Biomaterials Research (2000) 4(1) : 8-12

Biomaterials Research

Compliance of Surface Modified Polyurethane Tubular Scaffold for Artificial Esophagus

Hwal Suh[1], Yu-Shik Hwang[1], Yu-Bong Kang[2], Ryusuke nakai[2], Sadami Tsutsumi[2] and Jong-Chul Park[1]*

[1]Department of Medical Engineering, Yonsei University College of Medicine, 134, Shinchon-dong, Seodamun-ku, Seoul, Korea
[2]Institute for Frontier Medical Sciences, Kyoto University, 53, Kawara-cho, Shogoin, Sakyo-ku, Kyoto 606-8507, Japan
(Received January 10, 2000/Accepted March 10, 2000)

To evaluate the mechanical properties of a polyurethane tube, which is fabricated to use as a scaffold for artificial esophagus, the storage modulus of the material toward axial direction, dynamical elasticity, and compliance values of the tube was investigated. A polyurethane tube of which surface was oxidized to induce peroxide demonstrated the highest storage modulus and compliance, had the larger radial change than those of the others against the same internal pressure, and showed adaptable softness toward the radically directed pressure. These results indicate that mechanical compliance of the material increased although oxidization produced deterioration.

Key words : Compliance, Polyurethane, Tubular scaffold, Esophagus

INTRODUCTION

Currently, various kinds of stents are in use to expand lumen of the occluded esophagus to prevent or treat dysphagia which is mainly oriented from cancer metastasis or injury by swallowing chemicals that burn esophageal mucosa.[1)] Placing a meshed metallic stent is a representative of them, but the continuously penetrating mucosa through the wire of filaments of the stent was used to re-occlude the esophageal lumen with impinging the placed stent.[2)]

Although a silicone tube has been reported as an acceptable device to replace damaged esophagus, its high flexibility limits application to the lesion between laryngopharynx and cardicac part of the stomach.[3)]

To develop an artificial esophagus that would totally replace esophagus including laryngopharynx and cardiac part of the stomach, fabrication of polyurethane in tubular shape to use as scaffolds was considered.

The primary mechanical requirement for a material to be an artificial esophagus is the optimal compliance that the material should be dilated to provide smooth passage for the swallowed dietary mass from top to bottom without any interference during deglutition, and be shrunk during the rest time to prohibit reverse passage of food from the gastric contraction.[4)] Polyurethane (PU) is a well-known material as bioinert implantation with mechanical advantages including high durability against continuously affecting bending stresses, and surface modification to provide biologically adequate properties for tissue interactions on the material has also been widely investigated.[5)]

In this study, we evaluated the compliance value, storage modulus toward axial direction, and dynamical elasticity of variously surface modified PU tubes to produce a scaffold that has optimal mechanical properties and surface with acceptable tissue interactions.

MATERIALS AND METHODS

Fabrication of PU tubular scaffold

Thirteen % PU solution (Pellethane, 2363-81A, Dow Chemicals, Midland, MI), which is purified by dimethylacrylamide (DMAC) and methanol as previously described,[6)] was coated on a glass-rod with 3.8 mm of diameter, and to fabricate tubes with length of 50 mm and thickness of 0.5 mm.

The specimens were divided into 4 groups. Group 1 was the control without surface modification, Group 2 was the PU tubes whose outer-surface was treated by

*To whom correspondence should be addressed.

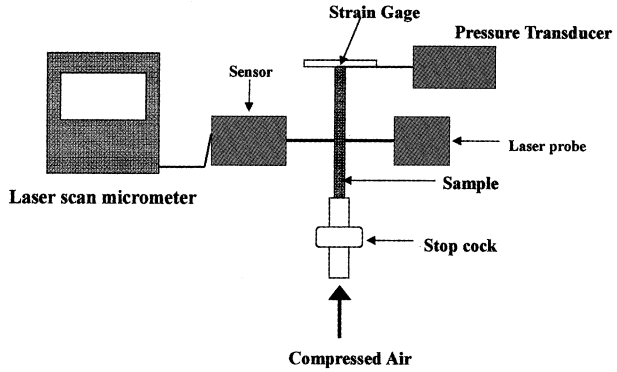

Fig. 1. Schematic diagram of the apparatus for compliance assessment

5% hexamethylene diisocyanate(HMDI), Group 3 was the tubes equally treated as the group 2 with additional Dimethylsulfoxide(DMSO), and Group 4 was the specimen, whose surface were ozone-oxidized.

Through an ozone generator (TOG-B1, Peak Scientific Inc., England, U.K.), dried oxygen gas passed with 4.5 L/min of oxygen flow rate, 1 bar of oxygen pressure, and 60 V of generator voltage at 37°C. The gas was supplied into a chamber where PU tubes and films were placed in. Ozone treatment was processed for 30 min, and tubes were purged by nitrogen gas to remove non-reacted ozone on polymer surface in the same way as described previously.7

Compliance Assessment

The change of the tubular diameter in response to the change of internal pressure was referred to compliance value. An extremity of a tube was closed and the compressed air was delivered into the specimen. The internal pressure was measured by using a strain gage (060S-35, KYOWA Co., Japan) through a pressure transducer (SMD-10A, KYOWA Co., Japan) placed in the tube, and changes of diameter were measured by a laser scan micrometer (LS5000, KEYENCE Co., Japan). (Fig. 1)

The compliance value was calculated by following equation;

$$C=2\times\{(D-D_0)/D_0\}/P$$

Here, C is the compliance, D_0 and D are the initial and measured diameter at the internal pressure P, respectively. (n=4/groups)

Storage modulus measurement

Storage modulus of a material was measured to investigate the complex stress, which occurs from the swallowed dietary mass, bolus, that passes esophageal lumen. To investigate the storage modulus, specimens were prepared to rectangular sheets (20×4×0.5 mm). Storage modulus toward axial direction, and dynamical elasticity of the specimens were measured by using a dynamic visco-elastic measurement equipment (Rheogel E-4000, UBM Co., Japan), at 37°C with frequency range from 1 to 20 Hz. (n=4/groups)

Observation of the modified PU surface

A scanning electronic microscopic observation (S-800, Hitachi, Tokyo, Japan) was carried to investigate surface textures of all the specimens prior to the assessment of storage modulus.

RESULTS

Compliance value assessment

Radial change ratio of the tubular PU scaffold was estimated by measuring changes of diameter versus the internal pressures, and the group 4, the ozone oxidation induced PU tube, permitted the larger radial change ratio than other groups. However, the HMDI treated group 2 and HMDI-DMSO treated group 3 permitted less radial change ratios than group 1, the control. (Fig. 2)

The compliance values (=1/Kpa) were obtained from calculating determined radial change. The compliance values of the control group, group 2, group 3, and group 4 was 0.0015±3.0E-4, 0.0012±2.2E-4, 0.0009±1.2E-4, and 0.0037±8.2E-4 respectively. This indicates that the group 4 has the highest flexibility toward the radial direction of all groups. Although either group 2 or 3 has modified surface, their compliance values are below than those of the control. (Fig. 3)

Storage modulus measurement

The storage modulus in the longitudinal axial direction reveals the strength toward the axial direction in tubes. All the surface modified PU groups demonstrated higher storage modulus than the control, and group 4 was the

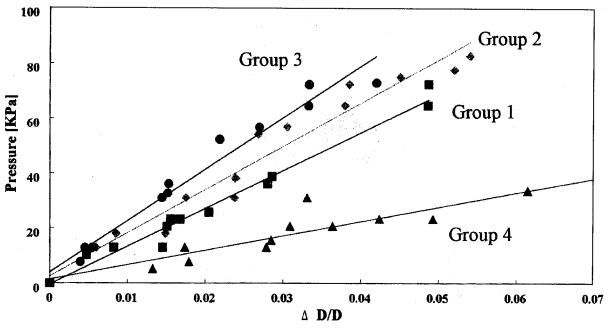

Fig. 2. Change of diameter in accordance with internal pressure

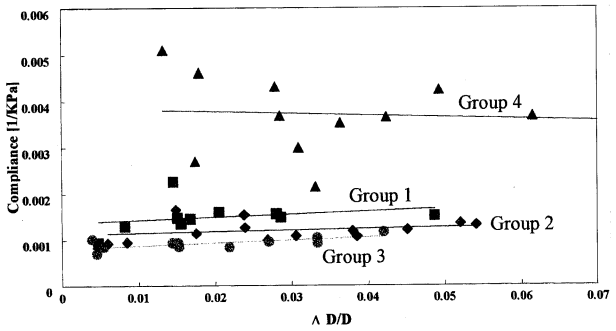

Fig. 3. Compliance in accordance with diameter changes

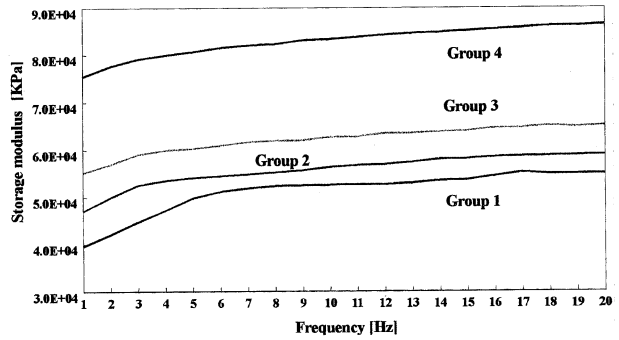

Fig. 4. Storage modulus with frequency

highest. In the HMDI-treated groups 2 and 3, additional DMSO-treated group 3 had the higher storage modulus. At low frequency (1~5 Hz), the values of storage modulus changed steeply than those of high frequency (5~20 Hz). (Fig. 4)

Modified surface texture

In scanning electron microscopic observation, relatively smooth surface appeared on the HMDI treated group 2 and HMDI - DMSO treated group 3. The surface of PU ozone treated group 4 demonstrated a diffuse and wavy texture, and was similar to uniformly wavy surface texture of control PU. (Fig. 5)

DISCUSSION

Esophagus is a muscular digestive tract that transports bolus from mouth to stomach, and consists of the internal mucous epithelium lining the tract lumen, inner circular layer and outer longitudinal layer of the external smooth muscle fibers. Peristalsis, which propels mass along the digestive tract, consists of waves of external muscular contractions of repeating circular and longitudinal contractions. A swallowed bolus inters esophagus with opening of upper esophageal sphincter, the bolus is pushed down by a primary peristalsis, the secondary lower esophageal sphincter opening follows, and this movement occurs repeatedly until the bolus enters stomach.[8)]

The ideal mechanical properties for artificial esophagus should have both high compliance in radial direction and low storage modulus in axial direction, because the esophagus must expand in radial direction and produces a tension in axial direction to provide esophageal peristalsis for passing bolus. If an artificial esophagus has the lower elastic modulus in radial direction and higher elastic modulus in axial direction than the normal esophagus, the tubular esophagus would easily derive the higher stress concentrations in the boundary area between the esophagus and the living tissues. And thereby the artificial esophagus would be removed from the connecting interfaces with the living body. In the reverse, the higher compliance value in radial direction and lower modulus in axial direction, the small expansion in radial direction

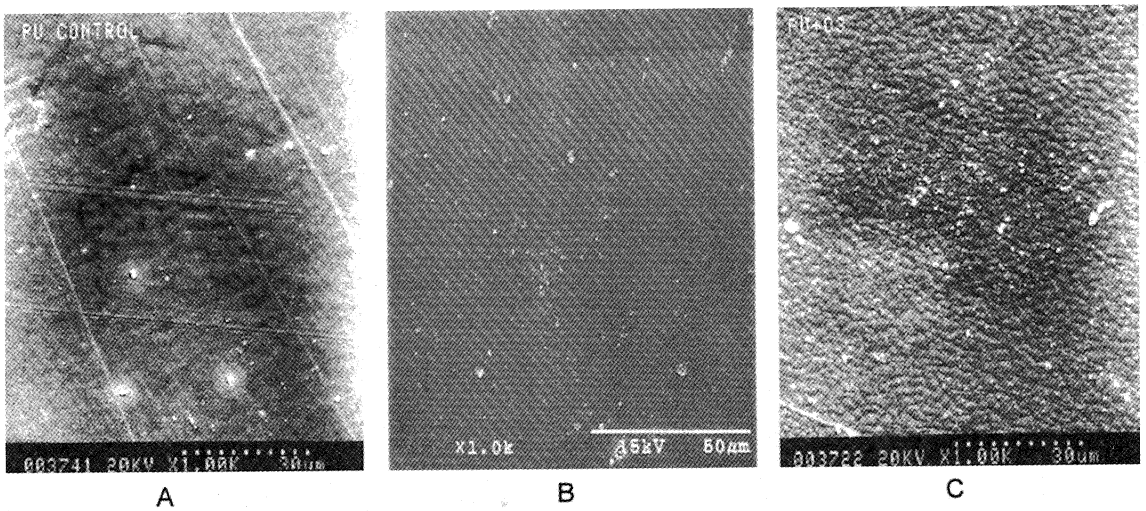

Fig. 5. Surfaces of a) non-treated PU, b) HMDI-treated, and c) ozone-treated PU observed by SEM

produces smaller deformation without generating the higher stresses in axial direction. Therefore, high elasticity in radial but low elasticity in axial directions would be necessary for fabricated materials.[9] Extensive work to develop practical and economical methods for surface modification of PU has been carried out, and many different biologically functional molecules have been chemically or physically immobilized on polymeric supports.[10-12] But these method limits their practical use because of the side effects of residuals from chemical treatment, or mechanical deformities after physical treatments. Previous study reported that hexamethylene diisocyanate (HMDI)-induced NCO- groups on PU surface to bind with amines of collagen molecules, which resulted CONH-covalent bonding, were effective. But it limits the selectivity of solvent for dissolving proteins to avoid diisocyanate-related toxicity.[6] To overcome the limitation, introduction of the active species using an oxidation reaction was considered to graft polymerization onto PU. Ozone oxidation easily produces carboxyls and hydroperoxides on the surface of molded polymers even with complicated shapes.[13-15] On the PU surface, active oxygen-atoms, which induce carbon and hydroxyl radicals, are produced by the ozone decomposition. The carbon radical immediately reacts with oxygen molecules, and leaves peroxyl radicals.[11] Such polymeric peroxides are convenient to initiate the graft polymerization with proteins onto PU surface. External surfaces of the tubular PU were modified to graft collagen molecules, and the effect of chemical modification to compliance and storage modulus was investigated in this study, because those procedures produce chemical erosion and molecular degradation on the PU surface.[16] In this study, several kinds of surface modification procedures were compared. The compliance value of the HMDI-treated group 2 was decreased as compared with that of control, and additional DMSO-treatment onto the HMDI-treated PU surface produced the lower compliance value in group 3 than in group 2. This phenomenon was related to the fact that the more chemical treatment induces the more material degradation, and the specimens lost radial flexibility due to re-aggregation of the degraded residues, in concerning with the previous report about elasticity of the HMDI-treated PU.[6]

In reverse, the ozone treated group 4 demonstrated the more increased compliance value than the control, and this was within the physiologically acceptable range. It would be assumable that using oxygen gas, instead of using HMDI and DMSO solution, produced less degraded chemical residues, but produced surface erosion leading to increased compliance value. This can be presumable according to the surface texture observed through scanning electron microscope. The surface of PU treated by ozone gas revealed uniform wavy texture due to surface deterioration by ozone attack[17], which was similar to the surface of control PU, but the HMDI treated PU surface was relatively smooth, which was greatly different from the control PU surface.

In investigation of storage modulus, the stress forward the longitudinal axis increased as the frequency increased, and group 4 demonstrated the highest value. The steeper modulus values were obtained in all groups at the low frequency than at the higher frequency, and this assumes to be affected by the surface viscosity of the PU.[18]

At this point of view, group 4 was appropriate to use as a scaffold for artificial esophagus, though the storage modulus was high, but it was in the applicable limit. But, the group 4 assumes to have the most degraded surface, and it is necessary to estimate the effect of surface treatments on durability of the materials in a further study.

CONCLUSION

In this study, compliance of chemically surface modified tubular PU scaffold was investigated.

1. The compliance increased in the ozone treated PU tubes, but decreased in the HMDI treated ones, while storage modulus decreased in the ozone treated Pus, but increased in the HMDI treated ones.
2. Inducing gas phase chemical is favorable one to modify surface of PU for fabrication of artificial esophagus.

ACKNOWLEDGEMENT

This study was supported by the Biotech 2000 Program (Grant No. 97-N1-02-05-A-03) of the Ministry of Science and Technology, Republic of Korea.

REFERENCES

1. B. G. Fallone,. Wallace, and C. Gianturco, "Elastic characteristics of the self-expanding metallic stents", *Invest. Radiol.*, **23**(3), 370-376(1988).
2. P. Rossi, M. Bezzi, F. M. Salvatori, F. Maccioni, and M. L. Porcaro, "Recurrent benign biliary strictures: management with self-expaning metallic stents", *Radiology.*, **175**(4), 661-665(1990).
3. M. G. Sarr, P. H. Harper, and M. G. W. Kettlewell, "Peroral pulsion intubation of malignant esophageal strictures using a fiberoptic technique", *Am. Surg.*, **50**(3), 437-440(1984).
4. H. Song, K. Choi, B. Cho, D. Ahn, and K. Kim, "Esophagogastric neoplasms: Palliation with a modified Gianturco stent", *Radiology.*, **180**(2), 349-354(1991).

5. J. E. Lee, J. C. Park, K. D. Park, Y. H. Kim, and H. Suh, "In vitro evaluation of PEG modified polyurethane in cellular toxicity", *Biomater. Res.*, **2**(2), 65-68(1998).
6. H. Suh, Y. S. Hwang, J. E. Lee, K. T. Kim, J. C. Park, K. D. Park, and Y. H. Kim, "Type I atelocollagen grafting on polyurethane tube and its mechanical property", *Biomater. Res.*, **2**(4), 158 - 162(1998).
7. H. Suh, "Treatment of collagen for tissue regenerative scaffold", *Biomed. Eng. Appl. Basis Comm.*, **11**(4), 167-173(1999)
8. S. I. Fox, Human physiology, Wm. C. Brown Pub., Dubuque, IA, pp. 487-489(1993).
9. S. M. Kim, T. McCulloch, and K. Rim, "Evaluation of the viscoelastic properties of pharyngeal tissue", *Tissue Engineering.*, **4**(4), 389-402(1998).
10. G. Soldana and R. Mercogliano, "Bioartificial polymeric materials obtained from blends of synthetic polymers with fibrin and collagen", *Int. J. Artif. Organs.*, **14**(5), 295-303 (1991)
11. J. Yamauchi, A. Yamaoka, K. Ikemoto, and T. Matsui, "Graft copolymerization methyl methacrylate onto polypropylene oxidized with ozone", *Ann. Appl. Polym. Sci.*, **43**, 1197-1203(1991)
12. T. Okada and Y. Ikada, "Modification of silicone surface by graft polymerization of acrylamide with corona discharge", *Macromol. Chem.*, **192**, 1705-1713(1991)
13. S. Dasgupta, "Surface modification of polyolefins for hydrophilicity and bondability : Ozonization and grafting hydrophilic monomers on ozonized polyolefins", *J. Appl. Polym. Sci.*, **41**, 233-248(1990)
14. J.O. Karlsson and P. Gatenholm, "Solid-supported wettable hydrogels prepared by ozone induced grafting", *Polymer.*, **19**, 4251-4256(1996)
15. J. Peeling, M. S. Jazzar, and D.T. Clark, "An ESCA study of the surface ozonization of polystyrene film", *J. Polym. Sci.*, **20**, 1797-1805(1982)
16. S. S. Sternstein, "Transient and dynamic characterization of viscoelastic solids", Polymer characteization, Vol. 203, Mapple Press Co., York, PA, pp 123-148(1981).
17. K. Fujimoto, Y. Takebayashi, H. Inoue, and Y. Ikada, "Ozone-induced graft polymerization onto polymer surface", *J. Polym. Sci.*, **31**, 1035-1043(1993)
18. M. Szycher, A. A. Siciliano, and A. M. Reed, "Polyurethane elastomers in Medicine", Polymeric Biomaterials, ed. S. Dumitriu, Marcel Dekker Inc., New York, NY, pp 233-244(1993).