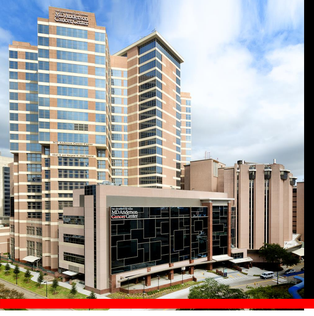

Electrospun bioresorbable polymer blends as vascular grafts

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Introduction

The most common vascular graft and vascular bypass surgeries use autologous vessels to replace damaged vasculature. However, many patients don't have sufficient healthy vasculature appropriate for these procedures. Current research and applications have yielded polymer-based vascular grafts, but these are limited to large-caliber vessel application and can induce stenosis and thrombosis along with other biological complications.

Our research seeks to incorporate a hydrophilic polymer into polymer-based vascular grafts to increase recruitment and patency of endothelial cells.

Methods

Synthesis:
PCL (polycaprolactone), PCL:PEG (polyethylene glycol), PCL:PLGA (poly lactic-co-glycolic acid), and PCL:PLA (polylactic acid)—were dissolved in 3:1 ratios and electrospun at 15 kV to yield polymeric grafts.

Hemolysis and Cytotoxicity:
The samples were incubated overnight, and the supernatant was used to test for hemolysis and cytotoxicity against RF24 or MOVAS cells.

Proliferation Assay:
The proliferation of RF24 or MOVAS cells on the scaffolds were also determined at 4, 24, 48, and 96 hours with an Alamar blue assay.

In Vitro Assay:
Samples were also placed in an in vitro pump system to simulate the in vivo degradation of the grafts under constant pulsatile flow. At 0, 2, 4, 6, and 8 weeks, the maximum stress and modulus of elasticity was measured using an MTest Quattro machine (ADMET, Shirley, NY).

In Vivo Assay:
A scaffold of each type was grafted onto the abdominal aorta of Sprague-Dawley rats. A 5th control rat had their abdominal aorta cut and sutured back together. After 4 weeks, rats were sacrificed, and the scaffolds were removed and imaged for analysis.

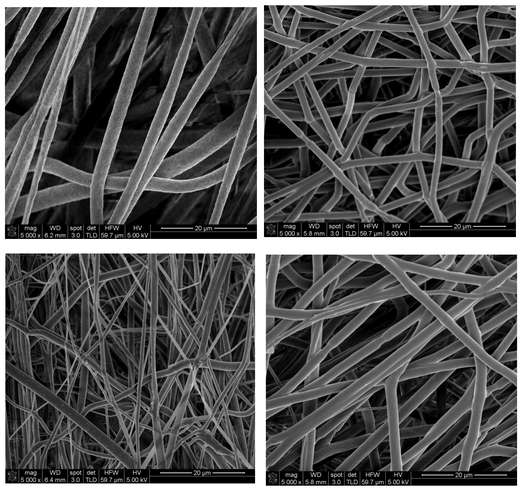

Fig. 1. SEM images of PCL (top left), PCL-PEG (bottom left), PCL-PLGA (top right), and PCL-PLA (bottom left) at 5000x magnification.

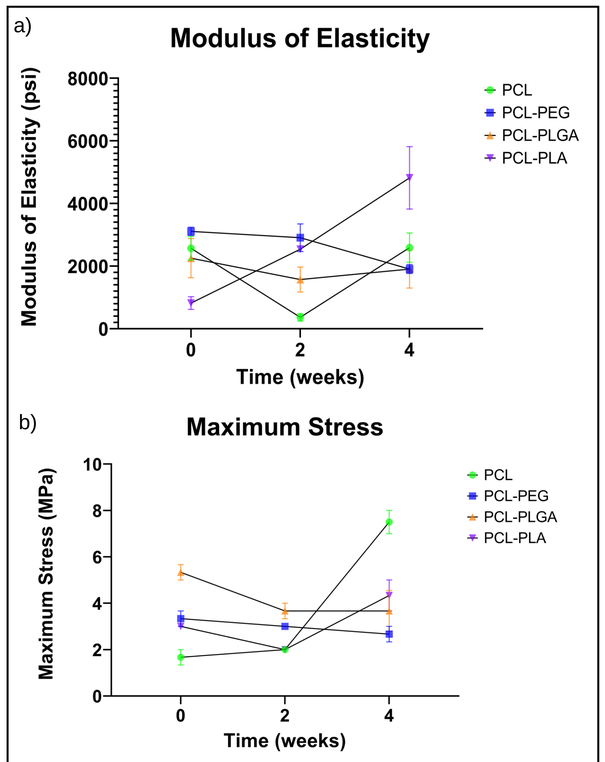

Fig. 2. Mechanical Properties. (a). Measured modulus of elasticity for stress at 0, 2, and 4 weeks after samples were placed into in vitro assay. (b) Measured maximum stress each sample was capable of handling at 0, 2, and 4 weeks after samples were placed into in vitro assay.

Table 1. Physiochemical properties

Sample	PCL	PCL-PEG	PCL-PLGA	PCL-PLA
Fiber Diameter (um)	3.057 ±0.098	1.317 ±0.249	1.760 ±0.406	2.377 ±0.394
Pore Size (um^2)	2.731 ±1.763	0.192 ±0.079	0.474 ±0.331	0.225 ±0.102
Porosity Value	0.502 ±0.051	0.478 ±0.012	0.429 ±0.006	0.456 ±0.022

Note: Image J analysis of n = 9 SEM images for each type of scaffold and DSC analysis of 5 mm lengths of each type of scaffold. Porosity value was determined through uptake of ethanol over 24 hours.

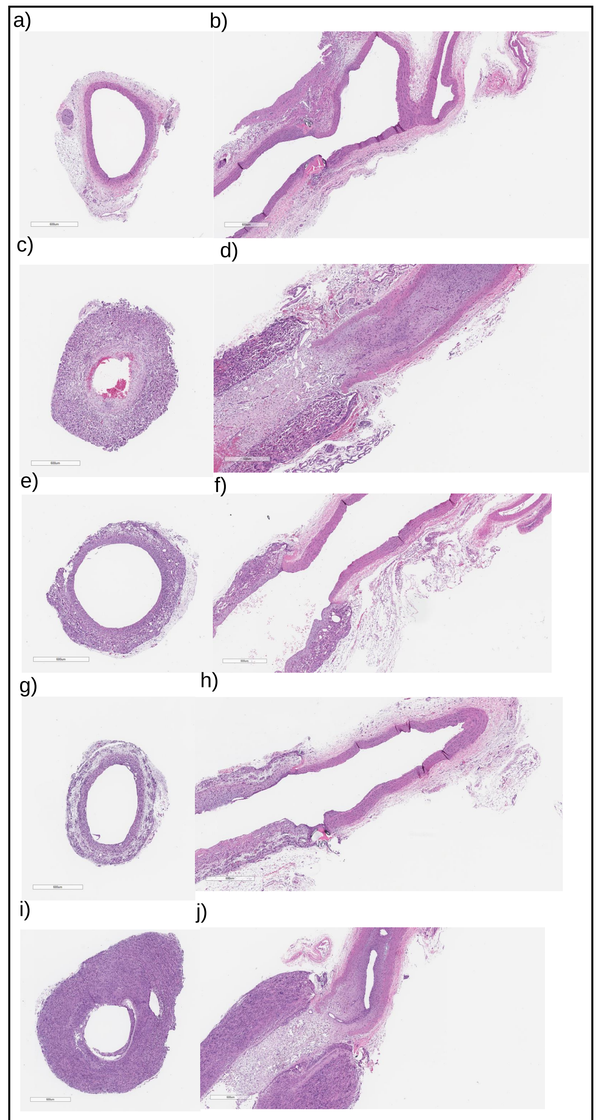

Fig. 3. Hematoxylin and eosin staining. (a-e) Axial cross-section of in vivo control (a), PCL (b), PCL-PEG (c), PCL-PLA (d), and PCL-PLGA (e) vessels. (f-i) Longitudinal cross-section of in vivo control (f), PCL (g), PCL-PEG (h), PCL-PLA (i), and PCL-PLGA (j) vessels.

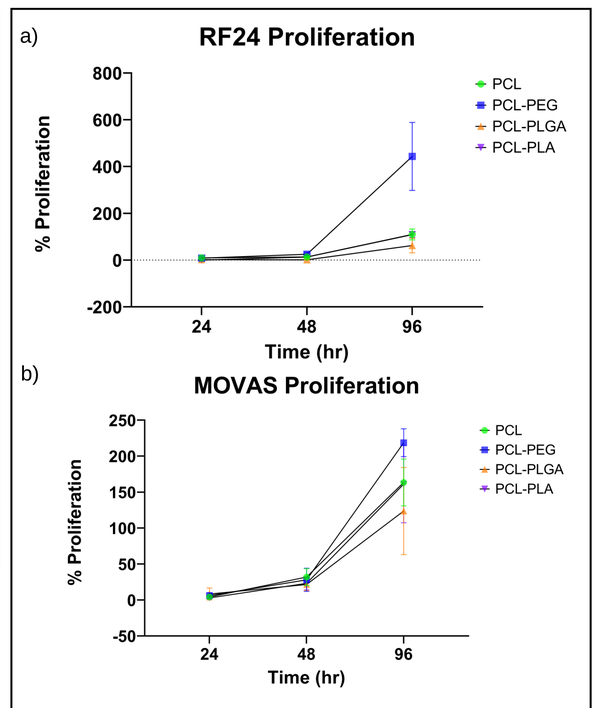

Fig. 4. Proliferation Assay. (a) Graph of RF24 proliferation on a 5 mm^2 as a percentage of the control. (b) Graph of MOVAS proliferation on a 5 mm^2 as a percentage of the control

Results

All polymer combinations were not hemolytic or toxic to the two tested vascular cell lines. For physiochemical properties, PCL-PLA had a smaller porosity value than the other 3 samples while the other 3 had statistically insignificant differences in porosity values. PCL-PEG and PCL-PLGA had the lowest moduli of elasticity, though there were statistically insignificant differences between PCL-PLGA and PCL. Meanwhile, PCL demonstrated the greatest ability to handle stress over time and it had an increasing trend. For the cell proliferation assay, PCL-PEG had the greatest amount of proliferation for both cell types, though there was no difference between it and PCL-PLA for MOVAS. Finally, analyzing our in vitro studies, we found that PCL and PCL-PLA induced significant stenosis and thrombosis. Clots can be seen best in the PCL scaffold. PCL-PEG and PCL-PLA demonstrated most signs of healthy vascular development, with little to no narrowing of the vessel. There were some interruptions to the endothelial monolayer for PCL-PLA. Additionally, PCL-PEG had the greatest wall-to-lumen ratio.

Discussion

PCL-PEG overall has the most ideal properties for vascular grafting. Its lower modulus of elasticity allows it to deform more like a biological vessel and although it cannot deal with stresses as well, there are limited stresses it would experience in vivo. It also experienced the greatest cell proliferation for both cell lines, showing promise of recruitment for vascular reconstruction, and in vivo, it performed the best. With minimal biological complications.

Conclusions

PCL-PEG is the most ideal polymer combination to continue testing against for vascular graft synthesis and the inclusion of a biocompatible hydrophilic polymer enhanced polymer grafts' ability recruit cells for vascular reconstruction with a decreased incidence of stenosis and thrombosis.

References

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