INTRODUCTION: Current tissue engineering efforts are aimed towards recreating tissues to repair those that have been lost or damaged—such as the development of in vitro 3D biomimetic platforms to recapitulate in vivo conditions. Specifically, in breast cancer research, surrounding ECM in vivo has a profound effect on malignant invasion of cancer cells and it has also been clinically observed that breast tumor tissue is denser than normal tissue. However, traditional cell culture systems employed to study tumor cell behavior are limited by the significantly different cell phenotype induced under 2D culture conditions. We have created intact functional vascularized channels in biocompatible collagen constructs with proper in vivo vascular physiology and alter collagen stiffness to study factors that influence tumor progression, and vascular remodeling.

METHODS: Type-I collagen was enzymatically stiffened with ribose solution to create a stock collagen solution. Pluronic F127 fibers, were sacrificed in the collagen, creating a central looped microchannel with a tumor spheroid embedded in the collagen bulk. A cell suspension of human aortic smooth muscle cells (HASMC) and human umbilical vein endothelial cells (HUVEC) was seeded into the microchannel. Mechanical compression testing was completed by ElectroForce-3200 Series III.

RESULTS: Confocal reflectance values showed no statistical changes of fiber length or pore area in enzymatically altered collagen, suggesting changing the stiffness would not affect bulk cell migration. Biomechanical testing of stiffened collagen revealed that 200mM of ribose dosed collagen increased the stiffness of the hydrogels to appropriate “tumor” stiffness (4kPa). After all time points, non-cancer containing constructs contained microchannels consisting of an anatomically correct robust vascular channel lining with increasing proliferation. However, in cancer constructs, degradation of the vascular lining and aberrantly organized HUVEC and HASMC were present. IHC and MPM imaging revealed the presence of breast cancer cells invading the endoluminal lining. Permeability studies using TexasRed Dextran revealed an increase of neovessel permeability correlating with increasing stiffness, suggesting metastatic potential of cancer also increased.

CONCLUSION: This model overcomes the limitations of previous 2D and 3D culture models and may be used to investigate any type of tumor cell and can lead to the further understanding of breast cancer signaling pathways, as well as potentially provide an effective platform for high throughput analysis of patient specific breast cancer cells.

Reference Citations:
1. Plewes, D., et al. Elastic moduli of normal and pathological human breast tissues: an inversion-technique-based investigation of 169 samples. Physics in Medicine and Biology. 52 (2007). 1565–76. doi:10.1088/0031-9155/52/6/002.

RESULTS of the XPAND II Multi-Center, Prospective Clinical Trial for the AeroForm Tissue Expander System used for Two-Stage Breast Reconstruction

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INTRODUCTION: Data from the XPAND II continued access clinical study are presented to confirm previously reported results for the AeroForm Tissue Expander System when used for two-stage breast reconstruction.

BACKGROUND: The XPAND II multi-center study was conducted as a continued access study under the U.S. FDA IDE regulations. The study was a multi-center, prospective, single arm study designed to confirm the results from the XPAND study, a multi-center, prospective, randomized study for breast reconstruction. In December 2016, the AeroForm device received clearance from the FDA based on the results of the XPAND trial, and adoption of this novel needle-free expansion system is underway in the U.S.
METHODS: Fifty (50) women were treated in the XPAND II study and implanted with the AeroForm device (89 devices). Study endpoint was successful completion of the second stage surgery and secondary endpoints were days to complete expansion and reconstruction, and patient/physician satisfaction. Inclusion criteria included age (18–70), BMI (<33) and tissue suitability for expansion. Following implantation, women self-administered 10cc doses of CO₂ up to three times daily. When adequate expansion was achieved, the expanders were then exchanged for standard breast implants.

RESULTS: The interim result by breast (89) with the primary endpoint (successful exchange to standard breast implant, precluding non-device related failures) is 100%. All-cause interim success is 95% with three subjects (4 breasts) failing primary exchange due to non-device related reasons (cellulitis / intolerance to antibiotics, seroma w/exposure, cellulitis / delayed wound healing). One subject withdrew from the study prior to completion of the second stage. For the 46 subjects completing the second stage surgery, median time to complete reconstruction was 112 days (range 55–494).

CONCLUSION: Results of the XPAND II continued access study build upon the previous results from the first randomized trial (XPAND) for two-stage breast reconstruction using the AeroForm Tissue Expander System. These results validate that the AeroForm patient-controlled, needle-free CO₂ tissue expander is safe and effective for two-stage breast reconstruction.

INTRODUCTION: Reconstructive failure (RF) following prosthetic breast reconstruction is often preceded by multiple complications, but there is a paucity of literature examining these sequences of events. Understanding the temporal relationships between associated complications can aid in managing patient expectations, timing surveillance, and planning interventions. We present a novel investigation of the “pedigree” of reconstructive failure, i.e. the patterns and temporal clustering of complications preceding it. Though previous authors have noted associations between complications like seroma, infection, and explantation, this is the first study to methodically explore the possible routes that lead to RF.

METHODS: We examined our prospective intra-institutional database of prosthetic breast reconstructions from 2004–2015. Patients lost to follow-up before six months were excluded. Missing variables were imputed over twenty iterations. Outcomes of interest were seroma, infection, flap necrosis, exposure, and RF defined as expander removal without replacement and/or conversion to autologous reconstruction. We mapped a complete pedigree of all complication sequences leading to RF, and analyzed the timing and interdependence of the sequential events using risk ratios, multivariate regression, and Cox regression.

RESULTS: The cohort comprised 1,867 breasts (1,225 patients). Median follow-up was 16.6 months. Complication rates and their median times-to-detection were: flap necrosis (8.7%, 21.5 days), seroma (3.1%, 27 days), infection (4.7%, 39 days), exposure (4.1%, 52 days), and RF (9.3%, 171 days).

Of the 373 breasts encountering some postoperative complication, 35.4% experienced more than one. Seroma increased the risk of subsequent infection (RR=6.52, p<0.001) and necrosis (RR=1.97, p<0.001). Necrosis increased the risk of subsequent exposure (RR=3.56, p<0.001). All complications increased risk of RF, particularly infection and exposure (RR=6.69 and RR=7.45 respectively, p<0.001). These findings remained significant after multivariate risk-adjustment.

The pedigree demonstrated three common, multi-step routes to RF: seroma, infection, RF; necrosis, infection, RF; and necrosis, exposure, RF. There was a stereotyped 14-to-21-day interval between first and second events in these sequences. If a