A Novel Murine Model of Chronic Ischemic Cutaneous Wound Healing
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INTRODUCTION: Chronic, ischemic wounds present immense clinical challenges by way of limited treatment options and potentially catastrophic complications. Various murine models which represent human cutaneous injurious states exist, including full thickness wound healing, pressure ulcers, ischemic flaps, burns, and radiation injury. We describe a novel model which we propose as a surrogate for chronic ischemic cutaneous wounds, as evidenced by a persistently patent wound defect and surrounding viable, yet relatively ischemic, wound border.

METHODS: Following dorsal depilation, C57BL/6 mice underwent complete excision of a 12mm diameter full-thickness skin graft which was subjected to a full-thickness wound centrally via 6mm punch biopsy. The resultant ring of tissue was rotated 180°, re-inset into its harvest site, and secured with 8x 5-0 silk sutures. Macroscopic and dermatoscopic imaging as well as scanning laser doppler flowmetry (SLDF) monitoring was carried out alongside routine dressing changes. Wounds were harvested at day 30 for standard and immunofluorescent histology.

RESULTS: All grafts took completely by day 14. All wounds remained patent throughout day 30. SLDF demonstrated relatively decreased perfusion in the wound penumbra. Histology exhibited patent wounds with ischemic borders, further confirmed via relatively decreased CD31 and Ki67 immunoreactivity.

CONCLUSION: A novel mouse model of chronic ischemic wound healing is described. The phenotype of this disease state is validated via gross, histological, and SLDF analyses. Investigations employing this model may serve to distinguish therapeutic means of improving perfusion and/or tissue regeneration in the context of wound healing.

Comparative Cytokine Profiling of Wound Tissue Homogenate From Irradiated and Non-irradiated Skin
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INTRODUCTION: Cutaneous radiation injury is an inadvertent side effect of targeted radiotherapy for cancer treatment. Operating in skin which has been subject to radiation damage is often necessary in oncoplastic reconstruction, yet poses inherent risk of adverse wound healing outcomes. Inflammation, mediated by cytokines, is one factor contributing to impaired tissue fidelity following radiation injury and wound healing. Herein, we compare the cytokine profiles of wound tissue from non-irradiated and irradiated murine skin.

METHODS: CD1 nude mice were subjected to 30Gy radiation to the dorsum(fractionated in 5Gy doses), with control receiving no irradiation. Mice received full-thickness, dorsal excisional splinted wounds within either irradiated or non-irradiated sites. Tissue was harvested, enzymatically digested, filtered, and centrifuged prior to aspiration of homogenate-supernatant for analysis. Luminex® 48-plex cytokine analysis was carried out to profile cytokine levels, performed with 2 technical replicates, normalized by BCA assay, and reported as absolute and fold-change values of averaged median fluorescent intensities (MFIs) between groups.

RESULTS: The majority of the 48 cytokines in the panel were elevated in irradiated-skin wounds vs. control-skin wounds, with the greatest fold change observed in EOTAXIN/CCL11(MF:395.96- >5385.71,13.6x), MIP1A/CCL3(MFI:564.71- >7067.71,10.1x), and MIP2(MFI:6266.96- >3659.46,5.8x). The only exceptions in which control skin wounds exhibited relatively higher levels was for that of IL-22(5.8x), IFNγ(3.2x), and IL-18(2.6x).

CONCLUSION: The inflammatory profile of wound tissue, as measured by cytokine analysis, is elevated in irradiated skin compared to control. Key cytokines elevated in response to radiation may be studied further to gain insight into pathophysiology and potential therapies for radiation damage and wound healing.

Craniopagus Separation Using a Novel Tissue Expander Design
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INTRODUCTION: Craniopagus twins occur at an incidence of 1 in 1.6-2.5 million births. The authors present their successful surgical approach to cranial separation and reconstruction in craniopagus twins.

METHODS: Babies A and B are female twins diagnosed with angular partial craniopagus. The occipital region of Baby A was joined to the left parietal region of Baby B. They demonstrated connection of the scalp, calvaria, and dura; they also had a venous fistula connecting the two sinus systems. Superiorly, the fused calvaria was a thick, rigid strip of bone, which was selected as a base for tissue expansion. A novel wedge-shaped tissue expander with a thin crescentic base was designed. At 6 months, it was placed in the subgaleal plane at the cephalad bony fusion point to gain soft tissue for reconstruction. Tissue expansion occurred over 4 months. At 10 months of age, the infants underwent cranial separation, venous fistula ligation, duraplasty, cranioplasty, and successful soft tissue closure using only native expanded scalp.
RESULTS: The twins underwent tissue expansion without complication; they had successful cranial separation at 10 months of age. Scalp flaps were of the exact shape and dimension required for soft tissue coverage; an aesthetically pleasing result was achieved.

CONCLUSION: Craniopagus twin anatomy should be closely studied to assess candidacy for separation and to determine what anatomic traits may be leveraged for reconstruction. In the presented case, the interplay between bony anatomy and tissue expansion allowed for tissue expansion at a young age, thereby expediting definitive separation.

Dermal Iron Chelation Reduces Indirect Radiation Injury
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INTRODUCTION: Indirect oxidative damage is more injurious to tissues than the preceding direct DNA damage caused by ionizing radiation. In studying deferoxamine’s (DFO) effect on radiation-induced fibrosis (RIF) of the skin, much of the focus has been on HIF-1α stabilization and healing through neovascularization. DFO’s antioxidant conserving effects have been under elucidated, even though reactive oxygen species (ROS) production is a well-known cause of local inflammation and fibrosis. Ferric iron is a reactant for Fenton-based chemistry and subsequent ROS generation. This study sought to investigate the effects of removing this reactant via chelation of labile dermal iron prior to irradiation (IR).

METHODS: CD-1 nude mouse dorsal skin was treated with transdermal DFO either prophylactically (PPxDFO), or during a 2 week IR regimen (IRDFO) (30Gy fractionated into 6 sessions). Skin was harvested 24h after the last session for the detection and quantification of oxidative stress biomarkers.

RESULTS: DFO treatment reduced dermal iron content (p<0.0001), IR increased 8-Isoprostane, a lipid peroxidation product, but iron chelation inhibited this increase (p<0.0001) with PPxDFO having the greater treatment effect over IRDFO (p=0.0082). Active glutathione (GSH) stores were spared with iron chelation (p<0.0001) and PPxDFO was more efficient than IRDFO (p=0.0004). p53 mediated apoptotic protein BAX was expressed in higher amounts following IR but decreased with DFO treatment (p<0.0001), particularly PPxDFO compared to IRDFO (p<0.0001).

CONCLUSION: Iron chelation decreases radiation-induced ROS production in the dermis (evidenced by oxidative damage biomarkers, preserved antioxidant stores, and decreased apoptotic protein quantities.)