

Experimental Study on Stability of a High-porosity Expanded Polytetrafluoroethylene Graft in Dogs

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Purpose: The purpose of the present study was to evaluate the stability of a high-porosity expanded polytetrafluoroethylene (ePTFE) graft, which has been shown to possess excellent biocompatibility and tissue integration.

Methods: The graft used in the present study was a high-porosity ePTFE graft, which had an average internodal distance of approximately 60 μm and a random node architecture with tortuous path channels extending from the outer to the inner surface. Eleven beagle dogs (each group n=3 or 4) weighing 10-12 kg were used. The graft, with a 6 mm inside diameter and a 30-40 mm length, was implanted into the canine abdominal aorta and retrieved after 2-80 weeks. The deformation of the graft was evaluated by conventional computed tomography (CT). The radial tensile strength, longitudinal tensile strength, and suture retention strength of the graft were measured after 2-80 weeks.

Results: CT studies showed no anastomotic aneurysm or deformation of the graft. Physical tests demonstrated no significant deterioration in suture retention strength, radial tensile strength or longitudinal tensile strength for periods ranging from 2-80 weeks compared to pre-implantation grafts.

Conclusion: The graft possesses adequate stability that ensures safe and effective clinical use. (*Ann Thorac Cardiovasc Surg* 2006; 12: 37-41)

Key words: stability, high-porosity, expanded polytetrafluoroethylene

Introduction

Polytetrafluoroethylene (PTFE) is a fully fluorinated polymer with a chemical formula $(-\text{CF}_2-\text{CF}_2)$. Since a process to expanded PTFE (ePTFE) was discovered by Oga of Sumitomo Electric Industries while conducting experiments on wire coating,¹⁾ the technique was ultimately re-

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financed and applied to the development of a viable vascular prosthesis. In 1975, the first ePTFE graft was introduced to the market by two manufacturers, Impra and W.L. Gore and Associates. Early observation of aneurysmal change of ePTFE grafts led manufacturers to add a thin outer reinforcing wrap of porous fibrous PTFE or sinter on the outer surface.²⁾

The biological behavior of ePTFE grafts is largely influenced by their physical dimensions, which can be controlled by their manufacturing process. The physical structure of ePTFE grafts comprises a microporous framework of solid materials (nodes) connected by fine fibers (fibrils). Several investigators were able to demonstrate improved graft healing by making the graft more porous.³⁻⁷⁾ However, in such experiments, high-porosity ePTFE grafts lacked an outer wrap and were not clinically available

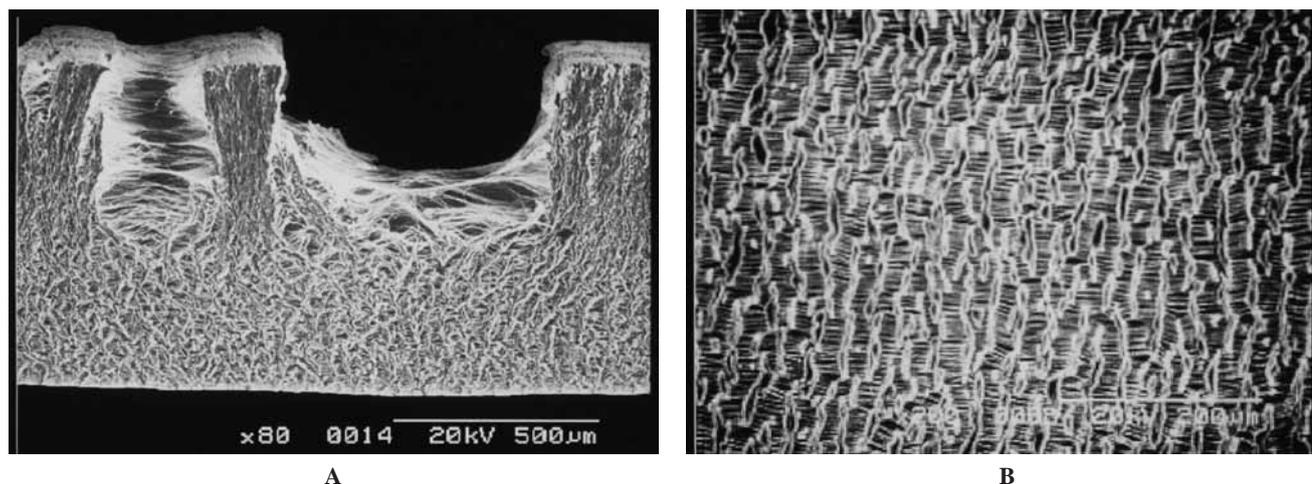


Fig. 1. Scanning electron micrographs of a high-porosity ePTFE graft with unique node-fibril morphology.

A: Longitudinal section.

B: Inner surface.

because of their physical fragility.

Recently, we developed a new high-porosity ePTFE graft with unique node-fibril morphology that possesses excellent biocompatibility and tissue integration.⁸⁾ The purpose of the present study was to evaluate the stability of the graft using a canine abdominal aorta replacement model.

Material and Methods

Vascular grafts

The graft used in the present study was a high-porosity ePTFE graft with unique node-fibril morphology. The graft had an average internodal distance of approximately 60 µm and a random node architecture with tortuous path channels extending from the outer to the inner surface (Fig. 1).⁸⁾ The graft had a 6 mm inside diameter and was 30-40 mm long. The graft was reinforced by a fluoropolyethylene filament.

Animal models

Eleven beagle dogs of either sex weighing 10-12 kg were used. The dog was chosen as a test animal because it has been reported to approximate the human in terms of vascular graft healing.⁹⁾ All animals have received humane care in compliance with the "Principles of Laboratory Animal Care" formulated by the National Society for Medical Research and the "Guide for the Care and Use of Laboratory Animals" prepared by the Institute of Laboratory Animal Resources and published by the National

Institutes of Health (NIH Publication No. 86-23, revised 1985).

The animals were anesthetized with an intravenous injection of butorphanol (0.025 mg/kg), midazolam (0.3 mg/kg), and ketamine (5 mg/kg), and were endotracheally intubated. Anesthesia was then maintained with 1% to 2% sevoflurane mixed with nitrous oxide and oxygen. A midline abdominal incision was made, and the abdominal aorta below the renal artery was identified and isolated from the surrounding structures. Heparin (150 IU/kg) was given intravenously, proximal and distal control of the abdominal aorta was obtained, and a 1-2-cm section of the abdominal aorta was excised. The grafts were interposed between the edges of the abdominal aorta, using a continuous 5-0 monofilament polypropylene. After complete hemostasis was secured, the abdomen was closed layer to layer. Ampicillin (50 mg/kg) was given intravenously before the operation. No anticoagulant or antiplatelet drugs were given postoperatively. The grafts were harvested at intervals of 2 weeks (n=4), 4 weeks (n=4) and 80 weeks (n=3). The animals were anesthetized and computed tomography (CT) was performed. The abdomen was then reopened. The entire graft with a portion of the host artery was removed under systemic heparinization (150 IU/kg). The specimen was fixed with 10% buffered formalin for 2 weeks. Finally, the animals were sacrificed by a sufficient dose of potassium chloride.

Computed tomography (CT)

The deformation of the graft was evaluated by conven-

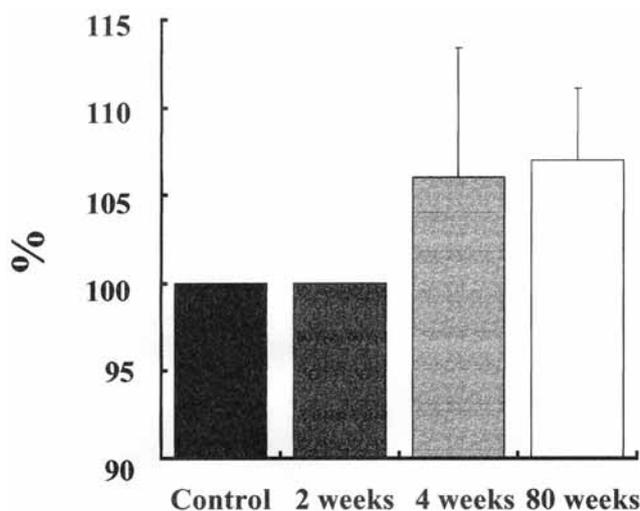


Fig. 2. Deformity ratio measured by using CT. There was no significant difference in the deformity ratio over the time course.

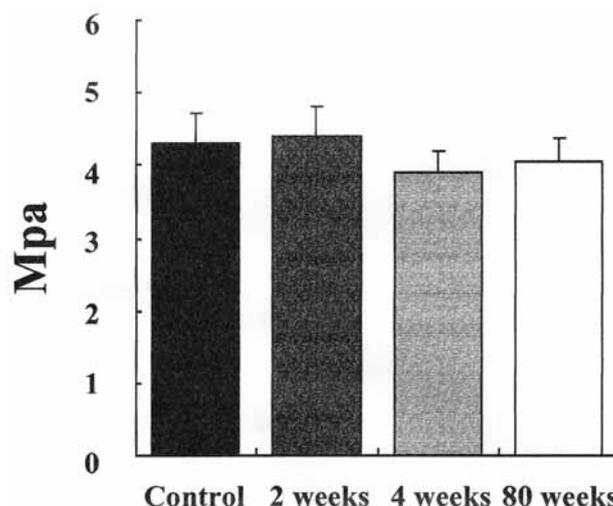


Fig. 3. Radial tensile strength. The strength did not change at all points as compared to pre-implantation.

tional CT. The CT was performed under the condition of 120 kV and 100 mA. The coronal sections were 1 mm thick. The maximum and minimum diameters of the graft were measured at the midpoint of the graft. The deformity ratio (%) was calculated as a percentage determined by dividing the maximum diameter into the minimum diameter.

Physical properties

The radial tensile strength, longitudinal tensile strength, and suture retention strength of the graft were evaluated according to test methods similar to those described by McClurken et al.¹⁰⁾ The reinforced filament was stripped from the graft wall, and the graft was cut into a test strip. To measure radial tensile strength and longitudinal tensile strength for the graft wall, a test strip, 1 mm in width and 10 mm in length, was clamped between a pair of jaw grips and stretched at a constant rate of 20 mm/minutes. The resulting force required to maintain this constant crosshead speed was indicated on a recorder that was synchronized with an Instron tensile strength machine. The radial and longitudinal tensile strengths were defined as the force at break (unit: megapascal, Mpa).

To measure suture retention strength for the graft wall, a test strip, 10 mm in width and 10 mm in length, was mounted in an Instron tensile testing machine and a 5-0 monofilament suture with a tapered noncutting needle was passed through one wall. The test was performed in the longitudinal direction. A 3-mm bite was stressed at a con-

stant rate of 20 mm/minutes. The resulting force was recorded on a strip chart recorder with the peak force noted in g. The suture retention strength was defined as the peak force at the breaking point.

Statistics

Statistical analysis of distortion ratio, radial tensile strength, and longitudinal tensile strength was performed by analysis of variance (ANOVA), followed by the Bonferroni-Dunn test. The suture retention strength was analyzed by the Student's t test. P values <0.05 were considered significant. All data are expressed as mean \pm standard deviation.

Results

Deformity ratio

No grafts were found to be occluded when the CT was performed. There were no anastomotic aneurysms or other complications. The deformity ratio was 100 \pm 0% at 2 weeks, 106 \pm 7.3% at 4 weeks, and 107 \pm 4.1% at 80 weeks. There was no significant difference in the deformity ratio over the time course (Fig. 2).

Physical properties

The radial and longitudinal tensile strengths for the graft wall were 4.3 \pm 0.4 Mpa and 17.2 \pm 2.6 Mpa at pre-implantation, 4.4 \pm 0.4 Mpa and 15.0 \pm 1.5 Mpa at 2 weeks, 3.9 \pm 0.3 Mpa and 12.2 \pm 2.4 Mpa at 4 weeks, and 4.1 \pm 0.3 Mpa and 16.0 \pm 0.4 Mpa at 80 weeks, respectively. The strength did

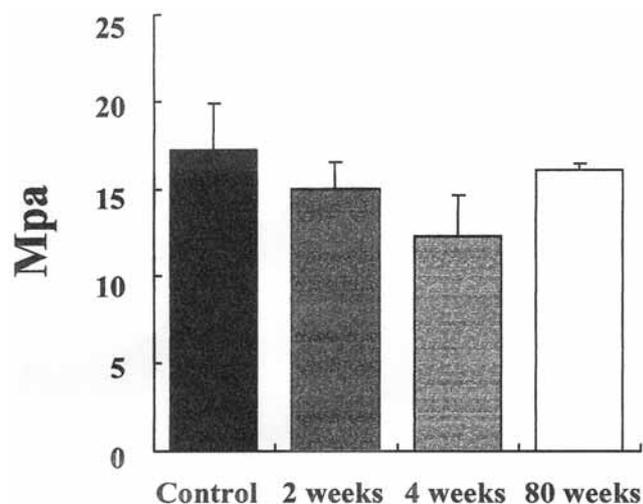


Fig. 4. Longitudinal tensile strength. The strength did not change at all points as compared to pre-implantation.

not change at all points as compared to pre-implantation (Figs. 3 and 4). The suture retention strength for the graft wall was measured at pre-implantation and 80 weeks. It was 479.3 ± 51.0 g at pre-implantation and 550.7 ± 81.6 g at 80 weeks. There was no significant difference in the suture retention strength between pre-implantation and 80 weeks (Fig. 5).

Comment

There is general agreement about the desirable characteristics of a vessel substitute that contribute to its function as an optimal vascular graft; it should be biocompatible with the host, resistant to infection, easy to sterilize and store, available in a variety of sizes, easy to implant, impervious to blood leakage, nonthrombogenic, compliant, low cost, easy to manufacture and physically durable.¹¹⁾ The graft should be free from deleterious dimensional instability over time, which would result in significant dilatation, aneurysm formation, rupture, or excessive elongation that could promote tortuosity, kinking, and eventual thrombosis. The graft should also be capable of being adequately sterilized without deterioration and conveniently stored in a sterilized condition for prolonged periods. Although a variety of synthetic materials were investigated as possible vascular grafts, including Vinyon-N, Nylon, PTFE, Ivalon, Orlon, and polyethylene terephthalate (Dacron), the fabric materials, except PTFE and Dacron, lost significant tensile strength following implantation or exhibited other problems for

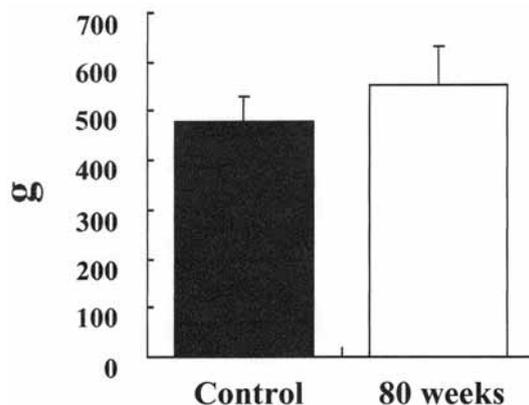


Fig. 5. Suture retention strength. There was no significant difference in the suture retention strength between pre-implantation and 80 weeks.

manufacturing or sterilization. Therefore, in Japan, only PTFE and Dacron grafts are commercially available as prosthetic grafts for peripheral vascular surgery.

It has been generally known that ePTFE grafts function well as vascular grafts. The internodal distance, which is defined as the average of the spacing between the nodes, has been widely used to describe the biological behavior of ePTFE grafts. In 1975, Campbell et al. performed extensive testing of ePTFE and concluded that an internodal distance of less than $22 \mu\text{m}$ was optimal.¹²⁾ They actually correlated increasing internodal distance with inferior patency in dogs, which appeared to be due to the development of a thicker pseudointima. Since then, the internodal distance in most commercially available grafts was set in the $17\text{-}20\text{-}\mu\text{m}$ range. However, in the 1980-1990s, several laboratories including ours revisited the relationship of internodal distance to graft healing.³⁻⁷⁾ ePTFE grafts with greater internodal distance, i.e., high-porosity ePTFE grafts, reportedly resulted in better graft healing as compared to standard ePTFE grafts. The large pore size allows rapid and unencumbered ingrowth of areolar tissue from the surrounding tissue through the interstices of the graft, thereby achieving a “healed” graft with an organized cellular, antithrombotic flow surface. However, high-porosity ePTFE grafts without an outer wrap were not clinically available because of their physical fragility.

Recently, we developed a new high-porosity ePTFE graft with unique node-fibril morphology.⁸⁾ The graft had a random node architecture with tortuous path channels extending from the outer to the inner surface. Our previ-

ous study demonstrated that, in the dog carotid interposition model, the graft exhibited satisfactory biocompatibility and tissue integration. The graft allowed adequate biologic communication to occur where cells and tissues could penetrate and venerate, resulting in a faster rate of healing.

The graft exhibited a degree of physical properties similar to other ePTFE grafts on the market. Some data has been published indicating that the suture retention strength, radial tensile strength and longitudinal tensile strength were 700 g, 5.5 Mpa and 12.0 Mpa for an Impra graft, 600 g, 9.0 Mpa and 11.8 Mpa for a Gore-Tex graft, and 520 g, 3.6 Mpa and 12.4 Mpa for a Vitagraft,⁹⁾ while 479.3 g, 4.3 Mpa and 17.2 Mpa for the graft, respectively. This result led us to test the stability of the graft, which is one of the desirable characteristics of an optimal vascular graft.

There have been several reports indicating that degeneration can occur in currently commercially available ePTFE grafts. Geiger suggested that, 12 months after implantation, the structure of ePTFE grafts was inhomogeneous with a widening of micropores, and both compressed and ruptured fibrils.¹³⁾ Vanmaele et al. also reported loss of mechanical strength in ePTFE grafts within a week.¹⁴⁾ However, the present study demonstrated that, in a canine abdominal aorta replacement model, the graft showed no significant deterioration in suture retention strength, radial tensile strength, or longitudinal tensile strength for periods ranging from 2-80 weeks. CT studies as well as macroscopic observation at sacrifice also demonstrated no anastomotic aneurysm or deformation of the graft.

In conclusion, the present study demonstrates that the graft possesses excellent stability. Taken together with our previous study, it is suggested that the graft be considered for evaluation in clinical trials.

References

1. Oga S. Japanese patent No.42-13560 (67/13560), 1967.
2. Campbell CD, Brooks DH, Webster MW, et al. Aneurysm formation in expanded polytetrafluoroethylene prostheses. *Surgery* 1976; **79**: 491-3.
3. Branson DF, Picha GJ, Desprez J. Expanded polytetrafluoroethylene as a microvascular graft: a study of four fibril lengths. *Plast Reconstr Surg* 1985; **76**: 754-63.
4. Golden MA, Hanson SR, Kirkman TR, Schneider PA, Clowes AW. Healing of polytetrafluoroethylene arterial grafts is influenced by graft porosity. *J Vasc Surg* 1990; **11**: 838-45.
5. Hirabayashi K, Saitoh E, Ijima H, Takenawa T, Kodama M, Hori M. Influence of fibril length upon ePTFE graft healing and host modification of the implant. *J Biomed Mater Res* 1992; **26**: 1433-47.
6. Nagae T, Tsuchida H, Peng SK, Furukawa K, Wilson SE. Composite porosity of expanded polytetrafluoroethylene vascular prosthesis. *Cardiovasc Surg* 1995; **3**: 479-84.
7. Nishibe T, Satoh Y, Iwashiro N, et al. Expanded polytetrafluoroethylene grafts for portal vein replacement: use of omentum wrap to promote graft healing. *Surg Today* 1997; **27**: 149-53.
8. Miura H, Nishibe T, Yasuda K, et al. The influence of node-fibril morphology on healing of high-porosity expanded polytetrafluoroethylene grafts. *Eur Surg Res* 2002; **34**: 224-31.
9. Abbott WM, Callow A, Moore W, Rutherford R, Veith F, Weinberg S. Evaluation and performance standards for arterial prostheses. *J Vasc Surg* 1993; **17**: 746-56.
10. McClurken ME, McHaney JM, Colone WM. Physical properties and test methods for expanded polytetrafluoroethylene (PTFE) grafts. In: *Vascular Graft Update: Safety and Performance*. Philadelphia: ASTM Publication, 1986; pp 82-94.
11. Brewster DC. Prosthetic grafts. In: Cronenwett JL, Głowiczki P, Johnston KW, Kempczinski RE, Krupski WC eds.; *Rutherford Vascular Surgery*, 5th ed. W.B. Saunders, 2000; pp 559-84.
12. Campbell CD, Goldfarb D, Roe R. A small arterial substitute: expanded microporous polytetrafluoroethylene: patency versus porosity. *Ann Surg* 1975; **182**: 138-43.
13. Geiger G. Deterioration of PTFE-prostheses wall. A SEM study. *J Cardiovasc Surg (Trino)* 1991; **32**: 660-3.
14. Vanmaele RG, van Schil PE, Demey HE, Rodrigus IE, de Maeseneer MG. Loss of mechanical strength in expanded polytetrafluoroethylene vascular prostheses. *Lancet* 1991; **338**: 755.