheters were still functioning at 5 years follow-up.

Conclusions: The single piece catheter has been a relatively durable component of this important drug delivery system. Infections present in proximity to surgery, with other mechanisms of catheter failure being evenly spread over a multiyear period.

Paper 35 *(DOI: 10.3171/2014.1.PEDSpaper35)*
Developing a Spasticity Center in a Rural, Underserved Area

David F. Bauer, M.D.

Introduction: Children with spasticity and dystonia are a vulnerable population of children who are at risk of being underserved by our medical system.

Methods: The author will discuss his experience developing a multi-disciplinary center for the treatment of children with spasticity and dystonia in a rural setting.

Results: Children in New Hampshire have received substandard care in the treatment of spasticity and dystonia. This was driven by a state-run neuro-motor clinic with an orthopedic surgery based model of care which treated these children exclusively with tendon lengthening, osteotomies, joint stabilization, and scoliosis surgery. Direct treatment of spasticity and dystonia with medications, botulinum toxin, selective dorsal rhizotomy, and intrathecal administration of baclofen were lacking and not offered to most patients. Careful utilization and coordination of resources has helped to create a state-wide spasticity clinic that has now identified and treated many children in rural Northern New England who have not been previously offered comprehensive care for their spasticity or dystonia.

Conclusions: A coordinated effort to capture the resources of a state run, orthopedic surgery driven neuro-motor clinic has resulted in a more comprehensive treatment paradigm for the state's children with spasticity and dystonia.

Paper 36 *(DOI: 10.3171/2014.1.PEDSpaper36)*
Motion Sparing Arthrodesis for Symptomatic Spondylolyis in Children: Results and Technical Considerations

Adele S. Riccardi, B.S., Ryan A. Grant, M.D., M.S., Rosamaria Didiano, B.S., Michael L. DiLuna, M.D.

Introduction: The current standard of care for symptomatic adults with chronic from pars defects is a single segment fusion. The so-called motion sparing, instrumented, direct pars repair first appeared in the literature in 2006. It has been used successfully to treat persistent pain from spondylolysis leading to isthmic spondylolisthesis. This technique is typically reserved for adolescents and young adults with the advantage of preserving motion across the segment affected. Furthermore it has demonstrated a low biomechanical profile. Herein we report our experience, technique and complications in children and young adolescents compared to the limited literature available.

Methods: Since 2010, eleven children presented with debilitating back pain. All surgical candidates had failed PT, direct pars injections, and had either an MRI or bone scan demonstrating the fracture/defect was chronic. Surgery was performed through a single midline incision. Screw-rod-hook or screw-wire-screw constructs were used. Bone graft was either iliac crest with DBM putty or local bone with DBM putty.

Results: All patients had bilateral spondylolysis. Average age at the time of presentation was 12 (range 9–15), average number of days of school missed was 26 (range 7–30). Disc degeneration was not present, four had Grade I slips. The average hospital stay was 2 days. Average blood loss was less than 100 cc. Mean operative time was 92 minutes. There were no neurological complications. Mechanical back pain and radiculopathy resolved within 3-4 months follow-up. Two patients required hardware removal because of recurrence of pain > 12 months after the procedure that resolved after surgery. All demonstrated radiographic evidence of pars fusion.

Conclusions: We present a technical description and small case series of pediatric patients undergoing a simple, instrumented pars repair. Complications were limited to hardware removal. This is a safe and effective way to relieve back pain in this population without biomechanically altering the lumbar spine of a child.

Paper 37 *(DOI: 10.3171/2014.1.PEDSpaper37)*
Hybrid Spinal Constructs Using Sublaminar Polyester Bands in Posterior Instrumented Fusions in Children and Transitional Adults for Neuromuscular Scoliosis: A Series of 17 Cases

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Introduction: We previously reported our early experience with sublaminar polyester bands in spine surgery. We now describe the use of sublaminar polyester bands in long segment posterior instrumented spinal fusions from the upper thoracic spine to the ilium in 17 children and transitional adults with progressive neuromuscular scoliosis. This dedicated study represents the first reported use of polyester bands in spine surgery for neuromuscular scoliosis in the pediatric age group and adult transitional patients in the United States.

Methods: The authors retrospectively reviewed the demographics and procedural data of children and transitional adults who underwent posterior instrumented fusion using sublaminar polyester bands for neuromuscular scoliosis.

Results: 17 pediatric and adult transitional patients, ranging in age from 10 to 20 years (mean 14 years), underwent posterior instrumented fusion for progressive neuromuscular scoliosis. Complications directly related to the use of sublaminar instrumentation included transient proprioceptive deficit (1 patient). Other complications seen in our series included post-operative wound infection (1 patient); pseudoarthrosis (1 patient); proximal junctional kyphosis (1 patient), non-infected wound drainage (2 patients); and perioperative death (1 patient). The lessons learned from these complications are discussed. Mean surgical time was 7 hours 30 minutes (range 3 hours 59 minutes to 10 hours 0 minutes). Average estimated blood loss was 914 cc (range 300–2400 cc). The average coronal Cobb angle measured 64.5 degrees before surgery

(range 37–108 degrees), and 39.3 degrees immediately after surgery (range 14–85 degrees). The average pre-operative thoracic kyphosis and lumbar lordosis measured 48.1 degrees (range 13–98 degrees) and 37.3 degrees (range 4–60 degrees), respectively. Immediately after surgery, the thoracic and lumbar angles measured 44 degrees (range 5–114 degrees) and 40.5 degrees (range 20–56 degrees), respectively. At last follow-up, the average coronal Cobb angle was maintained at 38.6 degrees (range 21–92 degrees), and the thoracic and lumbar sagittal angles were maintained at 42.1 degrees (range 8–97 degrees) and 39.6 degrees (range 29–57 degrees), respectively. Mean follow-up time was 13 months (range 1–47 months).

Conclusion: Pedicle screws, laminar/pedicle/transverse process hooks, and sublaminar metal wires have been incorporated into posterior spinal constructs and widely reported and used in the thoracic and lumbar spines and sacrum with varying success. This report demonstrates the satisfactory outcomes of hybrid posterior spinal constructs in pediatric and transitional adult neuromuscular scoliosis that include sublaminar polyester bands that promise the technical ease of passing sublaminar instrumentation with the immediate biomechanical rigidity of pedicle screws and hooks.

Friday's Abstracts

Paper 38 *(DOI: 10.3171/2014.1.PEDSpaper38)*

Visualizing Epileptogenic Networks in Surgical Planning: Granger Causality in Interictal iEEG Predicts Seizure Focus

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Introduction: We consider a new and emerging view of epilepsy surgery: the goal is to determine and deactivate the network which causes seizures, not to remove brain regions which happen to have seizures. Actual seizures may make the spatio-temporal networks more clear, but is there a way to "see" these networks even in interictal data? The current standard technique for delineating a seizure onset zone using intracranial electroencephalogram (iEEG) data is visual inspection of primarily *ictal* recordings by expert epileptologists, which is considered to be far more accurate than visual assessment of interictal data. This requires the electrocorticography to continue long enough to capture one or more seizures. We are developing an approach to predict seizure focus in the epileptogenic network from interictal intracranial EEG (iEEG) data based on Granger causality, a computational technique developed by the economist Sir Clive Granger and for which he won the Nobel Prize. If interictal iEEG data could be used then period of invasive recording can be shortened or even eliminated. We hypothesize that statistically valid prediction of seizure focus or resection area can be made with interictal iEEG data using Granger causality (GC) defined in the time domain.

Methods: We applied Granger causality analysis to interictal iEEG data recorded from ten consecutive pediatric patients who underwent invasive monitoring at for resection planning at our institution. For each of ten cases, we analyzed total of 20 min of interictal iEEG data (taken from before the first seizure) and created a map based on *causal source* (identifying nodes that influence the rest of the network) and *causal density* (measuring causal interactions involving each electrode; both in-coming and out-going direction with respect to the electrode) for each implanted electrode. The algorithm essentially performed pairwise analysis searching for causal influence of each electrode on each other electrode. We used conditional GC to consider interactions among multiple time series simultaneously. We then compared the GC-based map with the ultimate map of seizure onset zone created by neurologists (based on the ictal analysis of the entire invasive monitoring period). We also compared them with the map of final resection determined from operative records and postoperative imaging. Statistical significance was assessed by testing null hypothesis that the GC based maps are obtained by random chance using empirically created null distributions of rank order sum and of average shortest distance between randomly selected electrode set and electrode set identified as seizure onset and early spread as well as electrode set of resection area.

Results: Causality maps obtained from *interictal* data from ten patients are strikingly similar to the ultimate clinical determination of the seizure focus from *ictal* data. Statistical test (using rank order sum) of causal density map compared with map of seizure onset zone and early spread shows statistical significance of variation from random selection (seven cases with $p < 0.05$; four with $p < 0.0005$; as low as < 0.0001). Statistical test (using average shortest distance) of either causal density map or causal source map compared with either ultimate map of seizure onset zone created by neurologists or map of final surgical resection show statistical significance in both parametric paired t-test and nonparametric Wilcoxon signed-rank test (p-values < 0.02 (as low as 0.002) for all compared cases).

Conclusions: The result represents a dramatic potential for rapid identification of the seizure focus in the epileptogenic network, since the data were collected over a timescale three orders of magnitude longer (days versus minutes). Utilizing maps that guide neurosurgeons by quickly visualizing causal areas in the epileptic network could lower cost and morbidity of intracranial monitoring, ultimately encouraging more patients to be surgically treated for intractable epilepsy.

Paper 39 *(DOI: 10.3171/2014.1.PEDSpaper39)*

Technical Challenges Associated with Cell-Based Therapies in the CNS

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Introduction: Cell-based therapies offer the promise of correcting genetic and acquired brain disoders. An example is Pelizaeus-Merzbacher Disease (PMD), a rare leukodystrophy in which defective oligodendrocytes fail to myelinate axons causing global neurological dysfunction. Transplantation of allogenic human central nervous system stem cells (HuCNS-SC), which can develop into oligodendrocytes, was performed in four human subjects with an early-onset severe form of PMD in an open-label Phase I study.

Methods: HuCNS-SCs were surgically implanted into the frontal lobe white matter using frameless neuronavigation. One milliliter of cells suspension was injected by freehand into each of four targets. Serial neurological evaluations, developmental assessments and magnetic resonance imaging (MRI), including high angular resolution diffusion tensor imaging (DTI), were performed at baseline and up to two years following transplantation. Surgical procedures were reviewed to identify technical limitations.

Results: The neurosurgical procedure, immunosuppression regimen, and HuCNS-SC transplantation were well tolerated. No clinical or radiological adverse effects were directly attributed to the donor cells. Normalized DTI showed increasing fractional anisotropy and reduced radial diffusivity, consistent with myelination. The following potential technical limitations were identified after study completion: non-optimized delivery device, inability to identify exact site of cell deposition, reflux, and potential immunogenic effects of allogenic cell sources. Device limitations were addressed through the parallel development of a prototype designed for MR-guided cell delivery.

Conclusion: Results of a Phase I study indicate a favorable safety profile for cell-based therapies, although a new generation of techniques and tools are required.

Paper 40 *(DOI: 10.3171/2014.1.PEDSpaper40)*

Striving for Zero Shunt Infections: Our Successes and Failures with the Shunt Bundle

Greg Olavarria, M.D.

Introduction: Shunt infections remain a significant concern at children's hospitals worldwide. Our institution created a qual-

ity focus group to address infection rates, around the time the Hydrocephalus Research Network began collecting their data.

Methods: Our protocol began in 2010 and data collection ended in 2013. Culture positive infections were included as the outcome variable. Adherence to protocol was also assessed based on surgery check lists.

Results: 275 surgeries were reviewed, in 250 patients, minimum follow up of 6 months, children of all ages were represented. Infection rates of 16% in a quarter (10% for year 2010) prompted the bundle implementation, and rates dropped to 2.7% for 2011, 5.9% for 2012, and 3.6% for the first quarter of 2013. These were within or below established benchmark rates (5.6%). Statistical analysis and risk reduction calculations are ongoing. Initial bundle compliance is over 80%, and some cases with infection had 100% compliance. CSF leak, wound dehiscence, direct wound contamination were risk factors for infection.

Conclusions: Our goal is not to just report effects of shunt bundle protocol on infection rates. A more detailed analysis will be presented, including compliance, which measures were successful, and the measures discontinued due to non-compliance or lack of effectiveness. The bundle is a process in evolution, and further refinements to ensure compliance will be discussed.

Paper 41 *(DOI: 10.3171/2014.1.PEDSpaper41)*
Fusion Patterns of Major Calvarial Sutures on Volume-Rendered CT Reconstructions

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Introduction: Recently, we reviewed the volume-rendered head CT reconstructions of 338 pediatric trauma patients. While investigating the timing of fusion of lateral calvarial sutures (sphenoparietal, squamosal, parietomastoid), we found 21 subjects with prematurely-fused sagittal sutures. We describe these findings. Using the same CT reconstructions, we also describe the timing of fusion of the major calvarial sutures in children and adolescents.

Methods: We reviewed all head CT volume-rendered reconstructions performed January 2010 through September 2012 at Children's Hospital Colorado for trauma patients aged 0-19 years. Each sagittal, coronal, metopic, or lambdoid suture was graded as open, partially-fused, or fused. The cephalic index was calculated for subjects with prematurely-fused sutures.

Results: 18 subjects had premature fusion of the sagittal suture only. Their mean cephalic index was 79. One subject had fusion of the sagittal and medial lambdoid and coronal sutures. Two had fusion of the sagittal and medial lambdoid only. To our knowledge, no subject had previously been diagnosed with craniosynostosis. Metopic sutures normally began to fuse, halfway along their lengths, during infancy; fusion was usually complete only after 2 years. Coronal sutures started to fuse laterally early during the second decade but none were completely fused by 18 years. There was no normal closure of sagittal or lambdoid sutures.

Conclusions: The sagittal suture may close prematurely more commonly than is generally thought. This is of unknown significance. Normal metopic sutures may not completely fuse until 2 or more years of age. Normal coronal sutures may start to fuse early in the second decade.

Paper 42 *(DOI: 10.3171/2014.1.PEDSpaper42)*
Disruption of EAAT2-mediated, Astrocytic Glutamate Buffering in Epileptogenic Tissue

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Introduction: Approximately one third of pediatric patients with epilepsy will prove resistant to medication (MRE) and are potential candidates for surgical intervention. It is now widely recognized that most epileptogenic tissues are cortical dysplasia or hippocampal sclerosis but the exact molecular mechanisms of epileptogenesis have remained elusive. While most attention has focused on cortical neurons there is emerging evidence that non-neuronal cells may also contribute to epilepsy. One of the principal actions of astrocytes in the central nervous system is to dampen neuronal excitability through buffering of extracellular glutamate. EAAT2 and EAAT1 are astrocytic glutamate transporters responsible for clearance of glutamate from the extracellular space. Here we assessed the contribution of astrocytic dysfunction in glutamate clearance in 2 cases of MRE.

Methods: Fresh tissue was obtained from 2 individuals who underwent a grid based staged resection for intractable epilepsy (GBR). Precise localization of the region of epileptogenesis was made possible by precise localization from grid and depth electrodes. Tissue was separated between regions of epileptogenesis ("more" epileptogenic) and regions of adjacent spread ("less" epileptogenic). Using Western blotting and *in vitro* measurements of [^{3}H]-glutamate uptake, we measured glutamate buffering capacity of astrocytes via known glutamate transporters EAAT1 and EAAT2.

Results: In both cases we found that EAAT2 was downregulated (18%–31%), leading to a deficiency in EAAT2-mediated glutamate uptake. Using fresh tissue samples, we found that uptake of [^{3}H]-glutamate from the extracellular space was significantly diminished in more epileptogenic tissue, presumably due to a loss of expression of DHK-sensitive, EAAT2 glutamate transporters when compared with less epileptogenic adjacent tissue from the same subject. Although no change in EAAT1 expression was noted glutamine synthetase (GS), the enzyme that catalyzes the conversion of glutamate into glutamine after it is transported from the extracellular space into astrocytes, was also down regulated by 26% in more epileptic tissue.

Conclusion: Our data indicate that the ability of human astrocytes to clear glutamate from the extracellular space is impaired due to loss of EAAT2 and down regulation of other proteins involved in glutamate homeostasis in epileptogenic regions of pediatric human cortex.

Paper 43 *(DOI: 10.3171/2014.1.PEDSpaper43)*
Establishing a Pediatric Epilepsy Surgery Program: Pitfalls and Lessons Learned

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Introduction: Pediatric epilepsy surgery is a specialized area of medicine dealing with a diverse group of patients and parents. Navigating the multiple treatment options can be fraught with complications.

Methods: The Children's Hospital New Orleans began laying the groundwork for an epilepsy surgery center over a decade ago. Since that time we have encountered many obstacles and learned many things while developing our still-evolving system.

Results: Although our team is young, we have results and complication rates comparable with those in the literature.

Conclusions: Building a multi-disciplinary epilepsy team is an absolute necessity and can be accomplished even at a small regional hospital by a few dedicated personnel. We review our experience with emphasis on the logistics involved in developing such a team.

Paper 44 *(DOI: 10.3171/2014.1.PEDSpaper44)*
Stereotactic MRI-guided Laser Ablation of Epileptogenic Lesions in Pediatric Epilepsy

Daniel Curry, M.D.

Introduction: Surgical morbidity is one of the main reasons patient's families reject the option, resulting in a treatment gap. MR-Guided Stereotactic Laser Ablation (SLA) offers an opportunity to reduce the morbidity of intractable epilepsy in children.

Methods: A retrospective review of the ablative epilepsy surgery cases was performed at a single pediatric epilepsy center. 32 ablations

were performed on 29 patients. 3 patients had Tuberous Sclerosis Complex, 1 with focal epilepsy, and two with Subependymal Giant Cell Astrocytoma (SEGA), 5 had Focal Cortical Dysplasia (FCD), 16 had Hypothalamic Hamartoma (HH), and 4 had mesial temporal lobe epilepsy (MTLE). An MR-compatible laser applicator (1.6mm diameter) housing a 1cm or a 3mm diffusing tipped optical fiber was placed with framed stereotaxy into the target and secured with a plastic bone anchor. The Visualase thermal ablation system, which includes a 15W 980nm diode laser and MRTI software was to ablate the lesion. Safety limits (50^0C) were placed near the margin of the desired thermal ablation zone to protect critical structures. Post ablation T1-weighted plus gadolinium contrast (T1 + Gd) and diffusion images were acquired confirm ablation. Post ablation MRI was performed 3 months after ablation. Post-op seizure frequency and ablation related morbidity was obtained in 3, 6, 9, and 12 month follow-up visits.

Results: The one TS patient was sz free. For FCD, 2 are seizure free, two have 50% seizure reduction, and one is unchanged. For HH, 93% are currently seizure free after 3 HH patients underwent re-ablation. For MTLE, 50% are seizure free. The two SEGA patients have demonstrated lesion stability. There were 2 targeting inaccuracies, 1 subclinical subarachnoid hemorrhage, one post-op CSF leak, and 3 transient memory impairments.

Conclusions: MR-guided stereotactic laser ablation may reduce pediatric epilepsy surgery morbidity and thus narrow the treatment gap.

Paper 45 *(DOI: 10.3171/2014.1.PEDSpaper45)*

The Influence of Completeness of Resection and Perilesional Resection Volume on Seizure Outcome and Morbidity following Surgery for Resection for Cortical Dysplasia

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Introduction: Focal cortical dysplasia is one of the most common causes of intractable epilepsy leading to surgery in children. The predictors of seizure freedom following surgical management for FCD are still unclear. The objective of this study is to determine the influence of completeness of resection and perilesional resection volume on seizure outcome and morbidity following respective epilepsy surgery for cortical dysplasia.

Methods: The medical records and brain imaging scans of forty three consecutive patients who had undergone surgical treatment for refractory epilepsy with focal MRI abnormalities and pathological diagnosis of FCD were reviewed. Preoperative lesion volume and postoperative resection volume were calculated from the MRI scans by manual segmentation.

Results: Forty three patients underwent first time surgery for resection of cortical dysplasia. 28 patients (65%) were males while 15 patients (35%) were females. The mean follow up period was 26 months. The mean age at the time of surgery was 7.3 years with a range of 2 months to 21.8 years. Mean age of onset was 31.6 months with a range of 1 day to 168 months. With regards to seizure freedom, all patients with Engel IV seizure control outcome had documented residual cortical dysplasia identified on postoperative brain MRI scan while only 44% of patients with Engel 1 outcome had residual lesion on the postoperative brain MRI scan.

Conclusion: Completeness of resection of radiological abnormality is a significant predictor of seizure freedom following resection of FCD in children.
