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Abstracts*

PAPER 1 (DOI: 10.3171/2015.1.PEDSPAPER1)

Minimizing Radiation Exposure in Evaluation of Pediatric Head Trauma: Utilization of Rapid MR Imaging

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Introduction: Imaging of the pediatric patient with minor head injuries can often be a controversial topic. However, with more than 473000 annual emergency department (ED) visits for children with traumatic brain injuries in the United States, the risks related to the ionizing radiation incurred during CT examinations becomes a real concern. The purpose of this study is to assess the validity of rapid-sequence (or quick-brain) MRI in evaluating these patients, and its potential for replacing ionizing CT imaging for follow-up of patients with head trauma.

Methods: Retrospective review found 103 patients who underwent initial head CT and a subsequent follow-up rapid-sequence MRI between January 2010 and July 2013. Patients were between ages 0-19, presenting either directly or being transferred from regional centers with minor head injuries requiring imaging. The initial head CT was performed either at our institution or an outside institution with all MR imaging being performed within 48 hours at our institution. Two cases were excluded from the criteria group, as the follow up MR imaging was performed after surgical intervention. Images were then read by a certified neuroradiologist that was blinded to patient information and scan parameters. Statistical comparison was then carried out between CT and MRI findings.

Results: Evaluation of extra-axial hemorrhage demonstrates a *very good* level of agreement between MRI and CT (Kappa = 0.841). Evaluation of hemorrhagic contusion/intraparenchymal hemorrhage demonstrates a *good* level of agreement between MRI and CT (Kappa = 0.609). Evaluation of fracture demonstrates a *good* level of agreement between MRI and CT (Kappa = 0.705). Evaluation of diffuse axonal injury demonstrates a *poor* level of agreement between MRI and CT (Kappa = 0.154).

Conclusion: MRI is an adequate examination for follow-up imaging of head trauma in lieu of repeat CT in the management of extra-axial and parenchymal hemorrhages patients with mild traumatic brain injury.

PAPER 2 (DOI: 10.3171/2015.1.PEDSPAPER2)

Complications Following Pediatric Cranioplasty after Decompressive Craniectomy: a Multicenter Retrospective Study

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Introduction: In children, cranioplasty to repair the skull defect from decompressive craniectomy presents a unique set of challenges and complications. Single-center studies have noted different risk factors for the common complications of cranioplasty resorption and infection.

Methods: We conducted a multicenter retrospective chart review including all patients under 19 years of age undergoing cranioplasty to correct a skull defect from decompressive craniectomy at 13 institutions. Prior systematic review of the literature along with expert opinion guided the selection of variables to be collected. These included indication for craniectomy; history of abusive head trauma; method of bone storage; method of bone fixation; use of drains; size of bone graft; presence of other implants, including ventriculoperitoneal shunt (VPS); presence of fluid collections; age at craniectomy; and time between craniectomy and cranioplasty.

Results: 359 patients underwent cranioplasty at 13 centers. Mean age was 8.4 years, and 51.5% of patients were female. Presence of VPS was a significant predictor of infection (8.5% v. 20%, $p=0.006$). No other variable was associated with infection.

History of abusive trauma, age at craniectomy, method of bone fixation, and use of external ventricular drain were significant pre-

*PLEASE NOTE The theme of the ASPN meeting this year was Complications. We highlighted complications in a variety of topics relating to Pediatric Neurosurgery. The ASPN is only publishing the guest abstracts that pertain to original science, but not publishing the abstracts from members or guests that pertain to complications.

dictors of bone resorption on univariate analysis. Only age at craniectomy remained significant on multivariate analysis, including control for the “center effect.” For every year of increased age the risk of bone flap resorption drops by 1% (OR 0.99, 95% CI 0.983-0.995, $p < 0.001$).

PAPER 3 (DOI: 10.3171/2015.1.PEDSPAPER3)

Use of Silver-Impregnated Dressings to Reduce Neurosurgical Infections

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Introduction: The anti-microbial properties of silver have been exploited for centuries and have frequently been used to dress burns in recent times. A meta-analysis of randomized clinical data from the burn literature shows improved outcome measures when silver dressing was compared to traditional dressings.

Methods: A retrospective review of records of patients with consecutive procedures performed in the neurosurgical service from January, 2011 to December, 2013 was performed. The use of silver dressings was instituted in February, 2012. There were 224 patients in the standard dressing group and 284 patients in the silver dressing group. The prepping protocol, surgical technique and peri-operative care were similar for both groups. The standard dressing included application of antibiotic ointment and non-adherent occlusive dressing. ACTICOAT™ (Smith&Nephew, London, UK) was used as the silver dressing. Fisher’s Exact Test for independence was performed using 2 X 2 contingency table analysis.

Results: The overall surgical site infection (SSI) for all the neurosurgical patients was 3.1% (16/508). The SSI in the standard dressing group was 4.4% (10/224). With the use of silver dressings, the infection rate decreased to 2.1% (6/284), ($p = 0.19$). In addition, the cerebro-spinal fluid shunt infection rate dropped from 7.4% (7/94) in the standard dressing group to 1.4% (2/138) in the silver-dressing group. The type of dressing applied and the shunt infection rate were found to be significantly related ($p = 0.03$).

Conclusion: The results suggest that use of silver dressings reduces the risk of SSI in neurosurgical patients. This study supports the need for further investigation to elucidate the causal relationship between silver dressing and reduced SSI.

PAPER 4 (DOI: 10.3171/2015.1.PEDSPAPER4)

Targeting Histone Mutations in Pediatric Glioblastomas

David J. Daniels, MD, PhD

Pediatric high-grade gliomas including Diffuse Intrinsic Pontine Gliomas (DIPGs) are among the most lethal cancers known with no effective cures. Recently it has been reported that about 80% of DIPGs and nearly 70% of midline glioblastomas (GBMs) contain a lysine 27 to methionine (K27M) mutation at one allele of the H3F3A gene that encodes the histone H3.3 variant. In order to facilitate diagnosis, we have developed a quick and reliable method to identify the H3.3K27M mutation through real-time PCR tech-

niques. We were able to confirm our assay on a newly obtained patient derived cell line. Furthermore, our patient derived cell line has a favorable genotype and is a good pediatric GBM model for drug screening and other testing (it harbors the K27M mutation, has decreased p53 expression and overexpression of PDGFRα). We and others have shown the histone H3.3K27M mutation leads to global K27 hypomethylation and reprograms gene expression by changing the epigenetic landscape. Through shRNA techniques we have identified potential lead compounds that selectively target tumors with the K27M mutations. These results will be discussed.

In conclusion, we have developed a new technique to identify H3K27M mutant GBMs. We have established a patient derived cell line that we feel accurately recapitulates the genotype of these highly malignant tumors. Furthermore, these studies pave the way for developing molecularly targeted therapies as our understanding how these mutations lead to tumorigenesis unfold.

PAPER 5 (DOI: 10.3171/2015.1.PEDSPAPER5)

Convection-Enhanced Drug Delivery to Pediatric Brain Tumors – Individual Tumor Physiology and not Target Specificity will Determine Efficacy

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Introduction: Though intuitively appealing (circumvention of blood- brain barrier, independent of regional tumor blood flow) convection-enhanced drug delivery (CED) has been disappointing with several randomized-controlled trials having failed to demonstrate therapeutic benefit in gliomas. These trials have been based on fairly simplistic models of drug distribution and neglected the size of the extracellular space in tumors i.e the distribution space. As CED remains a very attractive modality in particular for deep-seated, non- resectable and radio-resistant tumors we have conducted a study into the physiology of pediatric brain tumors especially the size of the extracellular space, bidirectional capillary permeability and regional blood flow to evaluate how these parameters affect CED.

Methods: De novo medulloblastomas, malignant gliomas and lymphomas (N=7 each) were studied. Using a two-compartment model and fast spiral CT as well as stable xenon CT we measured the blood-to-brain transfer rate K1, the brain-to-blood transfer rate k2, the vascular volume RCBV and the size of the extracellular space ECS as well as regional blood flow rCBF.

Results: In medulloblastomas the mean K1 was $10.5 \pm 6.3 \mu\text{l/g/min}$ with a k2 of $0.044 \pm 0.017 \text{ l/min}$ and a mean RCBV of $0.08 \pm 0.1 \text{ ml/g}$. The rCBF was $19.9 \pm 6.8 \text{ ml/100g/min}$. The ECS ranged between 0.13 and 0.28 ml/g. In comparison lymphomas showed an ECS of $0.32 \pm 0.24 \text{ ml/g}$ ($p=0.07$) but malignant gliomas differed significantly with a median ECS of $0.61 \pm 0.21 \text{ ml/g}$ ($p < 0.01$). Lymphomas had a massively increased K1 ($38.9 \pm 10.2 \mu\text{l/g/min}$, $p < 0.001$) than all other tumors. In combination with the rCBF measurements the extraction fraction and drug efflux were calculated showing high uptake of blood-borne drugs in lymphomas and medulloblastomas versus low uptake but rapid washout in malignant gliomas. As intratumoral heterogeneity of ECS was also highest in malignant gliomas (ECS 0.4 – 0.82 ml/g) CED modeled for indi-

vidual tumors based on heterogeneity and actual regional size of ECS was significantly worse in malignant gliomas compared to medulloblastomas and lymphomas ($p < 0.01$) with a large sink effect for the delivered drug rendering CED inappropriate for sufficient drug delivery.

Conclusion: Individual tumor physiology measurements can hence be used to

1. select tumors with appropriate physiological variables (small ECS, low K1 and k2), and 2. to plan catheter placement based on individual distributions of the extracellular space as the distribution volume to target areas of the tumor preferentially with small ECS to minimize the sink effect which shunts drug away from the biologically active parts along pressure gradients.

Ideal tumors for CED are surprisingly non-resectable medulloblastomas with brain stem infiltration and highly cellular gliomas with small ECS.

PAPER 6 (DOI: 10.3171/2015.1.PEDSPAPER6)

Using iMR and iCT Together in Severe Pediatric Deformity Correction: Cervicothoracic Kyphosis with Myelopathy in a 13 Year Old Female with Chondrodysplasia Punctata

David F. Bauer, MD

Introduction: Treatment of severe cervicothoracic kyphosis with myelopathy can be difficult in children with skeletal dysplasias. We present a way to facilitate treatment in an innovative operative setting.

Methods: We will present a case review, focusing on the benefits and detriments of using combined iMR and iCT when treating a child with severe spinal deformity from skeletal dysplasia.

Results: Our patient is a 13 year old girl who initially presented at 11-months of age with rhizomelic short stature, macrocephaly, stippled epiphyses on radiographs, unique facial features, brachydactyly, and developmental delay. Genetics diagnosed chondrodysplasia punctata. She developed C1/C2 instability at 7 years of age requiring C1/C2 Harms fixation and fusion. Five years later she developed worsening myelopathy with kyphosis and dynamic instability at the cervicothoracic junction. Because of her skeletal dysplasia, bone anatomy was poorly seen on cross table radiographs. We facilitated her care in a novel operating room utilizing intraoperative CT and intraoperative MRI capability, with integrated neuronavigation. Anterior C7 and partial T1 vertebrectomy were performed, followed by C1 to T6 fixation and fusion. Screw placement and bone decompression were visualized with intraoperative CT, and spinal cord decompression was visualized with intraoperative MR. Our patient tolerated the procedure well, and she had post-operative improvement in myelopathy with a stable spinal construct during initial short-term follow-up.

Conclusion: Combined intraoperative CT and MRI were very useful when treating cervicothoracic deformity correction in a child with skeletal dysplasia. We plan further experience with this technique in order to determine the best uses for this technology.

PAPER 7 (DOI: 10.3171/2015.1.PEDSPAPER7)

Use of C1 Lateral Mass Screws in the Reduction of Atlanto-Axial Deformity: Technical Note

Jonathan E. Martin, MD

Introduction: C1 lateral mass screws (C1 LMS) coupled with C2 fixation are one of several options available for fixation of atlanto-axial pathology. Previous reports have discussed indications for the selection of C1 LMS constructs to include anatomic feasibility, biomechanical advantages versus alternative constructs, and surgeon preference. Independent fixation of C1 and C2 provides additional advantages over transarticular fixation that have not previously been presented- the potential for direct force application allowing reduction of translational and rotational deformities at C1-2. We present two illustrative cases demonstrating the utility of C1 LMS in reduction of C1-2 deformity.

Methods: Two patients with Down syndrome and fixed atlanto-axial deformity are discussed. Pre-, intra-, and post-operative radiographs as well as operative technique are presented.

Results: Anatomic reduction of fixed translational and rotational deformities was achieved in both cases. In Case 1 (Os Odontoideum with fixed translational deformity), reduction was achieved through set-screw delivery of the rod to a finitely-mobile polyaxial C2 pars screw. In Case 2 (Os Odontoideum with fixed rotational deformity), independent fixation of C1 and C2 allowed for the application of distraction and rotational moments which corrected the patient's rotatory fixation. Neither patient had intraoperative monitoring changes or suffered neurologic sequella from intraoperative reduction. Both achieved solid arthrodesis documented by 6 month follow-up CT.

Conclusion: C1 LMS provide potential advantages for deformity reduction that should be considered when selecting spinal fixation for atlanto-axial pathology.

PAPER 8 (DOI: 10.3171/2015.1.PEDSPAPER8)

Endoscopic Third Ventriculostomy and Ventriculoperitoneal Shunting: A Comparative Effectiveness Study Using Administrative Claims Data

Sandi Lam, MD, Thomas G. Luerssen, MD, Iwen Pan, PhD

Introduction: Large clinical studies have documented hydrocephalus treatment outcomes at specialized pediatric centers. This study aims to apply propensity score matched (PSM) methodology to compare outcomes of ETV and VPS in children using a large US administrative claims database.

Methods: The Truven Health Marketscan® database with data between 2003 and 2011 was used. Patients aged ≤ 19 years with their first occurrence of ETV or VPS during the study period were included. Surgery failure was defined as the need for further surgical treatment of hydrocephalus after initial ETV or VPS. Age, etiology of hydrocephalous, and history of CSF shunt were used to perform PSM for ETV and VPS samples. We used Kaplan-Meier survival curves, stratified log-rank test, and Cox proportional-hazard models to analyze the matched samples.

Results: 3231 cases (478 ETV and 2753 VPS cases) were eligible. 458 balanced pairs were obtained from PSM. For selected paired samples, 321 of 458 (70%) pairs were concordant while 137 pairs were discordant. Among discordant pairs, patients with ETV were more likely to have a failure within 3 months than patients receiving VPS (relative risk = 1.4, p-value = 0.016). Among patients < 1 year of age, patients had higher surgery failure rates with ETV than VPS (p-value = 0.002). No similar pattern was found in patients age $\Rightarrow$ 1 year.

Conclusion: Analysis of a cohort of pediatric hydrocephalus patients developed from a national administrative claims database reveals patterns of surgical outcomes consistent with previous clinical studies.

PAPER 9 (DOI: 10.3171/2015.1.PEDSPAPER9)

Efficacy of Hydromer-Coated Shunt Systems in Reducing Early Shunt Infections

Emil A. Pastrana, MD, Ivan J. Sosa, MD

Introduction: Shunt infection is the most common complication following a cerebrospinal fluid (CSF) diversion procedure with devastating consequences. This study analyzes the efficacy of hydromer-coated shunt systems (HC) in reducing early shunt infections in the pediatric population.

Methods: Retrospective analysis of 99 consecutive pediatric patients with hydrocephalus de novo shunted using a HC shunt systems, standard non-impregnated shunt systems and antibiotic-impregnated system (AIS) was performed and compared for the incidence of shunt infection in the early postoperative period.

Results: Group A consisted of standard shunt systems with 37 patients while Group B were HC shunt systems with 37 patients, and Group C consisted of 25 patients. In terms of shunt infections, HC group had 3 shunt infections (8.1%), as compared to the control group, where 10 patients (27%) had infections, and group C had 1 infection (4%).

Conclusion: Hydromer-coated shunt systems represent an alternative to standard shunt systems for the reduction of shunt infection in the early post-operative period. There was no statistical significance in term of infection between the HC group and the AIS group.

PAPER 10 (DOI: 10.3171/2015.1.PEDSPAPER10)

Ciliary Contributions to Progenitor Differentiation in Hydrocephalus

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Neonatal hydrocephalus is a common disorder of the developing human nervous system, accounting for approximately 2% of all pediatric hospital stays and 3% of all pediatric hospital charges. Hydrocephalus remains associated with elevated mortality rates in neonates. Moreover, treatment of infants affected by hydrocephalus relies solely on invasive surgical approaches developed over 60 years ago. Identification of the cellular and molecular mechanisms underlying hydrocephalus are therefore high priorities for the neuroscience and medical communities. Ciliopathies are a group of disorders that display overlapping phenotypes with ciliary defects. Among syndromic ciliopathies, Bardet-Biedl syndrome (BBS) is one of the best-characterized disorders, and recently, 20% of humans with BBS have been found to have hydrocephalus. Conventional ciliopathy models have described the development of hydrocephalus as a result of altered motile ependymal cilia leading to abnormal flow of CSF. Our recent study, however, has lead to the previously unrecognized finding that defects in primary cilia signaling in glial progenitors during late embryonic / early postnatal development are responsible for neonatal hydrocephalus. In this work, we identify glial progenitor cell populations whose differentiation is altered by Bbs3 mutation in primary cilia for our mouse models of neonatal hydrocephalus. We also identify the structural and cellular alterations in the subventricular zone (SVZ) that pre-date the onset of hydrocephalus, elucidating how the abnormal development of specific glial progenitor cells contributes to the genesis of hydrocephalus through aberrant primary ciliary function.

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