**AIM:** To examine the use of CD24 in enhancing the wound healing process.

**METHODS:** An incisional model of wound healing was used and wound healing was studied in wild-type (WT) mice treated by subcutaneous injections of CD24 derivatives from bacterial and mammalian cell sources.

**RESULTS:** 4 cm long full-thickness skin wounds were incised on the back of mice. The mice were locally treated by subcutaneous injections of CD24 derivatives from either bacterial or mammalian cell sources and compared to untreated mice. Wounds were histologically analyzed and scored, based on the degree of cellular invasion, granulation tissue formation, vascularity, and re-epithelialization. In the treated mice the wounds closed significantly faster then the untreated mice. No statistically significant difference was seen between bacterial and mammalian origin derivatives.

**CONCLUSION:** Increased levels of CD24, even in the normal state, may be used to enhance wound repair.

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**Remediation of Radiation Associated Vasculopathy Utilizing a Novel Angiogenic Nanotechnology**

**Presenter:** Alicia Elizabeth Snider, MD

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**INTRODUCTION:** Although radiotherapy is often necessary in oncologic management, it inhibits angiogenesis leading to devastating consequences in adjacent healthy tissues and subsequent tissue healing. Deferoxamine (DFO) has been demonstrated to bolster angiogenesis following radiotherapy, making it an attractive therapeutic to reconstructive surgeons treating oncologic patients. In current formulation, DFO would require frequent clinic visits for painful localized injections rendering it suboptimal for clinical use. This prompted us to develop an implantable nanoparticle formulation of DFO. We posit that the administration of nano-DFO will remediate an in vitro radiotherapeutic model of angiogenesis comparable to the levels achieved with standard DFO. Establishing equivalency of nano-DFO would offer promise for oncologic patients requiring both radiotherapy and reconstruction by providing a more clinically translatable single implantable dose of DFO.

**METHODS:** Three groups of irradiated (5Gy) endothelial cells (n=4/group) were treated with 50µM DFO, 50µM nano-DFO, or 100µM nano-DFO. All cultures were video recorded simultaneously with live cell imaging at 150x magnification over four hours. Hourly tubule counts, a measure of vascular architecture, was measured for each experimental group with comparison using ANOVA with \( p < 0.05 \) considered statistically significant.

**RESULTS:** We observed no statistical differences in angiogenic ability between normal DFO and nano-DFO for any doses through 3 hours. There were, however, trending increases between 50µM DFO and 100µM nano-DFO at 2 and 3 hours (\( p = 0.055 \) and 0.066). Furthermore, we observed a statistical increase in vascular networks between 50µM DFO and 100µM nano-DFO at 4 hours (\( p = 0.033 \)). Within two hours of incubation, 100µM nano-DFO cultures achieved more robust vascular architecture in comparison to the normal DFO experimental group.

**CONCLUSION:** Our data establishes in vitro angiogenic efficacy and translational dosing for a novel nano-DFO in a comparative analysis with the clinically cumbersome standard formulation of DFO. This study provides identification of a nanotechnology with a promising capacity to prevent radiation-induced tissue injury through enhanced angiogenesis with an improved method of delivery for facilitation of early clinical adoption.

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**The Enzymatic Dissolution of Human Fat**

**Presenter:** Zachary E. Gerut, MD

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INTRODUCTION: Assess the efficacy of Collagenase versus placebo in reducing the size of benign subcutaneous lipoma and assess the common short term side effects in a randomized, double-blind, placebo controlled study in subjects presenting with at least two benign lipomas of similar size.

METHODS: Collagenase derived from Clostridium Histolyticum was used in a randomized, double-blinded, placebo controlled study on a total of 19 healthy subjects, each with two biopsy-proven lipomas of similar size (one to receive drug and one to receive placebo) at two independent investigational centers (Office of Z. Gerut and Dept. of Plastic Surgery Vanderbilt Univ. Med Ctr.). An independent pharmacist prepared the research drug and the placebo for injection and the two indiscernible preparations were randomized for injection into the two lipomas of each subject; all staff including the investigators, as well as the subject were blinded.

EXPERIENCE: Patients were evaluated pre-injection and at day 1, 7, 14, 30, 90 and 180 post-injection. Efficacy was evaluated by MRI, caliper measurement and physical examination. All patients were tested for anti-Collagenase antibodies. All 19 patients that entered the study were followed to completion. There were no serious adverse events, no unsatisfactory therapeutic responses, no intercurrent medical problems. The visible surface area by caliper measurement of treated lipomas was reduced by an average of >80% vs. +2% for placebo lipoma (p=0.0001) with 11 of 19 drug-treated lipomas becoming invisible on physical examination. MRI of drug-treated lipomas revealed >50% decrease in lipoma volume while none of the placebo treated lipomas showed any significant diminution in size. In addition, one of the investigators has used Collagenase on human fat for contour modification.

RESULTS: By all employed metrics; MRI testing, caliper measurement, physical examination, the experimental drug showed significant efficacy in the treatment of lipoma. Many of the drug-treated lipomas clinically disappeared, all drug-treated lipomas showed significant diminution in size by both physical examination and MRI. All patients experienced some bruising and swelling; very few patients reported pain and in those cases, the pain was fleeting. There were no serious adverse events and none of the subjects were dissatisfied.

CONCLUSION: Collagenase is an effective treatment for treatment of lipoma as well as for the dissolution of human fat. The author has experience using the drug off label.

Oncologic Safety of Fat Grafting in Breast Reconstruction: A New Clinically Relevant Animal Model of Residual Breast Cancer

Presenter: Mayara M.A. Silva, MD
Co-Authors: Miguel Sabino Neto, PhD; Vera S. Donnenberg, PhD; Lauren Kokai, PhD; Liyong Zhang, PhD; Jeffrey L. Fine, MD, PhD; Damian Grybowski, MD; Kacey Marra, PhD; Albert D. Donnenberg, PhD; J. Peter Rubin, MD
Affiliation: Federal University of São Paulo, Sao Paulo

INTRODUCTION: Autologus fat grafting is becoming widely used for breast reconstruction. However, the bioactive adipose stromal cells have been shown in many in vitro and animal studies to promote cancer cell growth. We report a new animal model that accurately simulates the clinical scenario of reconstructive fat grafting.

METHODS: 40 female NOD-SCID gamma mice were injected with 1K MCF7 breast cancer cells in 4 sites of mammary fat pads. After tumor engraftment in 2 weeks, injections of human liposaprate prepared according to Coleman’s technique (N=20) or sterile saline (N=20, control) were performed at tumor sites. In 8 weeks, animals were euthanized and necropsied, tumor volume and mass were measured, and histological samples were assessed for presence of tumors, Nottingham histological grade, Ki67 positivity and metastatic spread.

RESULTS: In 8 weeks, all sites injected with breast cancer cells formed macroscopic tumors and all fat grafts were retained and colocated with breast cancer. Tumors from animals in the lipo group did not grow faster (p=0.54); and had lower volume (p=0.046) and lower mass (p=0.038) compared to saline group. Macroscopic invasion detected