Undergraduate Thesis Prospectus

# Improving Patient Outcomes for Breast Reconstruction Following Mastectomy

(technical research project in Plastic Surgery)

# Personal Readjustment Following Breast Reconstruction Surgery

(sociotechnical research project)

by

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On my honor as a University student, I have neither given nor received unauthorized aid on this assignment as defined by the Honor Guidelines for Thesis-Related Assignments.

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## General Research Problem

*Following disfiguring ailments or medical procedures, how can patients' quality of life be improved?* Disfigurements from diseases, birth defects, and medical procedures can be physically and emotionally debilitating, diminishing quality of life. Families of the affected individuals typically bear burdens too, such as caregiving, medical expenses, and lifestyle adjustments (Swift & Bogart, 2021). Developments in prosthetics and surgery can mitigate the physical effects of disfiguring medical procedures. The emotional effects of disfigurement can be diminished as well. Modes of personal adjustment vary, but patients who find informal or formal networks of caring support generally improve in their emotional wellbeing.

## Improving Patient Outcomes for Breast Reconstruction Following Mastectomy

*How can complications and failure rates for post mastectomy breast reconstruction be reduced?* Breast cancer is one of the most common forms of cancer, with approximately 315,000 women being diagnosed with breast cancer annually (Siegel et al., 2012). Most cases require a double mastectomy with some patients choosing to have breast reconstruction. Breast reconstruction has an associated complication rate of 32.9% two years following implantation, and can increase if radiation therapy is utilized following surgery (Bath, 2018). Complications such as infection, capsular contraction, implant malalignment, and skin necrosis can occur. Corrections for these complications can result in the need for multiple hospital visits, surgeries, and removal of the implant (Frey et al., 2018). Novel therapeutics and surgical techniques are required to help reduce the rates of complications.

Two primary implant locations are currently utilized in breast reconstruction following mastectomy, submuscularly or with an acellular dermal matrix (ADM) scaffold. An ADM

scaffold is a sheet of decellularized dermal tissue that provides implant support, support for the overlying skin envelope, and site where native tissue and vasculature can develop. Approximately 60% of all breast reconstructions utilize an ADM scaffold (Frey et al., 2018). Complications for this repair method occur due to a lack of incorporation and native tissue replacement of the ADM scaffold. Damage and inflammation of the overlying dermal tissue reduces healing kinetics and contribute to the development of infection, seroma, and necrosis of the skin (Kim et al., 2015). Radiation therapy is commonly administered following breast reconstruction, causing further tissue damage and leads to decreased vasculature, fibrotic development, and wound healing complications. As a result of these complications, novel therapeutics and surgical techniques are required to help improve angiogenesis and native tissue development following breast reconstruction.

In my senior Capstone project, I aim developing a flowable hydrogel derived from dermal tissue to help improve vascular development and cellular infiltration into ADM scaffolds, in models of breast reconstruction. This Capstone project is being advised by Patrick Cottler, Ph.D., in the Department of Plastic Surgery. Inflammation of the overlying dermal tissue due to surgical trauma and radiation leads to a lack of intimate contact between the dermis and the ADM scaffold. We hypothesis that a flowable hydrogel will allow for more complete contact between these two layers, promoting cellular migrate into the scaffold.

Special consideration as to the application and composition of the hydrogel are required to have potential and realistic applications to breast reconstruction surgery. Given the irregularity of the surgical space geometry, the hydrogel must be injectable in between the dermal layer and ADM scaffold. Due to this non-uniformity, a pre-solidified hydrogel would not be viable. Once injected the hydrogel must polymerize so as to ensure contact between the layers. Injectability

allows for minimally invasive application to the surgical sight. The hydrogel must not cause adverse immune reactions, which will be ensured by fully decellularizing the hydrogel. The hydrogel must be easily neutralized so as to allow for quick preparation immediately prior to surgery.

To synthesize the flowable hydrogel, a commercially available decellularized matrix is obtained from the plastic surgery department at the University of Virginia's hospital. The matrix is frozen, lyophilized, ground into a fine powder, and then enzymatically digested in dilute acid, followed by neutralization to physiological pH through the addition of a dilute base and salt solution. Gelation of the hydrogel is then achieved. To test the efficacy of the flowable hydrogel, an *in vivo* murine model is utilized that mimics the environment of breast reconstruction. Half of the mice receive a dose of radiation to the dorsal skin, 12 weeks prior to implantation, to simulate the damage from radiation therapy (Dassoulas et al., 2018). Once the *in vivo* trial is complete, the implant and surrounding tissue is excised, fixed, and stained. Histological analysis is performed using a microscope, and ImageJ is used for quantification of cellular count, infiltration distance, and vessel count.

Following the conclusion of this Capstone project, we aim to have developed a hydrogel capable of *in vivo* gelation following injection. We seek to show its efficacy at improving the integration of the ADM and effective soft tissue support of the native tissue in murine models of implant-based breast reconstruction. Evidence of its effectiveness can lead to future larger animal trials, with the ultimate goal of developing a therapeutic capable of improving the recovery and outcomes of patients following breast reconstruction.

**Personal Readjustment Following Breast Reconstruction Surgery**

*How have patient's quality of life following mastectomy and breast reconstruction been improved from a treatment and social perspective?* A diagnosis of breast cancer is a life-altering diagnosis that immensely burdens patients and their loved ones. The looming threat of death and strenuous treatments is compounded by the physical effects of medical procedures. Breast cancer and mastectomy have immense psychological impacts on patients. One patient described it as a "thief that can rob us of our identity making it hard to figure out life" (Slome, 2018). Patients face emotionally arduous personal and social readjustments. Their physical recovery and emotional wellbeing require extended medical and emotional care.

The emotional distress that follows mastectomy and breast reconstruction have consequences for mental health (Kornblith & Ligibel, 2003). Mastectomy alone can cause depression, anxiety, and distorted self-image due to the altered physical appearance of the patient's body. Breast reconstruction following mastectomy can relieve impaired body image and improve mental health (Crompvoets, 2006). However, complications in post-mastectomy breast reconstruction can entail additional surgeries, severe scarring, and even complete breast removal (Frey et al., 2018). Complication rates have fallen, but not enough (Bath, 2018). Complications only worsen the already difficult journey to physical and mental well-being

While many breast cancer survivors seek to recover a sense of normality following their ordeal, their means of coping are highly diverse. Many feel the painful loss of a "sense of self and femininity," as one breast cancer patient noted (Uyen, n.d.). The effects may include impaired relationships and work life. Many women endure cycles of extended emotional distress (Kornblith & Ligibel, 2003). The caring support of spouses or other partners can make a crucial difference (Sertoz et al., 2003). Yet spouses can also cause new conflicts, straining marriages or

committed partnerships. Women who have had mastectomies are more likely to divorce than other women (Sertoz et al., 2003). Children in homes with a breast cancer survivor both endure stress and may themselves be a source of stress; assistance with childcare responsibilities can help (Brown et al., 2006).

Besides the care of loved ones, many patients benefit from support networks of other cancer survivors. Young Survival Coalition, BreastCancer.org and other support groups offer women recovery advice, social support, and interpersonal connection. BreastCancer.org tells patients that its members can "teach you how to be the women you were before cancer" (Breastcancer.org, 2018). Support groups reassure women that they are not alone. Advocacies help too. The Maimonides Breast Center promotes awareness and body positivity for breast cancer survivors by organizing events, such as a fashion shows consisting of models who have all survived breast cancer (CeFaam, 2021). A breast cancer survivor noted that one such event "opened my eyes that I should be living more and not just going through life" (CeFaam, 2021).

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