In vitro Evaluation of Electrospun Nanofiber Conduits for Vascular Substitutes

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Introduction

Cardiovascular disease, including coronary artery and peripheral vascular disease, is the leading cause of mortality in the United States.[1] Biological and synthetic vascular grafts have been widely used as a blood vessel substitute for cardiovascular bypass procedures. However, these grafts have shown several limitations such as donor site morbidity, immunogenic response and thrombosis.[2-3] In addition, blood vessels are extremely diverse with regard to size, mechanical properties, biochemical and cellular content, and ultrastructural organization, depending on their location and specific function.[4] Therefore, vascular grafts should provide a variety of functionality for an optimal blood vessel substitute. Electrospinning technology offers a new potential for controlling composition, geometry and mechanical properties of vascular grafts. The present study suggests that electrospun nanofiber conduits fabricated by introducing synthetic biodegradable polymers possess tailored mechanical properties that overcome the compliance mismatch of other engineered vascular grafts.

Materials and Methods

We fabricated vascular grafts using an electrospinning method with blends of collagen type I, elastin and various synthetic biodegradable polymers such as poly(D,L-lactide-*co*-glycolide) (PLGA), poly(L-lactide) (PLA), poly(ε-caprolactone) (PCL) and poly(D,L-lactide-*co*-ε-caprolactone) (PLCL). Collagen type I, elastin and synthetic polymer are mixed at a relative concentration by weight of 45% collagen, 40% polymer, and 15% elastin to mimic the native blood vessel. The solutes are dissolved in 1,1,1,3,3,3-hexafluoro-2-propanol (HFP) in the concentration range from 5% to 20% (wt/vol). We investigated the feasibility of using electrospun conduits as a vascular substitute by testing morphology, dimensional stability, mechanical properties and *in vitro* biocompatibility.

Results and Discussion

The resulting electrospun conduits have a length of 12 cm and an inner diameter of 4.75 mm with a wall thickness of 0.5 mm. SEM images of the resulting fibers showed nanoscale fibers with a random orientation. The optimal concentration of the collagen/elastin/polymer blend solution in obtaining fine nanoscale fibers was 10% (wt/vol). The average fiber diameters of the electrospun conduits ranged from 477.35 ± 43.49 to 765.85 ± 175.42 nm. The biomechanical properties of the electrospun conduits were different depending on the compositions of blended synthetic polymers. The tensile strength of the electrospun collagen/elastin/PLLA conduit was significantly greater than that of the other compositions. Addition of synthetic polymers to the collagen/elastin blend improved the mechanical properties of the vascular grafts (Figure 1).

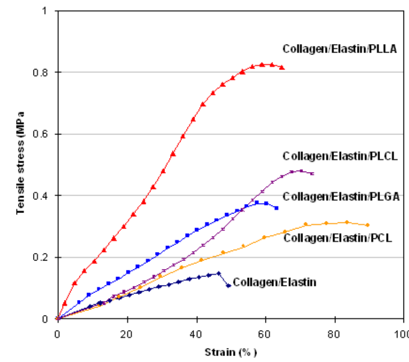

Figure 1. Stress-strain curves from tensile testing of the electrospun nanofiber scaffolds.

Biocompatibility of the biomimetic conduits was confirmed by cell viability and mitochondrial metabolic activity. There was no evidence of toxic effects of the electrospun conduits. *In vitro* studies revealed that the electrospun conduits support adhesion and migration of ovine smooth muscle cells (SMCs). The electrospun collagen/elastin/PLLA conduit showed extensive SMC infiltration into the conduit after 21 days in culture. These results indicate that the electrospun conduits using collagen, elastin and synthetic polymers possess adequate dimensional stability, controlled mechanical properties and good biocompatibility for vascular tissue engineering.

Conclusions

We have fabricated an electrospun conduits composed of collagen type I, elastin and synthetic polymers that possess ideal characteristics required for vascular substitutes. The conduits are biocompatible, biodegradable, dimensionally stable, easily fabricated and possess controlled mechanical properties. By introducing a variety of synthetic polymers, the electrospun conduits can be controlled the mechanical properties to match location and specific function of blood vessel. This study demonstrates the promise of the electrospinning technique as a fabrication method for functional vascular substitutes.

References

1. Ross, R. The pathogenesis of atherosclerosis: a perspective for the 1990s. Nature, 362(6423), 801, 1993.
2. Sayers, R.D., Raptis, S., Berce, M., and Miller, J.H. Long-term results of femorotibial bypass with vein or polytetrafluoroethylene. Br J Surg, 85(7), 934, 1998.
3. Stephen, M., Loewenthal, J., Little, J.M., May, J., and Sheil, A.G. Autogenous veins and velour dacron in femoropopliteal arterial bypass. Surgery, 81(3), 314, 1977.
4. Ratcliffe, A. Tissue engineering of vascular grafts. Matrix Biol, 19(4), 353, 2000.