Controlling Vascularisation Within Tissue Building Blocks
Using Internal and External Mechanical Cues

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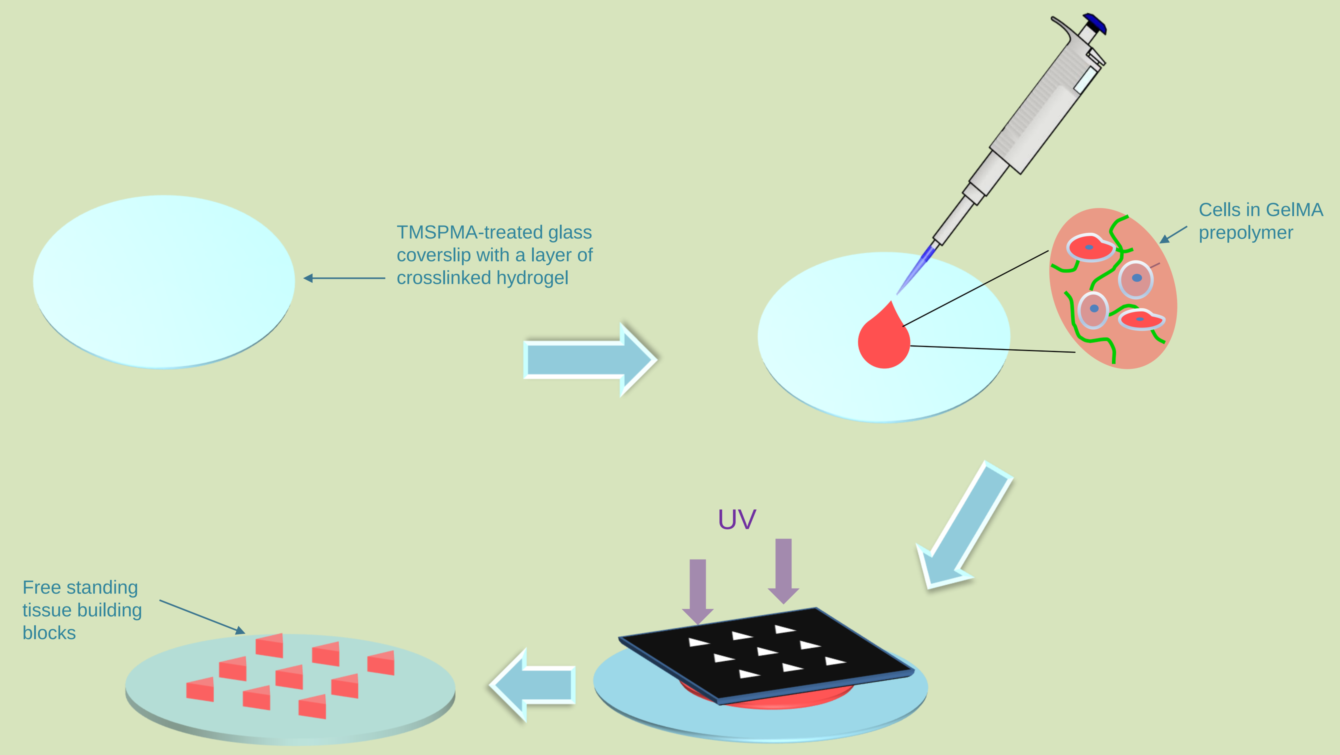
INTRODUCTION

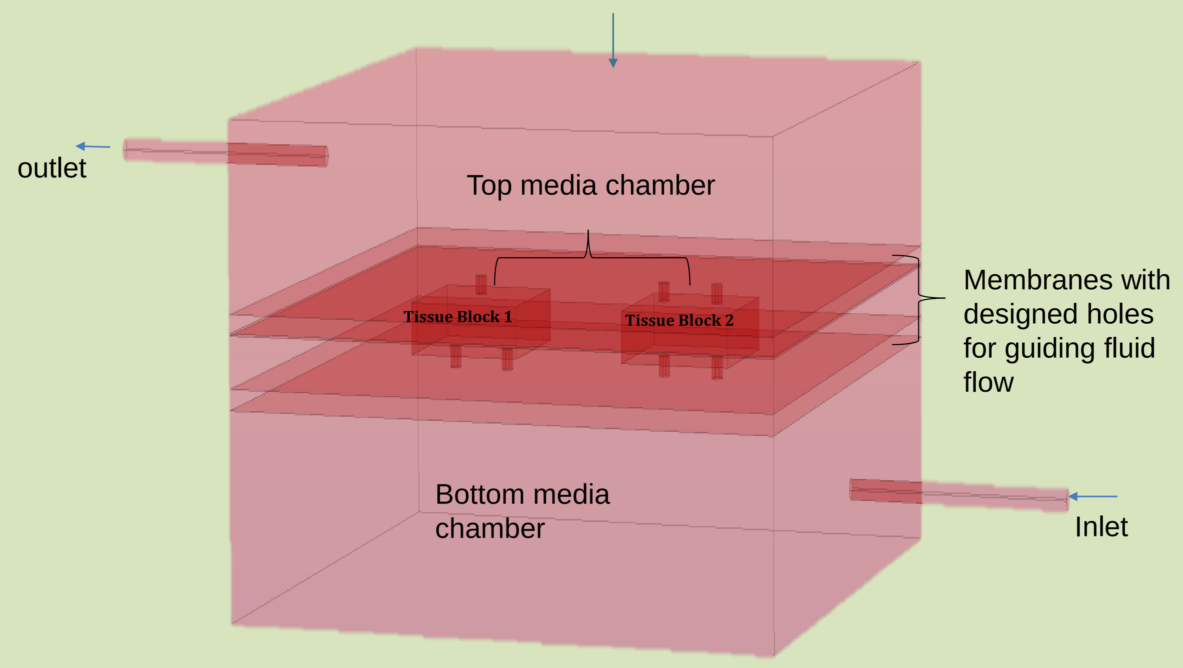
Modular tissue engineering, also known as “bottom-up” approach, has its ability to better mimic natural tissues and it allows a better control of the microenvironment. Mechanical cues (internal forces, such as cell contractile forces; and external forces, such as shear stress) have significant impacts on formation of vascular network.

- This project is to study if the physical forces generated by cells themselves within a hydrogel environment will induce various contractility according to the geometries. Tissue building blocks with different geometries were designed.
- Endothelium lining is constantly exposed to hemodynamic shear stresses. By applying fluid flow, we can mimic the natural condition and promote the endothelial alignment and initiate vascular network formation. For this aspect of our work, instead of creating channels, we are building a perfusion device to apply an interstitial flow to study how it affects cell orientation, alignment and endothelial sprouting. We have set the parameters of the device based on computational modelling.

MATERIALS AND METHODS



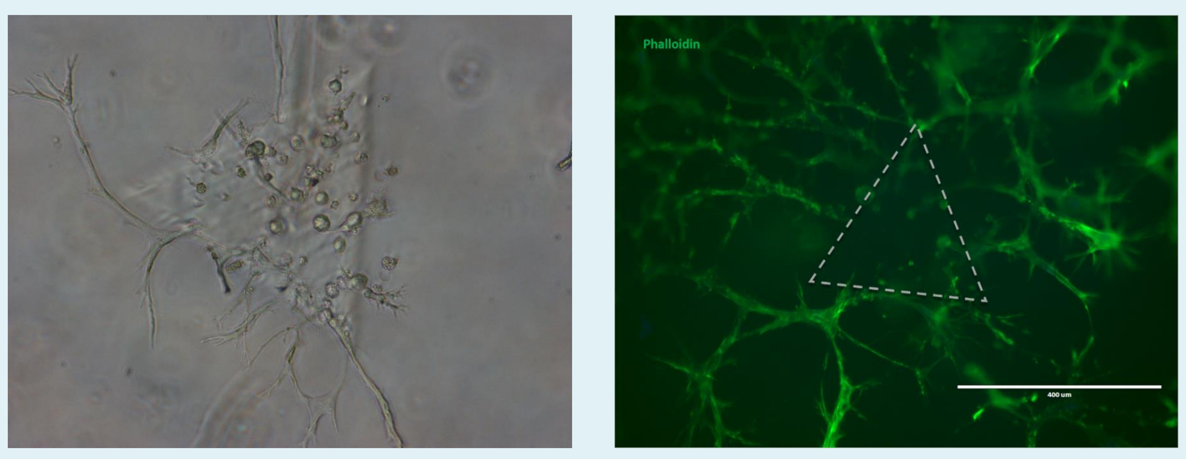
A perfusion device for applying patterned fluid flow through individual tissue building blocks



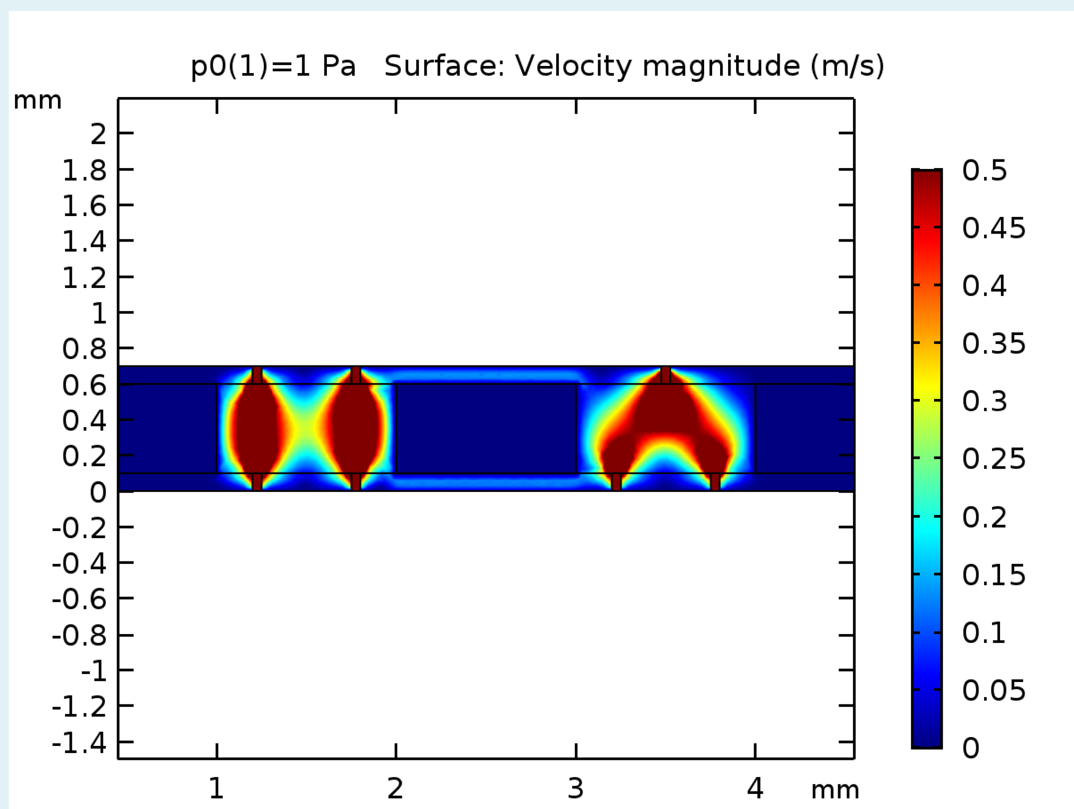
- GelMA was synthesised according to the predefined protocols. The degree of functionalization (DoF), as determined by NMR, was 82%.
- GelMA solutions of different concentrations (5%-10%) was prepared by dissolving in PBS at 80°C. The concentration of photoinitiator (Irgacure 2959) in the solution was 1% (w/v).
- A mixture of MSCs and HUVECs at the ratio of 1:1 were loaded into GelMA solution at the concentration of 5×10^5 cells/ml. Cell-laden GelMA prepolymer was crosslinked with UV at 365nm wavelength to obtain tissue building blocks. Tissue building blocks were encapsulated in hydrogel with different mechanical properties.
- Computational modelling is performed by using COMSOL Multiphysics version 5.3a. A perfusion device is designed based on the results.

RESULTS AND DISCUSSION

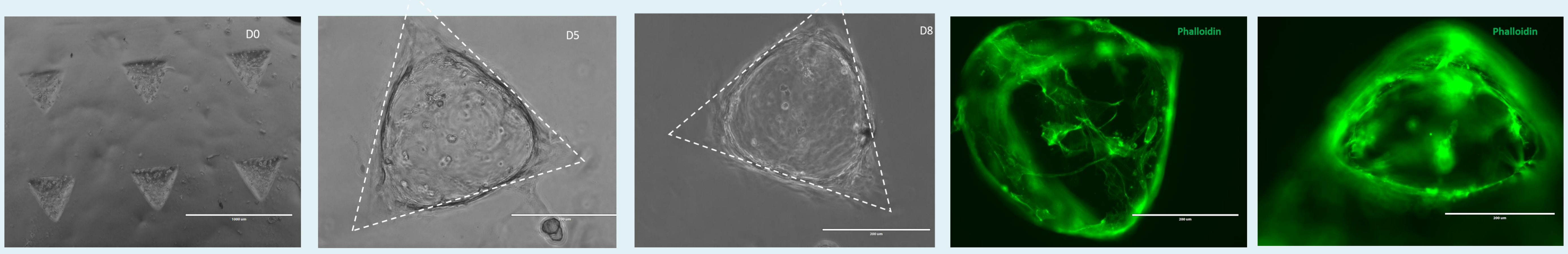
- The mechanical property of GelMA can affect cell spreading, migrating and sprouting. Cell-laden GelMA tissue blocks encapsulated in GelMA with lower storage modulus. Cells spread into the surrounding GelMA because its mechanical property allows them to migrate and proliferate better. Hence the mechanical properties of hydrogel have an significant effect on cellular behaviours. Dash-lined area indicates the original geometry.



- Free standing cell-laden triangular GelMA tissue blocks deformed anisotropically over time. More compaction occurs at sharp geometries can be observed. Quantification of the vascular structures will be conducted to compare the density between the corners and the centres of the blocks. Dash-lined areas indicate the original geometry.
- Tissue building blocks with other geometries, such as circular and square will be fabricated to compare the results with the triangular ones.



- Based on the computational modelling of applying interstitial fluid flow through individual building blocks， we can pattern and guide cell alignment hence the vasculature formation. Velocity profile indicates directed fluid flow patterns in tissue building blocks. Flow speed = 0.11m/s, cell experience 5dyn/cm^2 shear stress.
- A device for applying fluid flow profile through individual tissue building block will be built.



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