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Introduction

Cardiovascular disease (CVD) is a growing condition caused by the narrowing of blood vessels in a process termed atherosclerosis, resulting in angina, heart attack, stroke, and limb amputation due to ischemic tissues. End stage treatment for CVD seeks to restore blood flow to ischemic tissues through a grafted bypass conduit. Autologous vessel grafts require extensive harvesting time and have limited availability. Off-the-shelf synthetic grafts above 6 mm in inner diameter (ID) work adequately. However, current synthetic vascular grafts < 6 mm ID perform poorly and most frequently fail by graft occlusion via thrombosis and/or hyperplasia. Gore-Tex is a current, off-the-shelf vascular graft composition used in bypass surgeries. These grafts do not allow for cell infiltration to restore the damaged blood vessel which can lead to thrombosis and later mechanical mismatch. The goal of this project is to develop templates that serves as conduits while guiding *in situ* regeneration (Figure 1).



Results



Figure 4. Ultimate tensile strength of vascular grafts along A. the circumferential axis and B. the longitudinal axis (data represent mean, error bars represent standard deviation (n=6), * indicates p < 0.05, red line indicates literature values for Gore-Tex®, green line indicates literature values for SV and IMA).

Figure 1. Schematic of vascular template guiding *in situ* regeneration.

The primary mechanism of reendothelialization in humans is through transmural growth of perivascular capillaries. For functional *in situ* regeneration, the bioresorbable vascular graft should guide transmural angiogenesis to deliver endothelial cells into the lumen of the graft via pores of 60-200 µm. Because pore size and fiber diameter are intrinsically linked in traditional electrospinning, near field electrospinning (NFES), utilizing a reduced air gap, is used to generate grafts with precisely aligned fibers to produce grafts with tailorable pore sizes and fiber alignment that mimics the alignment of the extracellular matrix. It was hypothesized that grafts with larger wind angles would have higher mechanical properties than the grafts with smaller wind angles.

Methods

A consumer 3D printer was modified to obtain the desired degree angles of 15° and 30° for vascular grafts. The NFES print head was customized to contain a syringe pump that held a polypropylene 1 mL syringe with a blunt Luer-lock 23-gauge probe needle. A custom G-code translated the print head along the X- and Z- axis while the grounded 4 mm stainless steel rod rotated about the y-axis with Q-code. Each G- and Q-code were altered to meet the specification of translation and rotational speed determined by the desired angle (Table 1). Solutions of polydioxanone were prepared at a concentration of 100 mg/mL. The syringe was filled with 1 mL of PDO solution and mounted vertically on the NFES print head syringe pump connected to a DC voltage source. The applied voltage to the syringe needle was +1.6 kV with a polymer flow rate of 25 µL/h, air gap of 1.7 mm, and a resultant velocity of 80 mm/s (Figure 2).





Figure 5. Percent elongation of vascular grafts in A. the circumferential axis and B. the longitudinal axis (data represent mean, error bars represent standard deviation (n=6), * indicates p < 0.05, red line indicates literature values for Gore-Tex®, green line indicates literature values for SV).



Figure 6. Young's modulus of vascular templates in the circumferential axis (data represent mean, error bars represent standard deviation (n=6), * indicates p < 0.05, red line indicates literature values for Gore-Tex®, green line indicates literature values for SV).



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	Translational Velocity (mm/min)	Rotational Velocity (rev/s)
15°	1242	6.149
30°	2400	5.513

Figure 2. Schematic of angle determination with the green line representing resultant velocity and the red and black lines representing zero degrees from the needle tip.

The wind angle of the templates was verified using scanning electron microscopy (SEM) to obtain images and the Windows 11 snipping tool and protractor function to measure the angles between the fibers (Figure 3). Mechanical testing of the templates—ultimate tensile strength (longitudinal and circumferential), percent elongation (longitudinal and circumferential), and suture retention—was then performed until failure using a uniaxial testing frame in tension with a 25 lb_F load cell. Burst pressure was also performed using a custom apparatus with a pressure transducer, pumping water into the graft at a rate of 15 mmHg per second. The obtained values were then compared to internal mammary artery and saphenous vein target values and Gore-Tex® values. Statistical analysis was performed with a significance of p < 0.05, and wind angle differences were evaluated using a one-way ANOVA and post hoc Tukey-Kramer analysis.



Figure 7. A. Single wall suture retention and B. burst pressure of vascular grafts (data represent mean, error bars represent standard deviation (n=6), * indicates p < 0.05, red line indicates literature values for Gore-Tex®, green line indicates literature values for SV and IMA).

Discussion and Conclusions

- 1. Fiber angles were produced as programmed.
- 2. NFES PDO templates produced with various degrees of fiber winding provide flexibility in producing vascular grafts with biomimetic mechanical properties.
- 3. NFES grafts have appropriate tensile strengths, percent elongations, and suture retention strengths when compared to at least one native vessel value.
- 4. NFES shows promise in the fabrication of bioresorbable vascular grafts capable of mimicking native arterial properties and promoting full arterial regeneration.

Future Work

- 1. Explore decreasing fiber diameter used in construct fabrication.
- 2. Explore developing a pore size/fiber diameter model to better understand cellular interactions with scaffolds.
- 3. Explore the evaluation of the regenerative as well as inflammatory capacity of neutrophils interacting with NFES scaffolds.
- 4. Explore an in vitro model followed by an *in vivo* model to demonstrate the capacity of transmural capillary ingrowth.
- 5. Explore various grafts thickness to better approximate native values.



 20%
 SE
 20.00 kV
 1.06 mm
 Field-Free
 120 x
 1.5
 4.8 mm
 University of Memphis
 1.
 Stand

 20%
 SE
 20.00 kV
 1.06 mm
 Field-Free
 120 x
 1.5
 5.4 mm
 University of Memphis
 1.
 Stand

1. Standard AN. Revisions Proposed for Vascular Graft Prostheses Standard. Biomedical Safety & Standards. 1994;24(8):63. doi:https://doi.org/10.1097/00149078-199405010-00015

Figure 3. Representative images of fiber alignment angle verification of A. 15° and B. 30° templates (red indicates the reference line, green indicates the measured angle).

 Konig G, McAllister TN, Dusserre N, et al. Mechanical properties of completely autologous human tissue engineered blood vessels compared to human saphenous vein and mammary artery. Biomaterials. 2009;30(8):1542-1550. doi:https://doi.org/10.1016/j.biomaterials.2008.11.011