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Perfusion-Driven Vessel Organization in 3D Bioprinted Constructs Using bEnd.3 Endothelial Cells

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The tissue matrix plays a pivotal role in maintaining structural integrity and orchestrating tissue transport; however, conventional 2D cultures inadequately recreate their 3D architectural complexity and biomechanical microenvironment. Here, we present a dynamic 3D *in vitro* platform engineered to mimic vascularized tissue by combining extrusion-based 3D bioprinting with continuous perfusion bioreactor culture. Using computer-aided modeling, custom tubular structures were printed and subjected to fluidic forces, exhibiting robust structural stability and resistance to shear stress over extended periods. To establish functional tissue, brain endothelial cells, bEnd.3 cells were encapsulated into two distinct hydrogel precursors: a sodium alginate-gelatin matrix and a GelMA-fibrin crosslinked network. Comparative analysis revealed that while the alginate-gelatin bioink retained high spatial resolution during printing, it restricted bEnd.3 cell spreading and lumen-like alignment. In contrast, the permissive biomimetic properties of the GelMA-fibrin system promoted exceptional cell viability, robust elongation, and spontaneous capillary-like network formation within the hydrogel walls of the constructs. Long-term dynamic culture demonstrated sustained bEnd3 cellular metabolic activity for up to 21 days in GelMA-fibrin, marked by attenuated oxidative stress (low ROS) and negligible cytotoxicity (minimal LDH output). Overall, combining bioinspired GelMA-fibrin bioinks with fluidic stimulation offers a powerful, high-fidelity model of vascularized tissue, creating new avenues for translational drug discovery, tissue engineering, and vascular disease research.

Keywords: 3D Bioprinting; vascularized tissue; bEnd.3 Cells; dynamic bioreactor.