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Patterning vasculature within individual tissue building blocks

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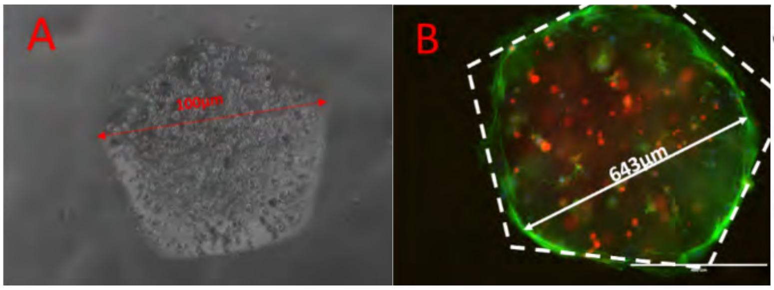
INTRODUCTION: Functional vascularization in engineered tissues is essential for its initial survival after implantation. In this project, we are aiming to study the vascular formation within individual tissue building blocks in two aspects: internal forces, such as cell contractile forces; and external forces, such as shear stress. Studies have shown that more vascular structures formation caused by the tissue contractility tends to happen in regions of higher deformations. We fabricated cell-laden GelMA tissue building blocks with different geometries to investigate how the physical forces generated by cells themselves within a hydrogel environment will induce various contractility. A perfusion device is built to apply an interstitial flow to study how shear stress affects cell orientation, alignment and endothelial sprouting. The primary parameters of the device are set based on computational modelling. By combining the effects of geometries and the patterned interstitial flow through individual tissue building blocks, we can guide the vasculature formation to obtain a tissue with desired properties.

METHODS: GelMA of 82% degree of functionalization (DoF) was synthesised according to the predefined protocols. 7.5% (w/v) GelMA solutions was prepared by dissolving in PBS at 80°C. The concentration of photoinitiator (Irgacure 2959) in the solution was 1% (w/v). A mixture of MSCs and HUVECs at the ratio of 1:1 were loaded into GelMA solution at the concentration of 5×10^6 cells/ml. Cell-laden GelMA prepolymer was crosslinked with UV at 365nm wavelength to obtain tissue building blocks. Computational modelling is performed by using COMSOL Multiphysics version 5.3a.

RESULTS & DISSCUSSION: Free standing tissue building blocks deform isotropically and more vascular structures were formed in the regions of higher deformation (figure 1). The primary computational modelling results (figure 2) demonstrated that we can pattern and guide cell alignment hence the vasculature formation by applying interstitial fluid flow through individual building blocks.



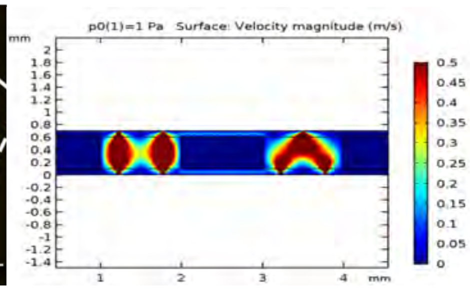


Figure 1: Deformation of the tissue building block. (A) A cell-laden tissue building block with the geometry of a pentagon was fabricated by photo patterning. (B) Deformation of the tissue building block on day 8 (left). **Figure 2:** Velocity profile indicates directed fluid flow patterns in tissue building blocks. Flow speed = 0.11m/s, cell experience 5dyn/cm^2 shear stress (right).

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