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Ph.D. DISSERTATION DEFENSE

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Degree:	Doctor of Philosophy
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Date:	Tuesday, April 23rd, 2024
Time/Location:	10:00 am, Carnegie 315
Title:	Multiscale Channel Formation to Promote Cell Viability in Volumetric Tissue Constructs
Chairperson:	Dr. Hongjun Wang**,** Department of Biomedical Engineering, School of Engineering and Sciences
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ABSTRACT

The fields of tissue engineering and regenerative medicine have made astounding progress in recent years, evidenced by cutting-edge 4D printing technologies, precise gene editing tools, and sustained long-term functionality of engineered tissue grafts. Despite these amazing feats, clinical success of tissue-engineered constructs is still limited to relatively simple tissues. Volumetric tissues (typically those larger than a few millimeters) suffer from poor oxygen supply due to limited diffusion. Large, complex tissues require a vascular network to supply the growing cells with nutrients needed to meet the metabolic demands of prolonged viability and tissue regeneration. To develop a vessel structure capable of immediately oxygenating cells while also forming a biomimicking vascular network, a combination of 3D printing and cell-driven self-assembly must be adopted. The focus of this dissertation is the fabrication of multiscale channel structures using 3D printed sacrificial templates and cell biology to mimic blood vessels from the macroscale (>100μm) to the microscale (<30μm). First, 3D printed sacrificial templates were combined with an elastomeric coating method to create free-standing, perfusable tubular networks with micropores in the tubular walls. Porous tubular networks showed improved proliferation and viability in cell-laden volumetric hydrogels compared to controls without vascular networks. Next, polymeric microfibers fabricated from near-field electrospinning were embedded within cell-laden hydrogels and then enzymatically digested to create microchannels to improve the viability of embedded cells. Finally, the 3D coculture of endothelialized microchannels with osteoblast progenitor cells demonstrated the synergistic effects of these two cell types to promote neovessel formation from the endothelialized microchannels via sprouting. Taken together, this work highlights the prospect of creating vascular-like channel networks at multiple scales by using novel 3D printed structures as sacrificial templates in conjunction with angiogenesis for neovascularization. Future studies will improve the complexity of these 3D printed sacrificial templates for developing hierarchical vascular networks while combining other cell types to develop more robust neovasculature. Altogether, the findings from this dissertation provide an important step forward in creating viable volumetric tissues.