Creating waved and aligned nanofiber composites to mimic the microstructure and match the compliance of blood vessels

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Introduction: Small diameter vascular grafts are used in revascularizaton and reconstructive functions such as heart bypass operations. Autologous vein grafts occlude over time, resulting in a 10 year patency of approximately 50% after coronary bypass operations [1]. Synthetic prostheses have much lower patency rates than natural grafts [1]. Differences in radial compliance between vascular grafts and the native vessel have been shown to cause intimal hyperplasia and thus luminal narrowing [1]. It is hypothesized that a synthetic vascular graft that mimics the histological structures and matches the compliances of natural blood vessels would have increased patency. To this end, we developed several fabrication technologies to construct synthetic vascular grafts by orienting nanofibers in a composite with interlacing wavy and aligned configurations similar to the arrangement of collagen and elastin fibers in natural blood vessels [2]. Elastic polyurethane was used to mimic the mechanical properties of elastin and polycaprolactone was used to mimic the mechanical properties of collagen. Similar technology can be used for the arrangement of elastin and collagen fibers.

Material/Methods: Elastic polyurethane (PU, Texoflex SG-80A) was dissolved in hexafluoro-2-propanol (Oakwood) at 8% w/v and polycaprolactone (PCL, M_n=80,000, Sigma) was dissolved in 3:1 dichloromethane/dimethylformamide (Sigma) at 18% w/v. In order to visualize and distinguish fibers from two different materials, DiI (Invitrogen) was added to PU solution and DiO (Invitrogen) was added to PCL solution at 0.03 mg/ml. The solutions were feed through a 23 gauge needle at 0.015-0.020 ml/min and a voltage of 8kV was applied to the needle tip to initiate electrospinning of polymer nanofibers. PU fibers were collected first and stretched. PCL fibers were then collected on top on the stretched PU layer. The composite fiber mat was relaxed to the original length of the PU fibers, which caused the PCL fibers to configure in a wavy configuration similar to the arrangement of collagen fibers in natural blood vessels. Aligned elastic polymer nanofibers mimicking elastin in natural blood vessels were collected and stretched using an expandable rotating mandrel or by using an expandable rectangular rack as shown in Figure 1.

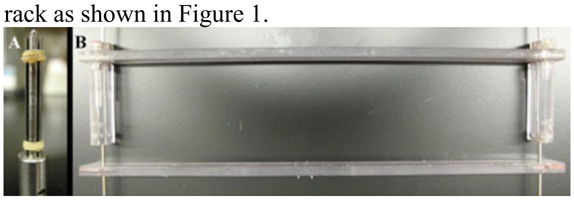

Figure 1: Expandable (A) Mandrel (B) Rack

Results/Discussion: Fiber mats were fabricated with alternating PU and PCL layers. In one case, 4 layers of aligned PU fibers and 3 layers of aligned PCL fibers were collected across a rack. PU layers were collected at a length of L_0 and stretched to 1.55× L_0. PCL fibers were collected at a length of 1.55× L_0 on top of the stretched PU layer. The stretching ratio can be readily controlled with both collecting device. Upon relaxation of the mat back to L_0, the PU fibers pulled the PCL fibers into a wavy configuration. Analysis by scanning electron microscope confirmed that some of the fibers were straight and aligned, while others were in a wavy orientation (Fig 2A). Fluorescent pictures (Fig. 2B) further confirm that polyurethane fibers (DiI labelled, red) are straight and PCL fibers are waved (DiO labelled, green). The nanofiber mats were mechanically tested for tensile strength and stress strain curves were obtained. In Figure 3 the shape of the normalized stress strain curves of a PU/waved PCL composite fiber mat, control PU/straight PCL mat, and native aorta tissue are compared. The blue curve [2] is from a native aorta, the pink curve is from a PU/wavy PCL fiber mat fabricated by the method described, and the orange curve is from a PU/straight PCL fiber mat fabricated without stretching the PU layer.

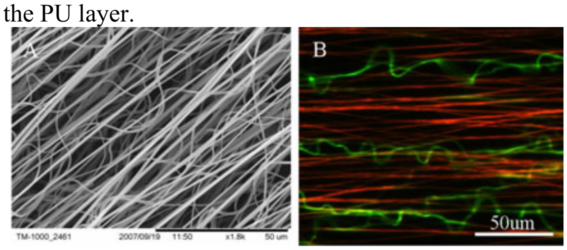

Figure 2: (A) SEM Image (B) Flourescent Image of composite fiber matter with interlacing waved and straight fibers.

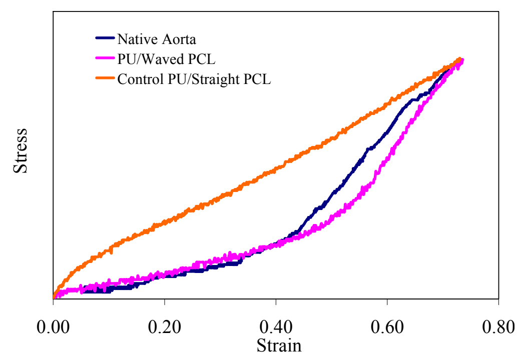

Figure 3: Stress vs. Strain for PU/PCL mats and Native Tissue

Conclusions: It was concluded that the structural and mechanical properties of the fabricated composite fibers mats were similar to that of native tissue in microstructure and compliance. This novel method of fabrication may be used to fabricate vascular grafts with the appropriate properties to improve the patency of vascular grafts.

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References:

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2. Sum-Tim et al. Ann Thorac Surg, 68, 2298-305, 1999