This entity is poorly understood. Therefore, we attempted to quantify the functional disturbance in patients with large cranial vault defects and changes after cranial vault reconstruction using accepted functional analysis.

**METHODS:** Patients with large cranial vault defects (>50cm²) were studied preoperatively and postoperatively (6 months) after cranial vault reconstruction using both: 1) Cognistat Active Form and 2) The FIM instrument (Functional Independence Measure) (n=35). Cranial vault reconstructive techniques varied from split cranial bone to alloplastic implants (PEEK) to titanium implants. Complications, reoperations, and patient scores on both outcome instruments were recorded.

**RESULTS:** Of the 140 patients treated with decompressive craniectomies, 35 with large cranial defects were studied. Defects ranged from 55cm² to 110cm² with a mean of 65cm². Reconstructions were: Split cranial bone (74%); alloplastic implants (PEEK) (15%); titanium implants (11%). Timing of postoperative symptom improvement varied with a range of 1 week to 3 months. Cognisant assessment showed functional improvement in 85% of patients undergoing cranial vault reconstruction; mean preop score 38 ± 9 and postop score of 69 ± 11. FIM also showed improvement (score=16 meant total dependence and score 126 meant complete independence): when comparing total preoperative 38 ± 7 to postoperative 98 ± 1 scores. Cognitive scores improved from 11 ± 4 to 26 ± 10 and Motor from 27 ± 10 to 71 ± 10. Type of reconstruction was not a determinant for functional improvement. Split calvarium was the longest procedure but had the least complications. In 2 patients, implants were removed due to infection and Syndrome of Trephined returned. Symptoms once again resolved after the patients underwent a second cranial vault reconstruction.

**CONCLUSIONS:** Syndrome of the Trephined occurs more frequently then previously described in post-traumatic patients with large cranial vault defects; Cranial vault reconstruction leads to symptomatic improvement in large number of patients.

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**Identifying New Mutations Of Fgfr1a After CRISPR/Cas9 Genome Editing**

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**PURPOSE:** Mutations in FGF receptor 1 are associated with numerous inherited skeletal disorders. We aim to develop a new zebrafish model of fgfr1a deficiency to study molecular mechanisms causing abnormal skeletogenesis. We used CRISPR/Cas9 genome editing method, that provides the ability to introduce heritable mutations in the gene encoding of the protein of interest. Here we aim to characterize an array of mutations within fgfr1a, generated by CRISPR/Cas9 technology ultimately to assess the effect of each mutation on cranium development.

**METHODS:** A CRISPR-fgfr1a constructs were used to edit the fgfr1a gene close to the P252R position frequently mutated in patients with Pfeiffer syndrome. Each identified allele was recovered as heterozygote and used for breading to obtain next generation of homozygote mutants. For genotyping, the genomic DNA was isolated from a small fragment of zebrafish caudal fin. Two different sets of primers were designed for PCR amplification of the targeted DNA. The product size was evaluated by electrophoresis on 3.5% MetaPhor agarose gel and selected samples were Sanger sequenced for conformation.

**RESULTS:** Nine different lines were initially characterized by allelic changes in the genomic sequence. The following mutations were recovered: three frameshift caused by deletion of 20 base pair (bp), 17bp and 13bp. These mutations cause changes in the reading frame and the premature termination of protein synthesis, which presumably leads to loss of fgfr1a function. In addition short, in-frame insertion of 6bp and deletion of 3bp were recovered. In this category, we also identified a small, in-frame rearrangement of genomic sequence, which consists of small deletion and substitution within the targeted region. No mutations have been found in fgfr2 or fgfr3 in any of the identified mutant lines.
CONCLUSION: The CRISPR/Cas9 method targeted to a highly conserved sequence of fgfr1a introduced a diverse array of mutagenized alleles providing the opportunity to investigate suture development in correlation with new pathologic alleles. These mutations are heritable and despite the high sequence homology among genes encoding Fgf receptors, no off-target mutations have been identified to date. Initial characterization of identified alleles will focus on embryonic stages to assess the effect of mutation on Fgf signaling target genes. This analysis will be complemented by histology of zebrafish head to assess the cranial suture development and maintenance of juvenile and adult animals.

An Analysis of Bleeding Complications in Plastic Surgery

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PURPOSE: Our aim was to identify patient characteristics and procedures associated with bleeding complications during plastic surgery.

METHODS: The American College of Surgeons National Surgical Quality Improvement Program (NSQIP) database was queried to identify all primary plastic surgery procedures from 2008 to 2013. Patients with bleeding complications as defined by NSQIP were identified. Patients who had a documented bleeding disorder were separately identified. Procedure CPT Codes, patient characteristics, and surgical outcomes were abstracted and analyzed to determine those procedures and conditions associated with bleeding complications. An analysis of co-morbidities, peri-operative characteristics, and post-operative complications between bleeding and non-bleeding cohorts was performed using a non-paired, 2-tailed t-test and a chi-squared test with Yates correction.

RESULTS: Of 59,184 cases identified, 1261 (2.1%) experienced bleeding complications. Regarding co-morbid conditions, 18.2% of patients had diabetes, 41.8% had hypertension, and 6.7% had bleeding disorders in the bleeding group compared with 7.4%, 25.9%, and 1.5% in the group without bleeding complications (p<0.0001). The most common primary procedures associated with bleeding complications were breast reconstruction with a free flap (20.7%) and myocutaneous trunk flaps (13.1%). The most common concurrent procedures associated with bleeding complications were breast oncology procedures (35.3%) and enterolysis (1.9%). The most common non-bleeding complication was difficulty weaning the patient off the ventilator. Twenty-five patients (2.0%) with bleeding complications died within 30 days of the procedure. Of the primary plastic surgery procedures identified, 953 (1.6%) patients carried a pre-existing diagnosis of bleeding disorder. The two most common primary procedures performed in this group were myocutaneous trunk flaps and reduction mammoplasty. The rate of bleeding complications in the group with a pre-existing bleeding disorder was more than four times the rate of bleeding complications for those without a bleeding disorder (8.9% vs. 2.0%, p<0.01). In addition, the rate of other non-bleeding complications was significantly higher in the cohort with a bleeding condition (1.29% vs. 0.35%; p<0.01). The most common non-bleeding complications in this cohort were prolonged ventilation requirement (2.9%) and septic shock (2.9%).

CONCLUSIONS: Plastic surgery procedures have an overall low rate of post-op bleeding (2.1%). Bleeding most commonly occurs with flap reconstruction, specifically breast and trunk flaps. A pre-operative diagnosis of hypertension, diabetes, or bleeding disorder was associated with increased incidence of post-operative bleeding complications. Two percent of patients undergoing plastic surgery procedures during our period of study had known pre-operative bleeding disorders. As these patients exhibit a significantly higher rate of post-operative bleeding as well as overall post-operative complications, recognition and appropriate management pre-operatively, potentially including risk stratification and a multi-disciplinary approach, may represent a realistic method for reducing complications in this cohort when undergoing plastic surgery procedures.

Ultrasound-mediated on-demand release from ionically cross-linked hydrogel: New approach for targeted Immunotherapy in Vascularized Composite Allotransplantation