Pliable Semi-Crystalline Polymer Scaffolds with Controlled Parallel-Channel Architecture for Nerve Repair

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Introduction: We present a simple and unique technique to create pliable biodegradable scaffolds with a plurality of distinct channels running parallel along the length of the scaffolds for repair and regeneration of peripheral nerve defects. Guidance channels help direct axons sprouting from the regenerating nerve end as alternatives to nerve autografts. They must *1)* be readily formed into a conduit with desired dimensions to support cell migration, *2)* be pliable and easy to handle and suture, but should maintain their shape and resist collapse during implantation, and *3)* protect the regenerating axons in the lumen from the external would-healing environment, but should be porous and semipermeable to provide a conduit from the diffusion of biomolecules such as growth factors (Schmidt CE. Annu Rev Biomed Eng. 2003:5:293.). In this study, we describe a novel technique for preparing pliable scaffolds composed of aliphatic polyesters which have their melting points around body temperature, and producing three-dimensional channels with desirable diameters using silica capillary fiber as the templates.

Methods: Pliable biodegradable scaffolds with controlled, parallel-channel architecture were fabricated by an injection molding technique. Briefly, branched poly(ε-carprolactone-*co*-D,L-lactide) macromonomers (P(CL-LA)) with various LC/LA compositions were synthesized by ring opening polymerization using pentaerythritol as an initiator (Uto K. J Contr Rel. 2006: 110:408). The branched P(CL-LA)s were then reacted with acryloyl chloride to introduce crosslinkable vinyl groups. The obtained macromonomers were dissolved in xylene and injected into cylindrical molds with diameter 1.6 mm containing a uniformly spaced 8-660 µm silica capillary fibers (Idota N. Adv Mater. 2005: 17:2723). The P(CL-LA) -filled molds were crosslinked at 80°C with benzoyl peroxide (BPO) as an initiator. The silica fibers were then dissolved by etching technique with hydrofluoric acid (HF).

Results: Four branched P(CL-LA) macromonomers were successfully synthesized using pentaerythriol which has four hydroxyl end groups. The crosslinked P(CL-LA)s demonstrated temperature dependent changes in elasticity over the melting temperature (T_m). *i.e.*, they are rigid below the T_m, while they become elastic above the T_m. Although pure PCL has a T_m around 60°C, the branched P(CL-LA)s shows lower T_m around body temperature (~37°C) (Figure 1). Indeed, prepared cylindrical P(CL-LA) scaffolds showed the pliable and elastic properties at 37°C (Figure 2*a* and *b*). The crystallinity of P(CL-LA) scaffolds were also controllable by changing the molecular weight, branched numbers, and concentrations etc. Scanning Electron Microscopy (SEM) images of the scaffolds revealed that fabrication with the etching technique successfully produced well-defined and highly aligned multiple-channels consistent with the mold design, as shown in Fig.2*c* and *d*. Channel diameters were measured with image analysis and found to be slightly less than that of the templates. Silica capillary fibers which were 8, 150, 350, and 660 µm in diameter created channels with diameters of 8.3±0.6, 130.0±18.0, 338.3±7.6, and 605.0±5.0 µm, respectively. The scaffolds' geometrical and dimensional properties were reproducible. Cell adhesion studies on the scaffolds were also demonstrated and both rat Schwann cells and Hela cells adhered and growth well on the scaffolds.

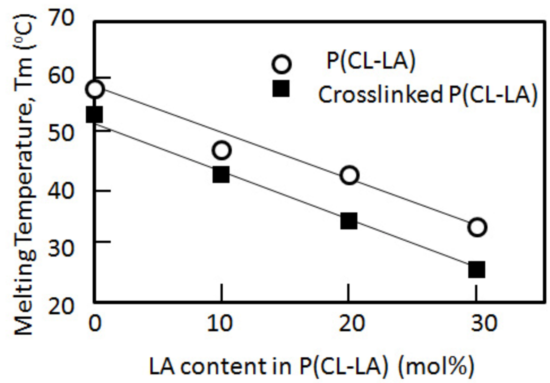

Fig.1 Effect of LA content in P(CL-LA)s on the melting temperature (T_m).

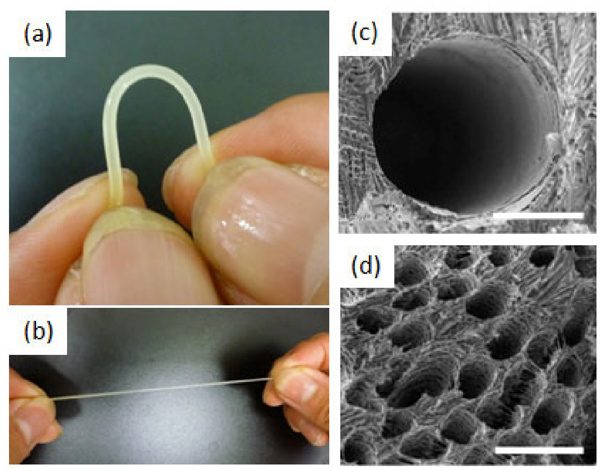

Fig.1 Photographs (*a, b*) and SEM images (*c, d*) of pliable and elastic P(CL-LA) scaffolds. Multiple-channels fabricated by HF etching technique are observed in panel *c* and *d* (scale bar represents 300 µm for panel (*c*), and 20 µm for panel (*d*)).

Conclusions: Injection molding of the crosslinked P(CL-LA) with silica capillary fibers as the templates resulted in producing pliable scaffolds with a plurality of distinct channels running parallel along the length of the scaffolds. The scaffolds also showed the good compatibility for cell adhesion. Therefore, they could serve as the basis for investigating the effects of the geometrical and dimensional properties on axonal outgrowth and regeneration of peripheral nerve defects.