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**INTRODUCTION:** The utilization of virtual surgical planning in pediatric reconstructive surgery has the potential to decrease intraoperative times with increased precision and improved patient outcomes. Such technology has been implemented in the creation of customizable, patient-specific three-dimensional printed tools to be used as intraoperative references. During open cranial vault reconstruction, three dimensionally designed templates have been used to guide osteotomies during calvarial remodeling. However, the final fixation of the bone is often subjective, relying on the surgeon’s expertise to restore the normative skull shape. Positional variations and miscalculations can sacrifice the symmetry of the cranium and threaten cosmetic outcomes. The recent development and implementation of three-dimensional printed positioning guides aim to improve this variability in reconstruction. Here, we describe a novel positioning guide design and its use in cranial vault reconstruction.

**MATERIALS/METHODS:** Virtual surgical planning was performed on patients diagnosed with craniosynostosis. A normative age-matched pediatric skull was superimposed onto a reconstructed DICOM digital patient image to guide the extent of repositioning. A novel, customized positioning guide was designed to fixate planned bony reconstruction with two goals in mind. The first being a solid articulation with reference skull landmarks with anchor holes articulating with the uncut portion of the skull. The second, novel feature, is a “tongue and groove” design that incorporates moving bony segments into the three-dimensional printed positioning guide. This articulation allows for the osteotomy segments to insert into the positioning guide and securely hold the bone in the precise, planned location allowing for accurate fixation.

**RESULTS:** The novel positioning guides have been implemented in two different case types, cranioplasty for sagittal craniosynostosis and fronto-orbital advancement for unilateral craniosynostosis. The novel tongue and groove feature allows for significant stability of the bone flaps, while resorbable plates are placed and fixated. Intraoperative measurements of the 3D printed guide and bony position matched precisely with the planned dimensions and gaps. The overall precision of the orientation and angulation of the bone flaps in relation to the VSP was preserved.

**CONCLUSIONS:** This is the first report of a customized positioning guide that has a novel feature of directly articulating with the bone to allow for objective fixation of remodeled bone in craniofacial reconstruction. Although there is a need for more data on both short and longer term outcomes with respect to the use of positioning guides for craniosynostosis, thus far, these cases have shown the successful implementation of this positioning guide with excellent surgical times and outcomes.

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**3D Transglutaminase Fibronectin Hydrogel Therapy for Healing of Chronic Irradiated Porcine Skin Wounds**

**Presenter: Anjali Raghuram, MD**

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**PURPOSE/BACKGROUND:** Chronic irradiated wounds are characterized by incomplete healing, with no effective therapies reported for the treatment of cutaneous radiation injury. Our group previously demonstrated that fibronectin, a key extracellular matrix glycoprotein involved wound healing, is significantly downregulated in radiation-damaged skin. We further found that an enzymatically cross-linked hydrogel is a suitable construct for sustained and incremental fibronectin release. Our present objective was to investigate the application of this fibronectin hydrogel...
dressing for the treatment of irradiated wounds in the clinically relevant porcine irradiated wound model.

**METHODS:** We created a chronic irradiation skin injury model in female Yucatan minipigs. Six 1-month-old minipigs underwent irradiation of the right dorsolateral neck region for five consecutive days in 5.5 Gy fractionated doses (total: 27.5 Gy). Following irradiation, the minipigs were allowed 6 weeks of recovery for chronic irradiation skin changes to develop. After recovery, 1 cm × 1 cm full-thickness wounds were created in the irradiated fields. After wound creation, 100 μl of fibronectin hydrogel was topically applied on experimental wounds, and 100 μl of phosphate-buffered saline hydrogel was applied on control wounds. Wound photographs were taken at weekly time intervals to calculate the percentage of wound closure relative to original wound size. Tissues isolated from the wound areas were evaluated histologically for wound healing quality and analyzed for gene and protein levels of radiation injury mediators with quantitative RT-PCR (RT-qPCR) and ELISA.

**RESULTS:** Wounds treated with fibronectin hydrogel demonstrated significantly faster wound closure and decreased scarring than wounds treated with phosphate-buffered saline hydrogel. By postoperative day 21, the mean percentage of wound area relative to original wound size was significantly higher in the control wounds (20.5 ± 2.6%) than in the fibronectin-treated wounds (4.3 ± 0.9%). By postoperative day 28, the mean percentage of control wound area was 6.1 ± 2.7% while all fibronectin-treated wounds were fully healed. Picrosirius red staining demonstrated that the fibronectin-treated wounds had decreased total scar area (10.3 ± 2.3 mm²) compared with control wounds (37.7 ± 3.2 mm²). In addition, fibronectin hydrogel treatment was associated with decreased levels of radiation-induced inflammatory mediators, TGF-β1 and SMAD3. RT-qPCR of tissue collected from fibronectin-treated wounds had significantly lower mRNA levels of TGF-β1 (0.40 ± 0.07) compared with levels in control wounds (1.0 ± 0.10). Similarly, RT-qPCR data revealed that relative mRNA levels of SMAD3 were significantly lower in fibronectin-treated wounds (0.34 ± 0.08) than in control wounds (1.0 ± 0.18). Lastly, protein level correlation with ELISA found significantly lower TGF-β1 concentrations in fibronectin-treated wounds (2682 ± 515.83 pg/mL) compared with control wounds (5245 ± 700.08 pg/mL).

**CONCLUSIONS:** Our novel hydrogel therapy functioned as a moisture-rich dressing and bioactive compound carrier. This dressing addresses irradiated skin fibronectin deficiency with topical glycoprotein supplementation, leading to improved rate and quality of chronic irradiated porcine wound healing.

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**Topical Antibiotic Elution in a Collagen-rich Hydrogel for Healing of Infected Wounds**

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**PURPOSE:** Chronic wounds challenged by biofilms have an impaired immune and healing response. Systemic antibiotics are less effective because of decreased blood flow and bioavailability to biofilm challenged wounds; a 10–1000 times increase in standard antibiotic concentration is necessary for treatment.

Collagen-rich hydrogel (CHG) is simple to manufacture from human cadaveric tendons. The material demonstrates a stable three-dimensional polymeric network, strong biocompatibility, and neovascularization enhancement that makes it a promising medium for sustained therapeutic delivery. CHG enhanced with antimicrobials has not been studied as a material for local biofilm disruption. This study examined a ciprofloxacin/collagen-rich hydrogel (CHG-ABX) preparation for the treatment of *Pseudomonas aeruginosa* challenged wounds in vivo.

**METHODS:** In total, 68 mice were divided into four groups: no infection and no CHG treatment (Control), infection without CHG treatment (Infection Only), infection with CHG treatment alone (CHG Only), and infection with ciprofloxacin-enriched CHG (CHG-ABX). Five millimeter skin excisions were performed on the animals’ dorsum and stented open. On postoperative day (POD) 2, infection groups were inoculated with cultured *Pseudomonas aeruginosa* biofilms. POD 4, 2% collagen-rich hydrogel, with or without 2 mg/ml ciprofloxacin, was applied. Wound dressings and hydrogel were replaced every other day until skin harvest days on POD 7, 10, 12, 14, or 17. Rate of wound healing was visualized by wound photography and Hematoxylin-eosin staining. Wound length was defined as the distance between intact hair follicles and a continuous basement layer. Healed length was defined as a percent of total wound length with keratinocyte return. Sterile, cardiopuncture, and blood draws were submitted for blood culture and diagnostic laboratory values.