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SCIENCE DIRECT®
Biomaterials 27 (2006) 1470–1478
Biomaterials
www.elsevier.com/locate/biomaterials

# Mechanical responses of a compliant electrospun poly(L-lactide-*co*-ε-caprolactone) small-diameter vascular graft

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Received 6 June 2005; accepted 23 August 2005
Available online 15 September 2005

**Abstract**

To design a "mechano-active" small-diameter artificial vascular graft, a tubular scaffold made of elastomeric poly(L-lactide-*co*-ε-caprolactone) fabrics at different wall thicknesses was fabricated using an electrospinning (ELSP) technique. The wall thickness of the fabricated tube (inner diameter; approximately 2.3–2.5 mm and wall thickness; 50–340 μm) increased proportionally with ELSP time. The wall thickness dependence of mechanical responses including intraluminal pressure-induced inflation was determined under static and dynamic flow conditions. From the compliance-related parameters (stiffness parameter and diameter compliance) measured under static condition, the smaller the wall thickness, the more compliant the tube. Under dynamic flow condition (1 Hz, maximal/minimal pressure of 90 mmHg/45 mmHg) produced by a custom-designed arterial circulatory system, strain, defined as the relative increase in diameter per pulse, increased with the decrease in wall thickness, which approached that of a native artery. Thus, a mechano-active scaffold that pulsates synchronously by responding to pulsatile flow was prepared using elastomeric PLCL as a base material and an ELSP technique.


*Keywords:* Poly(L-lactide-*co*-ε-caprolactone); Electrospinning; Tubular scaffold; Compliance matching; Circulatory apparatus; Strain

## 1. Introduction

Despite many years of efforts and various attempts, small-diameter (less than 6 mm in inner diameter) grafts have not been clinically applied [1–3]. This is due to thrombus- and excess tissue growth-caused occlusion, which is primarily determined by material factor and hydrodynamic and mechanical factor. As for the latter factor, it has been discussed over the years that the compliance mismatch between an implanted artificial graft and its host artery is a major detrimental cause of graft failure [4–9]. The incorporation of compliance matching into the designed artificial grafts has been carried out from various aspects including materials, structure, and fabrication [10–14].

Our strategy of developing a mechano-active vascular scaffold is based on a fabric-type tube made of elastomeric poly(L-lactide-*co*-ε-caprolactone) (PLCL), which is fabricated by an electrospinning (ELSP) technique. ELSP is a fiber spinning method of producing nano-to-micron-scale fiber meshes produced under a high-voltage electrostatic field. It enables the fabrication of an extracellular-matrix-resembling structure with a high surface-to-volume ratio [15–17]. Very recently, the initial phase of a study aimed at vascular application of an electrospun PLCL mesh has been reported by the other research group and our laboratory [18–21]. Our initial study focused on establishing a relationship between operation formulation parameters and the average diameter of electrospun fibers [20].

The purposes of this study are to fabricate "mechano-active" small-diameter tubes made of electrospun PLCL fabrics with various wall thicknesses, and to determine the dependence of pressure-dependent tube distensibility or compliance on the wall thickness of the tubes, and the

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doi:10.1016/j.biomaterials.2005.08.029

strain responses of these tubes under a biomimicked circulatory system.

## 2. Materials and methods

### 2.1. Polymer preparation

PLCL (molar ratio, 50:50; number-average molecular weight; $3.9 \times 10^4$) was polymerized and purified using the methods described previously [20].

### 2.2. Electrospinning of PLCL tube

A PLCL tube was fabricated using a custom-designed ELSP apparatus as reported in our previous work [22,23]. The polymer solution was delivered at a constant flow rate (5 ml/h) using the infusion pump to the needle with an air gap between the rotating/traversing mandrel (3 mm in outer diameter, 20 cm in length) and the needle tip (inner diameter; 0.8 mm) of 20 cm at a driving voltage of 20 kV. To easily detach the fabricated PLCL tube from the mandrel, poly(ethylene glycol) (PEG) (molecular weight $5 \times 10^5$; Wako Pure Chemical Industries, Ltd., Osaka, Japan) dissolved at 2 wt% in chloroform was pre-electrospun onto the mandrel for 3 min. Then, PLCL solution containing 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP; Sigma Chemical Co., St. Louis, MO) solution (3 wt%) was electrospun for 10, 30, 60 or 100 min, and tubular PLCL fabrics produced were detached from the mandrel after immersing in distilled water for 1 h.

### 2.3. Scanning electron microscopy

The electrospun PLCL tubes were sputter coated with platinum and their microscopic structure was observed by scanning electron microscopy (SEM; JSM-840A, JEOL Ltd., Tokyo, Japan) at an acceleration voltage of 8 kV. The wall thickness of the tube was determined as the average taken from 16 randomly selected points, whereas the mean fiber diameters at the luminal and outer surfaces of the tube were calculated using 60 fibers seen on SEM images.

### 2.4. Elasticity of fabricated electrospun PLCL tube

The elasticity of the processed electrospun PLCL tube was measured as described previously [23]. Briefly, all the tubes were sealed with fibrin glue (BOLHEAL; Kaketsuken, Kumamoto, Japan) to avoid water leakage upon pressure application. The intraluminal pressure–diameter relationship was determined using an apparatus designed by Takamizawa and Hayashi. The elasticity of the tube was determined as the stiffness parameter ($\beta$) defined by Hayashi et al. [24], which is described as

$$\ln(P/P_s) = \beta(D/D_s - 1), \quad (1)$$

where $P$, $P_s$, $D$, and $D_s$ denote the intraluminal pressure, standard pressure (100 mmHg in this study), external diameter, and diameter at $P_s$, respectively. The slope in the linear relationship of the ln $(P/P_s)$ vs. $(D/D_s-1)$ plot, which holds empirically in the physiological pressure range (60–140 mmHg), gives $\beta$. A smaller $\beta$ indicates a more compliant tube. The diameter compliance ($Cd$) was calculated using [25]

$$Cd = \Delta D/(D \times \Delta P), \quad (2)$$

where $\Delta D$ is the diameter change associated with $\Delta P$ (pressure increment) at the intraluminal pressure of 100 mmHg. The unit was expressed as percentage diameter change per mmHg $\times 10^{-2}$.

### 2.5. Simulated circulatory apparatus

A custom-designed pulsatile circulatory apparatus, schematically shown in Fig. 1, was composed of a centrifugal pump (Yasuhisakoki Bio-Mechanics Co., Tokyo, Japan), a tube-installed chamber, a compliance tank, a flow control valve, a flow meter and a reservoir, which were connected to each other with silicon tubes to form a closed circuit. After a fabricated tube, approximately 6.5 cm in length, was installed in the chamber and a closed circuit was assembled, such a circuit was filled with medium 199 with 10% fatal bovine serum. The outer diameter of the tube was determined using a laser sensor (LX2-V10; Keyence Co., Osaka, Japan), as shown in Fig. 1B. To biomimic a pulsatile flow similar to arterial flow, a centrifugal pump periodically produced alternate minimal and maximal rotation rates as shown in Fig. 1C. The minimal rotation rate was attenuated down to 70% of the maximal rotation rate, whereas the minimal rotation period ($t_1$) and maximal one ($t_2$) were fixed 0.7 and 0.3 s,

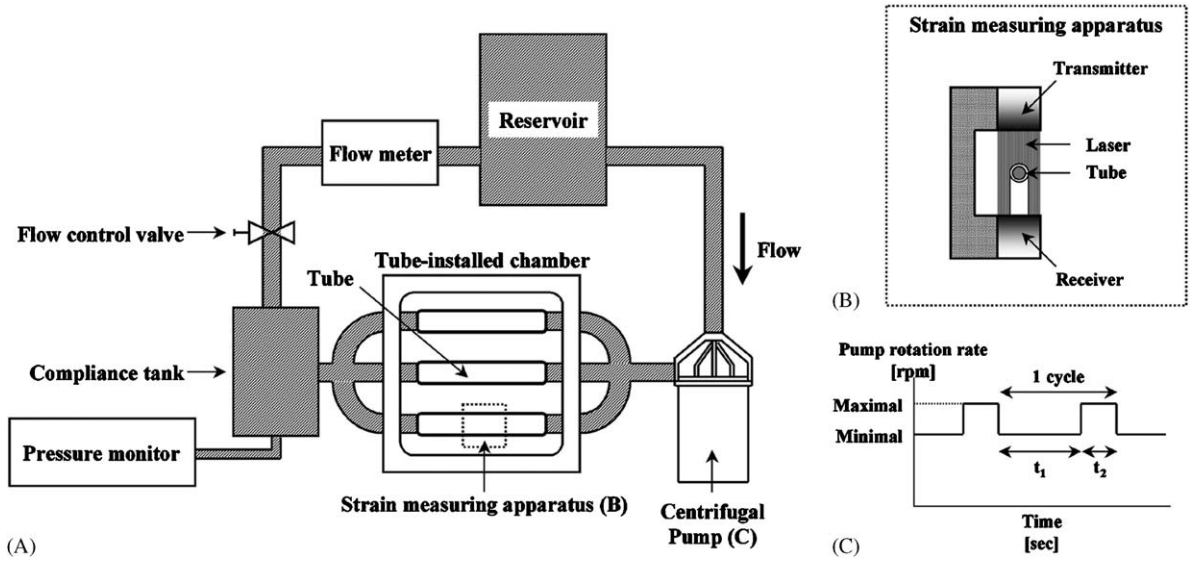


Fig. 1. (A) Schematics of simulated circulatory system. (B) Strain measuring device: for detecting outer diameter of tube by laser sensor placed at tube-installed chamber. (C) Schedule of periodic pump rotation rate generating pulsatile flow. The minimal rotation rate (duration; $t_1 = 0.7$ s) was attenuated down to 70% of the maximal one (duration; $t_2 = 0.3$ s), which produced physiologically simulated pulsatile flow at 1 Hz (60 beats per min).