Purpose: Breast cancer is the third highest cause of death among all cancers in women. Patients who undergo mastectomy for tumor removal often undergo adjuvant radiation therapy and elect to have breast reconstruction. An adverse side-effect of radiation therapy is radiation-induced fibrosis (RIF), causing thickening and tightening of the tissues on the chest wall and around the reconstructed breast. This can result in pain and/or aesthetically displeasing results. Of the many studies investigating potential mechanisms for RIF production, none to our knowledge, have measured the whole-transcriptome response in local tissues around the reconstructed breast. Thus, we utilized whole-transcriptome sequencing to understand the potential expression pathways for clinical intervention.

Methods: Unilateral breast cancer patients undergoing a bilateral mastectomy with reconstruction were recruited for the current study. A total of 7 patients were recruited for this study. During the initial surgical mastectomy procedure, tissue expanders were placed in the sub-pectoral plane. Patients subsequently underwent unilateral radiation therapy of the affected breast. Approximately three months after completing radiation therapy, the tissue expanders were removed and the final definitive reconstruction performed. At this time, skin, the fibrotic capsule surrounding the expander (capsule) and muscle tissues were collected. From these samples, transcriptome-wide RNAs were extracted, processed, and sequenced. After sequence alignment, transcripts were counted and filtered, requiring at least ten counts per gene to be included for subsequent analyses. Differential expression analyses for each tissue type, between non-radiated and radiated samples, were performed incorporating RIN score, tissue type, and radiation status into the statistical model. Using the Gene Ontology (GO), an enrichment analysis was performed on the significant genes from the differential expression analyses.

Results: After applying quality control metrics, 39 samples remained. On average, samples had an alignment of 84.5%, quality scores above 32, and RIN value of 7.5. The total number of significant genes and GO terms identified for the skin, capsule, and muscle was 29, 39, 48 genes; 25, 29, 42 GO terms, respectively. In skin tissue, multiple keratin genes and TCHH were identified, contributing to the GO process: keratinocyte differentiation, cornification, intermediate filament organization, hair follicle morphogenesis. Significant genes in the capsule tissue included collagen genes (COL4A5 and COL6A6), SLC6A13, and CLCA2. CDKN1A and PDGFRA contributing to the significant GO process of positive regulation of fibroblast proliferation. In muscle tissue, significant genes of interest include BAX, TOP2A, MDM2, and CXCL10, which are associated with processes such as DNA damage and response to radiation.

Conclusion: In the current study, we have identified differentially expressed genes in the skin, fibrotic capsule, and muscular tissue that received radiation therapy. Signs of typical side effects can be observed by the presence of genes involved in DNA damage and fibroblast proliferation GO processes. Additionally, significant genes were identified that are involved in biological processes not previously associated with RIF, such as intermediate filament organization and hair follicle morphogenesis. These results contribute to a deeper understanding of RIF development in breast cancer patients receiving radiation therapy and may advance the potential for improving RIF mitigation.

QS9

Host Biofilm Interaction In Breast Implant Illness

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Purpose: Breast Implant Illness (BII) is patient-described constellation of symptoms that are believed to be related to their breast implant. The symptoms described include fibromyalgia, chronic fatigue and a host of other symptoms that are often associated with autoimmune illnesses. In this work, we report that bacterial biofilm associated with

breast implant, metabolize fatty acid oleic acid present in the breast tissue milieu to oxylipins, one such oxylipin identified from this study is (10S)-hydroxy-(8E)-octadecenoic acid (10-HOME). We hypothesize that immunomodulatory effects of oxylipin 10-HOME produced by biofilm present on the implant could be correlated with BII pathogenesis.

Methods: Capsulectomy and breast implants from clinically indicated procedures for patients requesting prosthetic removal were collected using clinical parameters outlined in previous studies, and questionnaire screened for the commonly reported symptoms associated with BII. Predictive variables included age, diabetes status, co-morbidities, nature and duration of implant. Scanning electron microscopy (SEM), Wheat Germ Agglutinin (WGA) and 16SrRNA sequencing were used for bacterial biofilm bacterial identification. 10-HOME was quantitated through targeted and untargeted lipidomic analyses using LC-MS-MS.

Results: Sixty eight Implant, associated capsules and breast tissue specimen were collected for BII (n=46) and two control groups, group I, (non-BII, n=14) patients with breast implants, no BII symptoms. Group II (normal tissue, n = 8), patients without an implant, whose breast tissue was removed due to surgical procedures. Bacterial biofilm was detected through SEM in both BII and non BII cohorts. However, WGA analysis (quantitative analysis) indicated increased abundance of biofilm in the BII cohort (n=7, p=0.0036). 16SrRNA (genomic) sequencing identified increased abundance of Staphylococcus epidermidis (Fisher's exact test, p<0.001) in the BII group (63.04%) compared to non-BII group (14.3%) and the normal group. The BII group was 9.8 times significantly more likely to have Staphylococcus epidermidis colonization compared to the non-BII group (p=0.003, logistic regression), compared to normal, it is 17.4 times significantly more likely to have Staphylococcus epidermidis (p=0.0021). Elevated levels of 10-HOME BII compared to non-BII samples, (p < 0.0001) were observed through mass spectrometry. Positive correlation was observed between bacterial abundance and concentration of 10-HOME in BII subjects (R2=0.88). Similar correlation was observed in BII subjects with Staphylococcus epidermidis (R2=0.77).

Conclusion: This study investigated the biofilm hypothesis of breast implant illness through a host-pathogen interaction. The breast microenvironment led to formation of biofilm derived 10-HOME from host oleic acid. The study provides the first evidence of a possible correlation between bacterial biofilm and biofilm derived 10-HOME in the context of 10-HOME. In consideration of reports of biofilm association with other metal implants, the findings of this study can possibly explain autoimmune response associated with those implants.

QS10

TOWARD AN OBJECTIVE OUTCOME IN FACIAL REJUVENATION SURGERY: AN EYETRACKING STUDY

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Purpose: The availability of an objective outcome measure for facial reconstructive surgery remains elusive. Evaluations submitted by external raters or by patient self-report are subjective, and may unreliably convey how one is perceived by others. We are interested in observers' instantaneous responses to the human face. The goal of modern facelift and associated procedures for facial rejuvenation are to achieved subtle differences that lead to the perception of youth and attractiveness, yet the observer cannot pinpoint what exactly have been done to the patient's face. We explored the visual markers that lead to differential perception of patients before and after facial rejuvenation surgery (high SMAS facelift, neck lift, fat grafting, brow lifts and blepharoplasty).

Methods: 40 images were obtained which portrayed pre and post operative photos of patients who underwent high SMAS facelift, fat grafting, and browlifts and blepharoplasty for facial rejuvenation. Photographs were obtained before and after surgical correction (>3 months postop). 40 observers examined the images while an infrared eye-tracking camera recorded their eye movements. The observers were then asked to rate the image for character attributes (attractiveness, trustworthiness, sociability, healthy, and capability, 1-7 scale, and also estimate the age of the patient).

Results: (i) The surgical intervention was found to decrease observers' attention to the cervical region, but did not change how other areas are perceived significantly.(ii) The surgical intervention was found to significantly increase the character ratings for all five attributes compared to pre op controls: (sociable 3.53 to 4.18, trustworthy 3.85 to 4.20, attractive 3.34 to 3.3.90, health 4.07 to 4.61, capable 3.91