**Thesis Project Portfolio** 

## ECM Hydrogel Derived from Decellularized Adipose Tissue for Adipose Derived Stem Cell Differentiation to Augment Breast Reconstruction (Technical Report)

Evaluating The Sociotechnical Factors Behind Racial and Ethnic Differences in Utilization of Breast Reconstruction Services Post Women's Health and Cancer Rights Act (WHCRA) (STS Research Paper)

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## **Executive Summary**

A woman in the United States has a 1 in 8 chance of developing breast cancer at some point in her life. Consequently, 100,00 U.S. women each year require a mastectomy, the surgical removal of one or both breasts, to achieve adequate locoregional disease control. Better prognosis and a decline in breast cancer mortality rates over the years have shifted the focus from the treatment of breast cancer to post-mastectomy care. From 2009 to 2014, the rate of breast reconstruction post-mastectomy for women ages 18 years and older increased by 62%. The increasing trends have led to greater demands for safer and more optimized procedures for breast reconstruction, an important process in many breast cancer patients' healing journeys. Improved postoperative quality of life is a goal of many breast reconstruction techniques, both physically and psychologically. As a result, both the technical and the science, technology, and society (STS) project of the study aims to answer the overarching question: how can the quality of life for recipients of bread reconstruction be improved and sustained?

To address the demands and different types of mastectomies, there are several common strategies for soft tissue replacements, which include autologous tissue transfer (ATT) and prosthetic implants, which are augmented by autologous fat grafting (AFG). However, there are limitations associated with AFG that include variable and unpredictable volume retention rates, and fat necrosis in which the injected fat dies. One of the most promising methods for soft tissue repair is tissue engineering using decellularized biological biomaterials. Thus, the technical project aimed to develop and characterize a decellularized adipose tissue (hDAT) extracellular matrix (ECM) hydrogel seeded with adipose-derived stem cells (ADSCs) that are able to effectively differentiate into mature adipocytes, providing controlled fat growth to improve traditional fat grafting procedures post-mastectomy. In this study, it is demonstrated that the hydrogel is a soft and elastic platform that supports cell viability and promotes adipogenesis. Ultimately, this approach can be applied clinically to improve or replace traditional fat grafting procedures post-mastectomy or lumpectomy, thus improving the overall quality of life physiologically for patients.

However, the quality of life extends far beyond the scope of the technical project alone. There are many long-term psychological consequences of breast mastectomy that impact identity, self-satisfaction, and overall quality of life. Due to the significant outcomes of breast reconstruction on quality of life, it must be accessible to all eligible patients. The Women's Health and Cancer Rights Act (WHCRA) was enacted in the U.S. to address accessibility by mandating insurance coverage for breast reconstruction post-mastectomy (Xie et al., 2015). Despite the importance of the WHCRA, the effects remain poorly understood, and the accessibility of breast reconstruction remains limited for non-white patients. The significant implications of breast reconstruction stressed the need for a policy review of the WHCRA. The STS paper aimed to explore potential sociotechnical factors that create or exacerbate racial/ethnic disparities in the utilization outcomes of breast reconstruction post-WHCRA mandate by conducting a policy review and comprehensive literature review. Despite the increase in overall utilization post-mandate, the racial/ethnic differences remained. In 2014, a higher utilization rate was found among white patients with differences in overall breast reconstruction utilization of 8.17%, 14.77%, and 19.03% with Black, Asian, and Native American patients, respectively. Factors such as economic status, access to insurance coverage, and quality of care have been identified as significant determinants of utilization. These factors indicate a health disparity within breast reconstruction, which necessitate a plan to address them to achieve equitable care as intended with the original WHCRA.

The results from the technical and STS project were significant, especially for future work in the field. For the hDAT ECM hydrogel, future work includes an *in vivo* mouse model using irradiated mice to mimic breast cancer treatment conditions to test for adipogenesis, immune response, and integration into host tissue. The characterization of the hydrogel can be improved by including mechanical testing for Young's modulus to observe how stiffness affects ADSC differentiation into adipocytes. Regarding the ST'S exploration of the WCHRA, the policy review can inform future legislation or reform efforts on the underlying reasons behind why there is such a difference in receipt of breast reconstruction and potential ways to address and reduce such differences. The findings from both projects would address current limitations to breast reconstruction and provide sustained long-term outcomes to ensure a good quality of life for patients who receive it.