Purpose: Craniosynostosis (CS) treatment is complex and varies widely. Large-scale outcome studies are difficult given the practice variation, low incidence of disease, and long time between intervention and final outcome. Established in 2016, the Synostosis Research Group (SynRG) is the largest multi-center consortium focused on prospectively evaluating the diagnosis and management of patients with CS. Here we present a preliminary analysis of these data.

Methods: Institutional review board at each SynRG institution approved this study prior to data collection. Patients diagnosed with CS who presented to any of 5 institutions from 2017 to present were enrolled in this study. Clinical data in 276 categories including history, diagnosis, radiographic imaging, intra-operative details, hospital course, and follow-up were recorded prospectively and stored in a REDCap database.

Results: Of 298 patients registered, 62.7% were male. Average age at registration was 10.4 months. Single suture CS accounted for 80% of patients and multisutural 20%; 3% of patients were syndromic. Mean age at surgery was 11.3 months. 46% underwent open vault reconstruction, 43% underwent strip craniectomy, and 11% underwent other types of reconstructions. Of those who underwent open reconstructions, 50.1% were fronto-orbital advancements. Of those who underwent strip craniectomy, 66.2% were sagittal, 16.9% metopic, and 13.6% coronal. Drains were used in 40% of patients. Antibiotics were given before incision in 98% of patients and continued post-op in 25% for a mean of 25 hours post-op. Tranexamic acid was used in 46% of patients and steroids in 60.5%. Intraoperative transfusion occurred in 42% of patients (80% in vault reconstructions and 11% in strip craniectomies). Postoperative hematocrit was on average 27.0, and 4.6% of patients required post-op transfusion. In-hospital complications were hematoma in 2.3%, early wound breakdown in 0.5%, seizure in 0.5%. No CSF leaks, infections, or deaths were reported. Early reoperations were necessary in 1.9% of patients. Mean length of stay was 2.7 days. Narcotics were prescribed at discharge for 73% of patients.

Conclusion: Large, prospective, multicenter studies of CS treatment have the potential to identify opportunities to optimize care and improve outcomes. This preliminary analysis of the SynRG data reveals clear trends in treatment of CS and will be useful in improving outcomes moving forward as the consortium continues.

Neurologic Functional Connectivity In Unicoronal Craniosynostosis: A Side-based Comparison

Anusha Singh, BS, Kitae E. Park, BA, Cheryl Lacadie, BS, Omar Allam, BS, Michael Alperovich, MD, MSc, John A. Persing, MD

Yale School of Medicine, New Haven, CT, USA.

Purpose: Unicoronal synostosis has been associated with impaired reading, language, and social function. Functional MRI (fMRI) can evaluate brain connectivity in targeted brain regions to compare imaging analysis to previously published clinical performance. fMRI was used in this study to compare brain function connectivity in unicoronal synostosis (UCS) and compare outcomes by cerebral dominance (left versus right-sided UCS).

Methods: Twelve adolescents with surgically treated UCS, 7 right-sided and 5 left-sided, were individually matched to age, gender and handedness controls. Resting state fMRI was acquired in a 3T Siemens TIM Trio scanner (Erlangen, Germany). Data was collected with intrinsic connectivity distribution and seed-connectivity analysis with BioImage Suite (Yale School of Medicine). Region of interest (ROI) analysis was performed based on Brodmann’s areas (BA) related to emotional, executive, language, motor and visuospatial function, left BA5, 6, 7, 18, 19, 37, 39, and 44. BA5, 6, 7 are areas of the frontal and parietal cortex important for visuomotor coordination and complex movement. BA18, 19 are areas of the occipital lobe related to visual information processing. BA 37, 39, and 44 are areas of the fusiform, angular gyri and temporal lobe important for language function. P<0.05 was significant.

Results: Compared to controls, all UCS patients demonstrated decreased connectivity in left BA7, bilateral BA39, and right BA41 (p<0.01)), which are areas of the parietal and
temporal cortices responsible for vision, language function, and motor coordination. Right UCS patients demonstrated increased connectivity in right BA17, BA18, BA19, BA20, BA36 when compared to controls (p<0.05). In the ROI analysis, right UCS exhibited decreased connectivity between the anterior cingulate cortex and right BA18, 19, and 37 compared to controls (p<0.05). The increased connectivity in BA17-20 (visual processing regions) supports our previous neurocognitive study results of increased visual perception abilities in right UCS patients. The subsequent decreased connectivity between BA18-19 and the anterior cingulate cortex (a section of which is implicated in complex motor coordination) is supported by neurocognitive data that shows decreased visual-motor integration ability in right UCS. This decreased connectivity between the aforementioned areas and the anterior cingulate gyrus despite increased intrinsic connectivity may also imply discordance in connecting emotion and executive function to language and visual information in right UCS patients. Connectivity between the left parahippocampus and right BA36, 37, and 54 was increased (p<0.05). Compared to controls and right UCS, left UCS demonstrated decreased connectivity between left BA6 and left BA17 and 18 (p<0.05). Left UCS patients did not demonstrate significantly different intrinsic or seed-based connectivity to right UCS or controls otherwise.

**Conclusion:** Unilateral coronal synostosis had decreased connectivity and greater potential for neurocognitive dysfunction in regions associated with memory, visual information processing, and motor function. Moreover, left-sided UCS had decreased connectivity in circuits crucial in complex motor movement when compared to right-sided UCS. This study provides data suggestive of long-term sequelae of UCS that varies by sidedness, which may underlie the different phenotypes of neurocognitive impairment found in previous cognitive analyses.

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**Development Of A Novel Murine Distraction Device To Investigate Bone Regeneration In Long Bone Distraction Osteogenesis**

*Harsh N. Shah, MPH, Ankit Salhotra, BS, Courtney A. Stockman, BS, Derrick C. Wan, MD, Michael T. Longaker, MD, MBA*

*Stanford University, Stanford, CA, USA.*

**Purpose:** Distraction osteogenesis (DO) promotes endogenous bone formation across a mechanically controlled environment, providing anatomical and functional replacement of deficient tissue. The application of DO, to the appendicular skeleton, has revolutionized the treatment of many congenital and acquired defects. Here, we describe the development of a novel mouse distraction model for the tibia.

**Methods:** Tibial distraction devices were manufactured using computer-aided design (CAD) software (SolidWorks) and 3D-printing (AW3D AXIOM 3D Printer). One 0.6 mm hole was drilled 3mm anterior and one 3mm posterior to a line dividing the tibial crest. An osteotomy was performed at the tibial crest using a diamond disc saw (Brasseler, Inc.). Distraction plates were secured with insertion of tight fit 0.65 mm screws (McMaster-Carr). Animals were divided into four groups: sham (exposure of the tibia and device placement without osteotomy), fracture (osteotomy without distraction), acutely lengthened, and gradually distracted. The gradual distraction protocol consisted of a 5-day latency period after the initial osteotomy and fixation of the distraction device, followed by 10 days of distraction at a rate of 0.15 mm every 12 hours, and 28 days of bone consolidation and remodeling. For our acute lengthening protocol, a 3.0 mm lengthening was performed following a 5-day latency period, with a consolidation period ending at 43 days post-operation.

**Results:** Bone successfully regenerated within the surgically created gap using the novel distraction device. Micro computed tomography (CT) images of the sham group presented native, unperturbed bone, while the acute lengthening group images showed the absence of bone regeneration at the site of the osteotomy. Bone regeneration occurred in the fracture group and the gradual distraction group. Upon quantitative analysis, the bone volume per tissue volume (BV/TV) (**P<0.001**) and callus volume (CV) (****P<0.0001) were significantly higher in the distraction group compared to the sham group. Finally, histological staining through Movat Pentachrome determine the tissue types present within the gap of the four groups. Pentachrome staining of the fracture group stained for fibrous tissue at the site of the osteotomy. Pentachrome staining of the fracture group indicated an overt presence of cartilage, and the staining in the distraction group showed the formation of new bone.

**Conclusions:** We have developed a new model for long bone distraction osteogenesis in the mouse. Future work will include applying this model to investigate the mechanisms underlying bone regeneration, and potential therapeutics that can quicken regeneration.