Developing a Synthetic Hydrogel for Breast Tissue Engineering

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Introduction: Current clinical approaches to repair breast damage from cancer resection, injury, or deformity focus on synthetic implants or autologous muscle grafts. While there are drawbacks and benefits to each, neither restore the function lost should the woman desire to nurse children. Tissue engineering methods have the potential to restore breast tissue volume and function that circumvent the reconstructive limitations of contemporary surgical procedures. There is a large body of research on breast tissue engineering; however, much of the research focuses on restoring breast volume rather than breast function and seek to replace the missing tissue with fat or muscle.[1] Here, we aim to develop a scaffold capable of supporting both breast adipose and glandular tissue (the main components of breast tissue) towards restoring both form and function to the breast.

Materials and Methods: Poly(ethylene glycol) diacrylate (PEGDA) hydrogels were synthesized as previously described.[2,3] All hydrogels were prepared using 10 kDa PEGDA. The hydrogels intended to replicate adipose tissue were formulated with HEPES buffer solution, 1.0% w/v eosin Y, 3.75 µL/mL 2,2-Dimethoxy-2-phenylacetophenone in 1-Vinyl-2-pyrrolidinone (acetophenone in NVP; 300 mg/mL), and 1.5 % w/v triethanolamine (TEOA). The hydrogels mimicking glandular tissue were formulated with HEPES buffer solution and 10 µL/mL acetophenone in NVP. PEGDA concentrations were varied at 6%, 8%, and 10% w/v for each formulation to achieve Young's moduli reported for breast adipose and glandular tissue, 18 kPa and 35 kPa, respectively. Compressive tests were performed at a ramp rate of 1 mm/min at various strains. Based on the resulting moduli, the hydrogel formulations that most closely recapitulated the elastic properties of fat and glandular tissue were used to form whole breast tissue composite structures. These composites were constructed by embedding "glandular" hydrogels within "fat" hydrogels. Three composite groups were formed by varying the number of hydrogel "glands". The composites were then subjected to compressive tests as described above to evaluate their moduli in relation to that of whole breast tissue.

Results and Discussion: Hydrogels formed with eosin Y, TEOA, and 10% w/v PEGDA had Young's moduli of 17.3 ± 2.03 kPa, similar to that measured for breast fat tissue (18 kPa), while 8% w/v PEGDA hydrogels formed with a greater concentration of the acetophenone solution but without eosin Y or TEOA had Young's moduli of 35.2 ± 2.28 kPa, similar to that of glandular tissue (35 kPa). The Young's moduli of the tissue engineered breast constructs were all within 5-25 kPa, the reported range of the Young's modulus for whole breast tissue (Fig. 1).

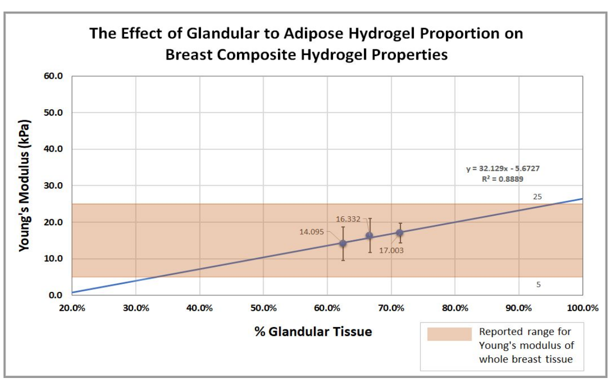

Figure 1. The proportion of "glandular" hydrogels within the tissue engineered construct reveals a trend where the amount of glandular tissue included increases the stiffness of the breast. Line shows levels for actual breast tissue, which is within.

Conclusions: In this study, we have developed a biomechanically relevant hydrogel scaffold with PEGDA hydrogels at concentrations demonstrated to support cell viability. In future work, we will evaluate our scaffold's ability to support adipocytes and luminal epithelial and myoepithelial cells (main components of glandular tissue).

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References:

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