Biomechanics of Cell Sheets Based Arterial Tissue using a Novel Force Sensor

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Statement of Purpose: There is a significant clinical need for a tissue engineered blood vessel (TEBV) to replace high pressure, small diameter vessels such as the carotid artery. Current techniques fail because the replacement vessels develop aneurysms, become thrombogenic, and suffer from anastomotic intimal hyperplasia[1]. Cell sheet engineering technology using thermo-responsive polymers is a viable candidate for constructing the basic functional unit for a tissue engineered blood vessel. By stacking cell sheets, one can control tissue microstructure so that it mimics a native artery. In order to develop a successful TEBV that doesn't develop an aneurysm or develop intimal hyperplasia, the graft must have suitable mechanical properties. Therefore, the aim of this project is to characterize the mechanical properties of cell sheets using a low-cost force sensor developed for this purpose.

Methods:
Using micro-textured poly(dimethylsiloxane) (PDMS) molded from soft lithography masks, we have created both non-patterned and patterned substrates that were subsequently grafted with thermo-responsive poly(N-isopropylacrylamide) (pNIPAAM) as previously described[2]. PNIPAAM allows cells to attach at 37 °C; following a temperature drop below 32 °C, pNIPAAm can spontaneously detach a confluent cell layer as an intact cell sheet without disrupting the intercellular connections without enzymatic treatment. The micro-textured substrates have 50 µm wide grooves and 20 µm ridges with a depth of 5 µm. Bovine vascular smooth muscle cells (BVSMCs) were seeded onto the pNIPAAM-grafted PDMS substrates and grown to confluence in a cell sheet monolayer. After reaching confluence, cells were treated with 50 µg/ml of ascorbic acid.

Cell sheets were mechanically tested on a uniaxial tensile tester that is controlled using a LabVIEW (National Instruments) interface. The force sensor design exploits bending beam mechanics to measure force. Since tip deflection is linearly proportional to applied force, force can be correlated to measured tip deflection, which can be measured using a Hall-Effect sensor. A Hall-Effect sensor is capable of measuring magnetic field strength. Embedding a magnet in beam tip allows the Hall-Effect sensor to function as a low cost displacement sensor. The current sensor uses a small rare-earth neodymium magnet (K&J Magnetics) embedded into the beam tip and also uses an Allegro Microsystems Hall-Effect Sensor (A1321) to measure beam displacement. Cell sheets were tested at room temperature in PBS and strained at a constant strain rate of 0.001/sec.

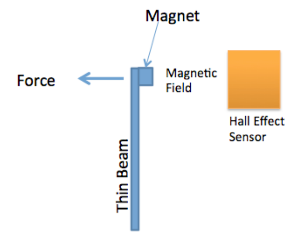

Figure 1: Force Sensor Schematic.

Results: Experimental characterization of Hall-Effect force sensor has shown that the force sensor is capable of measuring forces ranging from 0-10 mN. Furthermore, the Hall-Effect sensor has greater than 10 bits of resolution and is capable of detecting changes in beam tip displacement smaller than 1 µm. Figure 2 shows the results from the sensor calibration and confirms the expected linear relationship between beam tip displacement and applied load. Furthermore, the apparatus has been successfully used to measure the mechanical properties of non-patterned cell sheets.

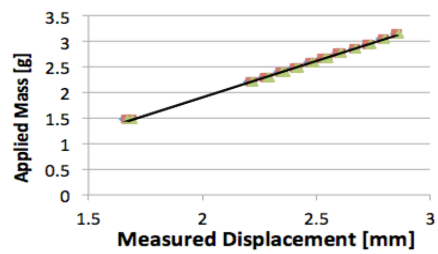

Figure 2: Sensor Performance Characteristics

Conclusions: In this study, a low cost, Hall-Effect based sensor has been develop to successfully measure the mechanical properties of single layer cell sheets. Currently, a study is underway that aims at characterizing the degree of mechanical anisotropy in aligned cell sheets in relation to amount of structural anisotropy in the cell sheets. Furthermore, a computational model is being developed that uses the microstructure of the cell sheets to predict it's mechanical properties. This ongoing work applies engineering methodologies to design a blood vessel with suitable mechanical properties to replace native arterial tissue.

References:
1. Isenberg, BC, Backman, DE, et al., J of Biomech.2012;45(5)756-761.
2. Lin, JB. et al., Colloids and Surfaces B. 2011;99:111-118

Acknowledgements:
NIH T32 Training Grant on Cardiovascular Biology (T32 HL007969), The Hartwell Foundation