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 subjects 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
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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...
in necropsy was higher in saline group (p=0.003). Proliferation index assessed by Ki67 positivity was significantly lower in lipo group (p=0.01). No metastatic lesion was identified in lung, liver or spleen of any animal.

CONCLUSION: Reconstructive fat grafting performed in the setting of residual breast tumor in a clinically relevant animal model does not increase tumor size, mass, proliferation or metastatic spread. This supports the oncologic safety of fat grafting for breast reconstruction after cancer therapy.

Chromatin Structure Regulation in Human Adipose-Derived Stem Cell Aging

Presenter: Ivona Percec, MD, PhD  
Co-Authors: Xiaoyin Shan, PhD; Cleresa Roberts, BS; Yemin Lan, PhD  
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INTRODUCTION: Aging and age-related diseases have been linked to both genetic and epigenetic changes. The chromatin structure is critical to the transmission of epigenetic information impacting transcription and genomic stability. Adult stem cells play a pivotal role in the maintenance of tissue and organ homeostasis during aging and are frequently exploited in regenerative medicine and plastic surgery. Although many studies have been focused on mechanisms of regulating chromatin structure in somatic cells, the mechanism in aging adult human stem cells is not well understood. We hypothesize that understanding the chromatin structure regulation of these stem cells will provide novel therapeutic strategies for both aesthetic and reconstructive applications. Towards this end, in this study we examine global chromatin structures of adipose-derived stem cells (ASCs) from young and old patients and compare them to those of age-matched somatic fibroblasts.

METHODS: Human primary ASCs and fibroblasts were isolated from 13 and 8 donors, respectively. The chromatin structure of these cells was examined with the assay for transposase-accessible chromatin using sequencing (ATAC-seq). The data was analyzed to identify genome accessible by Tn5 transposase. Principle component analysis (PCA) was used to assay chromatin structure similarities of all the samples. The Database for Annotation, Visualization and Integrated Discovery (DAVID) was used for pathway enrichment analysis of the accessible promoter regions in the genome of young and old ASCs.

RESULTS: Our data demonstrated that 1.2% of the genome in old ASCs, 1.1% in young ASCs, 0.33% in old fibroblasts and 0.51% in young fibroblasts were accessible by Tn5. PCA results demonstrated distinctively different chromatin accessibilities between ASCs and fibroblasts and specific differences between these cells with respect to aging. DAVID pathway enrichment analysis identified several pathways, including DNA damage and repair, nonsense-mediated mRNA decay, and Wnt signaling pathway, to be more accessible in ASCs from old donors.

CONCLUSION: In conclusion, our data demonstrated that genome accessibility in ASCs is overall significantly higher than in fibroblasts, consistent with their stemness phenotype. At the global level, ASCs maintain a more stable chromatin structure with advancing age compared with fibroblasts that appear more susceptible to age-related defects, consistent with our prior studies. These data support the benefits ASCs impart to regenerative medicine and will be valuable to the development of novel therapeutics.

Does Non-Smoked Nicotine Intake Increase Risk of Post-Operative Complications?

Presenter: Patrick A. Craft, DO  
Co-Author: Basil M. Michaels, MD  
Affiliation: Berkshire Medical Center, Pittsfield, MA

INTRODUCTION: The detrimental health effects of smoking tobacco are well known. Smoking tobacco increases the risks of many post-operative complications, many of which are germane to plastic surgery. The use of non-tobacco nicotine sources has proliferated in the hope that non-smoking delivery methods are safer than smoking; however, there is little data to support or refute this theory.

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