Development of Porous polyurethane Arterial-Venous Shunt by Thermal Phase Transition

G. H. Ryu, J. S. Jeong*, H. K. Jeong, H. K. Lee, K. B. Lee**, J. Kim*, B.G. Min*, H. Y. Lee
Department of Medical Devices and Radiation Health, Korea Food and Drug Administration, *Department of Medical Engineering, College of Medicine, Seoul National University, **Biomedical and Science Center, Korean Institute of Science and Technology

온도 변화에 의한 상전이를 이용한 다공성 동정맥 누관의 개발

유규하, 정재승*, 정희교, 이해광, 이규백**, 김종원*, 민병구*, 이해룡
식품의약품 안전본부, *서울대학교 의과대학 의공학과, **한국과학기술원 의공학센터

ABSTRACT

A new technique for the preparation of porous vascular prostheses was investigated. Polyurethane solution (10 to 14wt%) was injected into a mold. After freezing at low temperature (0 ℃ ~ -40 ℃), solvent was dissolved out with water at 0 ℃ to form porous tubes. The average pore size (< 10 ㎛)and pore occupation (10% to 51%) were easily changed by changing polyurethane concentration, freezing temperature, and freezing methods. This technique can give a proper pore size (30~60 ㎛) for tissue ingrowth, and suitable compliances for matching with arteries and veins. This method might give a desired compliant graft for artificial implantation with the presently valid medical polymers.

Introduction

The surgical reconstruction of diseased arteries with synthetic vessels was significantly satisfactory for patients.[1-4] However, surgical operations have been limited to the relatively large-diameter high-flow, low-resistance vessels (greater than 6mm in inner diameter) including the aorta, iliac, and femoral vessels. Small-diameter vessels (less than 6mm in inner diameter) are not in general clinical use due to their limited long-term biocompatibility and low patency rates in experimental trial.

For the artificial vessels, long-term patency is considered to depend critically on the properties of the material and the fabrication process of the graft[5]. Synthetic vascular grafts with porous walls have been widely proposed, since strength, suture retention, kink resistance, and other handling properties can be improved over those with nonporous solid walls. A variety of methods have been developed to allow the reliable production of porous vessels based on spinning technology. For example, Leidner and Wong[6] reported the extrusion of a concentrated polymer solution (or a polymer melt) on a rotating mandrel to form the desired thick porous vessels. In their process, a high-pressure source and a large number of passes were required. Other techniques for the manufacture of vascular have also been used for the preparation of compliant grafts.

However, these methods always need some special apparatus and can not change the compliance of the vessels over a large range to match the compliances of the native veins and arteries. Generally, the compliance of veins and arteries change from several percent to about 20% in the physiological pressure range (60-160mmHg). And, it is very important and practical to fabricate vessels with adequate compliance to match the arteries or veins to be replaced. Thus, it is necessary to develop a technique which can form vessels with various compliances. In this study, a simple and convenient technique to form compliant vessels was investigated. The porosity (pore size and pore occupation) and compliance could be easily controlled to match those of living tissues.

Methods and Materials

Materials

Pellethane® 2363-80AE(PU pellets) was provided by DOW Chemicals Co. U.S.A. and N,N-Dimethylacetamide(DMAc) was purchased from Shinyo Ltd, Japan.

Vessel fabrication

PU pellets were extracted with methanol for 3 days to remove low-molecular-weight components. After extraction, the pellets were dried under vacuum at 60 ℃ for 48 h to remove residual solvents.
The methanol-extracted PU pellets were dissolved in DMAc to make 10, 12, 14% (wt/vol) solution, respectively. The experimental mold is shown in Figure 1.

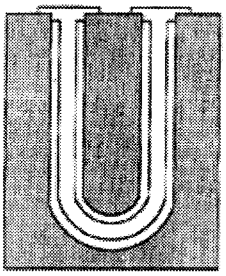

Figure 1. Diagram of mold for fabrication of porous vessels

Briefly, stainless steel rod having desired diameter was used as inner part and duralumin cases were used as upper and lower parts. The inner part was fixed centrally on an adapter. The mold was sealed with the bolts and nuts at five sites to protect the leakage of polymer solution. Polymer solution was injected into the mold, and frozen at a definite temperature. After keeping the polymer-solution-injected mold at the freezing temperature for 5 h, the bolts, nuts and outer cases were removed. The inner mold was moved into the cold methanol. The cold methanol was changed every 12 h to permit solvent in the frozen polymer graft to dissolve out. The solvent exchange was carried out for 2days to form a uniformly porous vessel. Porous vessels were moved into the distilled water to removed the methanol solution and dried under vacuum for 3 days for following experiments.

Scanning electron microscopy and image analysis

The surface morphology of modified PU grafts was examined with a Hitachi S-510 scanning electron microscopy (SEM) at an accelerating voltage 15kV. Samples were mounted and then sputter coated with gold using an ion coater.

Compliances

Compliance is defined as the percentage change in diameter over the physiological pressure range (60-160mmHg), and is expressed as $(D_{160mmHg}-D_{60mmHg})/D_{60mmHg}$, where $D_{160mmHg}$ and D_{60mmHg} are diameters at the corresponding pressure. Compliance was determined with a pressure regulator, pressure meter, and image analysis system.

Heating treatment and stretching

Porous vessels were treated in phosphate buffered saline (PBS, pH 7.4) at 60 ℃ for a definite time. For the stretching treatment, samples were stretched to 150% and 200% of the original length, and kept at 60 ℃ for 20 h. The treated samples were returned to room temperature (20 ℃), incubated into PBS at 37 ℃ for 24 h, and used for compliance measurement and microscopic observation.

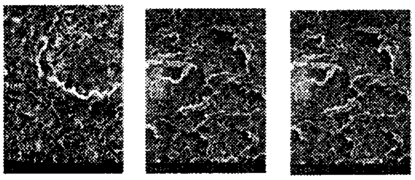

Figure 2. SEM photographs of inside, outside and cross-section of the vessel wall

Results

Vessel preparation

Vessels of wall thickness between 0.19 and 0.46mm were fabricated using the acute freezing method. All vessels were opaque(white) and very flexible, especially those formed with low polymer concentration solution. Typical SEM photographs of the cross-section, inside surface, and outside surface of the wall, are shown in Figure 2. From these photographs, a uniform distribution of pores on the surface is observed. Pores sizes are 6 ㎛ to 10 ㎛. Pore characteristics are a function of freezing temperature. The pore size was decreased with decreasing of freezing temperature. However pore occupation did not change. When the polyurethane concentration was decreased, the pore occupation was increased.

Compliances

The compliances changes with porosity, pore size and distribution, and nonuniformity as well as the mechanical properties. Usually, larger porosity and pore size increase the compliance.

Heat and stretching treatment

Polyurethane macromolecule are rearranged when in contact with solvent and this rearrangement is expected to modify surface and mechanical properties. To avoid continuous changes of surface properties, heat treatment with phosphate buffered saline was performed to make the rearrangement complete. Heat treatment displayed a decrease in compliances. When the polymer solution concentration was changed to increase or reduce the pore occupation, the compliance was also changed. The compliances decreased by increasing the polymer concentration. This is ascribed to the reduction of pore number and size induced by the increase of polymer concentration.

The compliances of porous vessels can be controlled by changing polymer concentration, freezing temperature, and methods as mentioned above. Compliance also changes through heat treatment. Thus, vessels which have different compliances but the same pore size, distribution, and occupation can be easily formed through post-treatment after fabrication under the same conditions.

Stretching treatment of samples changed pore shape. Pores became longitudinal in the stretching direction. These might be due to reorientation of polyurethane molecules under the stretching treatment[7].

Discussion

A convenient and simple technique for porous vessels has been developed. The vessels with a large range of compliances having different pore size and distributions or the same pore size and distribution can be easily formed by this technique without special apparatus. These parameters are very important for the performance of artificial vessels. To eliminate compliance mismatching, the compliance of the blood vessels is considered to make the corresponding grafts. To match the compliance completely, a series of grafts with various compliances can be prepared. This technique provides a series of compliant grafts conveniently and quickly for clinical selection.

References

1. L. M. Taylor, H. M. Edwards, E. S. Phinney, and J. M. Porter, "Reverse vein bypass to infrapopliteal arteries. Modern results are superior to or equivalent to in-situ bypass for patency and for vein utilization", *Ann. Sur.*, **205**, 90-97 (1987)
2. A. D. Callow, "Problem in the construction of an small diameter graft", *Int. Angiol.*, **7**, 246-253 (1988).
3. R. J. Dilley, J. K. McGeachie, and F. J. Prendergast, "A Review of the histologic changes in vein-to artery grafts, with particular reference to intimal hyperplasia." ***Arch. Surg***., **123**, 691-696 (1988)
4. J. L. Cronenwett and G. B. Zelenok, "Alternative small arterial grafts in *Biological and synthetic vascular prostheses*, j. C. Stanley, W. E. Burke, S. M. Lindenauer, R. H. Bartlett, and H. G. Turcotte (deds.), Grune Stratton, New York, 1982, pp. 565-620.
5. R. Walden, G. H. L'Italien, J. Megerman, and W. M. Abbott, "Matches elastic properties and successful arterial grafting." *Arch. Surg*., **11**, 1166 (1980)
6. J. Leider, E. W. C. Wong, D. C. MacGregor and G. H. Wilson, "A novel process for manufacture of porous grafts: Process description any product evaluation." J. *Biomed. Mater. Res.*, **17**, 229-247 (1983)

7. Shu Qin Liu and Makoto Kodama, "Porous polyurethane vascular prostheses with variable compliances." **JBMR**, **26**, 1489-1502 (1992)