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Title: Repair of Radiation Damage in a Novel Skin Injury Model with Microstructural Fat Grafting

Introduction: Anecdotal clinical reports suggest that subcutaneous fat grafting can ameliorate radiation skin damage. Adipose derived progenitor cells may play a role in this process. In order to study this phenomenon, we have developed a novel mouse model of radiation-induced skin injury and used low pressure, high pass fat transfer (Coleman method) to deliver lipoaspirate beneath the irradiated skin.

Methods: The dorsal skin of adult wild-type FVB mice was isolated with a low-pressure, non-ischemic clamp and exposed to a single dose of 45Gy XRT (dose determined through preliminary experiments). Skin changes were assessed by insonation, gross examination, H&E, and immunohistologic (COX-IV stains) evaluation every other week up to 6 weeks after irradiation. Human lipoaspirate was harvested from healthy female donors and processed (Coleman method). Refined fat was transferred (1cc syringes) for immediate transplantation. Six weeks after XRT, mice with visible partial thickness radiation ulcers were infiltrated subdermally with 1.5mL of human fat using an 18-gauge Coleman cannula (fan-like pattern over mouse dorsum, 0.033mL fat injected/ pass). Controls were not irradiated. All animals were used in strict accordance to protocols approved by the NYU institutional animal care and use committee (IACUC).

Results: All mice tolerated irradiation. Visible erythema, dermal thickening and skin changes were observed at each post-irradiation time point. Sirius red staining of skin biopsies demonstrated increased collagen and fibrosis of the dermal layer. Doppler analysis also demonstrated decreased dorsal skin perfusion. Human fat xenograft administration yielded only minimal inflammation in control and treatment groups alike. Whole mount analysis showed vascular infiltration and incorporation of human tissue elements, indicating that vascularity was human-derived. Histological analysis demonstrated vascularized viable human adipose tissue with nominal peripheral fat necrosis and fibroblastic infiltration. By gross examination, fat grafting resulted in rapid improvement in XRT skin changes compared to controls.

Conclusion: This novel murine model of radiation injury is the first to limit injury to the skin and reveals consistent, nonlethal dermal changes similar to human injury. Xenogeneic fat transfer incorporated into the host animal and was not acutely rejected. Lastly, subdermal fat grafting improved overlying irradiated skin quality and promoted ulcer repair.