A Laminated Perfusion Channel Scaffold for Creating Thick Tissue Engineered Constructs

James Kennedy, Laura Williams, Sean McCandless, Robert Hitchcock
Department of Bioengineering, University of Utah, Salt Lake City, UT

Statement of Purpose: A major challenge in the field of tissue engineering is oxygen and nutrient transport in scaffolds thicker than ~100-200 microns. Media perfused scaffolds have shown potential for allowing development of thicker tissue engineered constructs that may be used therapeutically or as research models. Recent focus has been directed towards connected channels that mimic the capillary networks found in native tissue. (Radisic, M. Am J Physiol Heart Circ Physiol. 2005;288:H1278-89) We report here a method for fabricating thin sheet scaffolds that can be patterned and laminated to form thick constructs with networks of channels that allow perfusion of the interior region of the scaffold with nutrients and oxygen.

Methods: Scaffolds were fabricated from polyether polyurethane through a sprayed phase separation method as previously described by our group (Kennedy JP, Biomaterials. 2009; doi:10.1016). Briefly, two spray nozzles were mounted on a computer controlled milling machine. One nozzle sprayed 4% polyurethane dissolved in dimethylacetamide (DMAc), while the other nozzle sprayed the nonsolvent onto a patterned substrate. Upon mixing of the solvent and nonsolvent, the polyurethane precipitated onto the substrate. The scaffolds were then removed from the substrate and laminated to form scaffolds of the desired thickness. These thick scaffolds were allowed to cure for 24 hr in water.

Perfusion Channels. A network of channels for media perfusion was designed into the thick scaffold structure using 3D design software and a 3D printer. A mold with channels ranging in size from 50 – 500 µm wide was designed using SoldWorks 3D design software. This mold was then printed using an Objet 3D printer and used to create a patterned spray substrate from PDMS (Fig. 1).

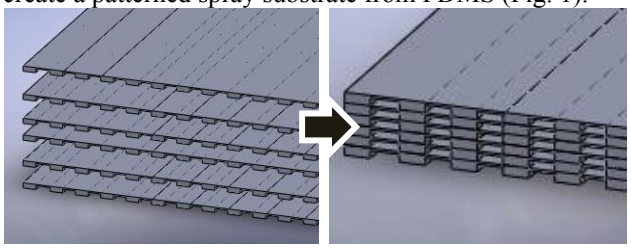

Fig. 1. Schematic of lamination method.

Hydraulic permeability. Hydraulic permeability (HP) was assessed to compare axial flow through the channels to transverse flow through the pores. Flow rate was measured at pressures from 3.4 kPa to 20.7 kPa. The flow rate was then normalized to cross sectional area, length, and pressure to determine the hydraulic permeability of the scaffold. Measurements were both normal (transverse) to the channels and in the direction of the channels (longitudinal).

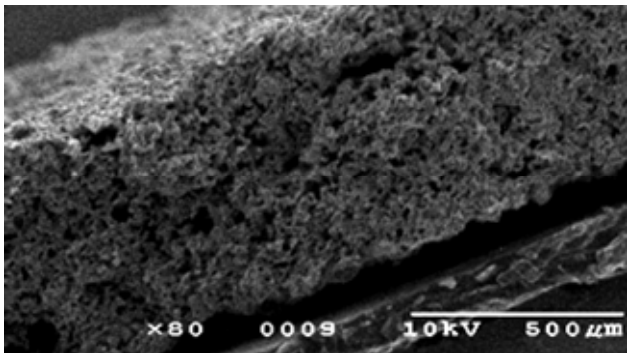

Fig. 2. SEM image of laminated scaffold without perfusion channels.

Results: Individual sheets were fabricated using a computer controlled phase separation technique. The scaffolds were laminated to form scaffolds ~1.5 mm thick. EM imaging revealed no traces of lamination boundaries (Fig. 2).

Perfusions Channels. Perfusion channel scaffolds were fabricated using the thin sheet lamination technique and the patterned spray substrate. Channels are visible in the cross sectional image of the scaffold (Fig. 3a).

Hydraulic permeability. HP was measured both in the longitudinal and transverse directions at varying pressures.. When normalized to the pressure, the HP of scaffolds in the longitudinal and transverse directions were measured to be 1.18±0.34 and 0.19±0.02 $cm^2/min \cdot kPa$, respectively (Fig. 3b).

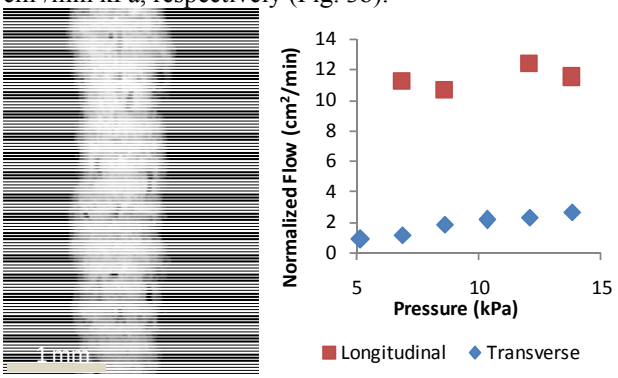

Figure 3. (a) Cross section of scaffold showing perfusion channels. (b) Normalized hydraulic permeability of scaffolds with respect to pressure.

Conclusions: Scaffolds for tissue engineering require systems for delivering nutrients and oxygen to the interior. Perfusion channels are a method that allow for scaffolds to be perfused with media. We have fabricated thin sheet scaffolds that can be laminated to form scaffolds of desired thicknesses. Spraying onto a patterned substrate allows perfusion channels to be designed and fabricated into the laminated scaffold. Hydraulic permeability testing confirmed that resistance to flow through the channels is reduced compared to flow through the porous scaffold.