BIOMEDICAL ENGINEERING
Carnegie Mellon University

Ph.D. Thesis Defense
Thursday, April 27, 2017
3:00 p.m. – 6:00 p.m.
Scott Hall, 4N200

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Rapid Prototyping Tissue Models of Mammary Duct Epithelium

Ductal Carcinoma in Situ (DCIS) does not have a clinically useful indicator of malignancy, and it is often benign, except in 20% of cases. Even more important, it has a cure – removal of the affected breast. DCIS patients overwhelmingly elect for invasive therapies to escape that 20% malignant chance. Overtreatment such as this costs the patients, and it highlights the need for a DCIS model capable of distinguishing the 20% in need of treatment. Some labs have taken steps toward three-dimensional, complex, and biomimetic models of mammary tissues using a variety of endogenous and synthetic gels and 3D printing. We developed FRESH (Freeform Reversible Embedding of Suspended Hydrogels) as the first method capable of 3D printing highly biomimetic shapes from endogenous gels. Utilizing FRESH, we aim to rapid prototype models of mammary duct epithelia that are biomimetic, parametric, and capable of iterative evolution. First, we investigate the principles of 3D printers modified for extruding fluids and construct a comprehensive hardware and software platform for printing gelling fluids. Second, we apply the FRESH method to 3D print collagen and alginate hydrogels, demonstrating patency of printed vascular models, topological fidelity, and the synergistic combination of hydrogel properties in multi-material prints. Finally, we rapid prototype an epithelial monolayer by seeding a 3D printed collagen manifold, and we demonstrate maintenance of the tissue's geometry across a week of culture. We provide evidence of fidelity in prints such as an epithelial tree printed at 200% scale using unmodified collagen type I, and we investigate the combination of hydrogel properties in multi-material prints by utilizing a second hydrogel (alginate) to reinforce and preserve the fidelity of this collagen tree during handling. Our approach utilizes faster (>40 mm/s), cheaper (<$2000) hardware, and it is capable of greater geometric freedom than previously established approaches which are hindered by "overhangs". Additionally, we demonstrate superior, 99.7% printed cell viability and material compatibility (collagen, fibrin, alginate, and Matrigel®). It is hoped that this work will enable researchers to inexpensively rapid prototype endogenous hydrogels; furthermore, through the efforts of these individuals, we hope our impact will hasten the pace of tissue engineering.