Experimental studies on application of small-caliber vascular prosthesis produced by polyurethane

Miyamoto, Katsufumi

(Degree)
博士（医学）

(Date of Degree)
1999-03-31

(Date of Publication)
2012-08-10

(Resource Type)
doctoral thesis

(Report Number)
甲1971

(JaLCDOI)
https://doi.org/10.11501/3156372

(URL)
https://hdl.handle.net/20.500.14094/D1001971

Experimental studies on application of small-caliber vascular prosthesis produced by polyurethane

Polyurethane製小口径人工血管の有用性に関する実験的検討

Katsufumi Miyamoto M.D., Takaki Sugimoto M.D.

Masayoshi Okada M.D., Sakan Maeda M.D.*

Department of Surgery , Division II , Department of Pathology* ,

Kobe University School of Medicine, Kobe, Japan

Key words : carcium carbonate, small caliber vascular prosyhesis, polyurethane

[Abstract]

It has been suggested that a microporous structure enhances fast and complete endthelialization. For long-term patency, antithrombogenicity and microporous structure are very important factors. In this paper, we have developed a new technique to give a microporous structure to small-caliber vascular prosthesis produced by polyurethane which has favorable antithrombogenecity. A mixed solution (tetrahydrofuran:dimethylformamide=1:1) containing 13 wt% of segmented polyurethane and variable amount of calcium carbonate (mean particle size of 8 μm in diameter) was dip-coated on a glass mandril of 3 mm and 6 mm in diameter and, placed into distiled water for 24 hours. After glass mandrill was removed, this polyurethane tube was placed into 1 mmol hydrochloric acid for 1 hour, and a microporous polyurethane vascular prosthesis of 20 mm in length was completed. These prostheses of 3 mm and 6 mm in diameter were implanted into the femoral and the carotid arteries, and the abdominal aorta of the dogs, respectively . Patency were recognized by arteriography and Duplex scanning and the removed grafts were inspected macro- and microscopically . The more hydraulic permeability of this graft was obtained with the more quantity of calcium cabonate mixed with polyurethane. In elasticity, this graft was more similar to the canine juglar vein than the polytetrafluoroethylene graft . Patency was observed 8 weeks after implantation on the arteriogram, and neointima was observed microscopically on the smooth and lustrous lumen. The new polyurethane vascular prosthesis we developed might provide a potentiality as a prosthesis for small-caliber vascular reconstruction.

[Introduction]

Recently , patients population with coronary artery disease or peripheral occlusive arterial disease has been increasing . Bypass surgery is the standard treatment for these disorders , and saphenous vein graft has been commonly used as the bypass conduit . However saphenous vein graft is sometimes not proper because of too small , too short , and varicosities . Therefore, a new small-caliber vascular prosthesis has been eager to be developed now . In this paper , we developed a new technique to give a microporous structure to vascular prosthesis produced by polyurethane which has favorable antithronbogenecity[1.2.3.], and studied the availability of this original modified polyurethane vascular prosthesis

[Materials and Methods]

Fabrication method of microporous polyurethane tubes

A mixed solution (tetrahydrofuran:dimethylformamide=1:1) containing 13 wt% of segmented polyurethane and variable amount of calcium carbonate (mean particle size of 8 μm in diameter) was dip-coated on a glass mandrill of 3 mm and 6 mm in diameter , and was placed into distilled water for 24 hours. Then , glass mandrill was removed, and this polyurethane tube was placed in the 1 mmol hydrochloric acid for 1 hour. Carcium carbonate particle in the wall of polyurethane tube was dissolved into the hydrochloric acid, and a microporous polyurethane vascular prosthesis was completed. The graft was white , pliable , and elastic . The inner surface of the graft was rough . This prosthesis was provided 3 mm and 6 mm in internal diameter and 20 mm in length .

Determination of water permeability

The polyurethane graft was provided with calcium carbonate to polyurethane ratio of 1:1 , 4:1 , 6:1 , respectively . The flow rate of water through a given area of the prosthesis was measured under a pressure of 120 mmHg in each 6 grafts[4] . Porosity of polyurethane graft was 1.2 ± 1.0 ml/min/cm^2 (1:1) , 21.5 ± 3.4 ml/min/cm^2 (4:1) , and 34.4 ± 2.7 ml/min/cm^2 (6:1) . Therefore , the more water permeability of the graft was obtained with the more quantity of calcium carbonate mixed with polyurethane (**Fig. 1**) .

Determination of elasticity

Compliance of the prosthesis was calculated in the following formula, (dV / dP) / V×100 (% / mmHg) , where V was luminal volume under some luminal pressure , and dV/dP was the corresponding changes of luminal volume in response to internal pressure changes . Water was induced into the canine jugular vein , polyurethane graft and expanded polytetrafluoroethylene (e-PTFE) graft at a rate of 5 cc/hour and the luminal pressure was simultaneously measured with a transducer[5] . The relationship between the intraluminal pressure and the time was evaluated in each tube . As the compliance under a pressure of 100mmHg, the canine jugular vein was 5.06 %/mmHg , the polyurethane graft was 1.16 %/mmHg ,and the e-PTFE graft was 0.08 %/mmHg . The polyurethane graft was more similar to the juglar vein than the e-PTFE graft in elasticity (**Fig. 2**).

In vivo experiments of polyurethane graft

Three kinds of these polyurethane grafts were provided according to porosity , and implanted in mongrel dogs weightly between 12~15 kilograms : Type I (n=4) ; porosity = 0 , Type II (n=4) ; porosity = 20 , Type III (n=10) ; porosity = 30 Anesthesia was induced with ketamine hydrochloride of 15 mg/kg intramuscularly and

pentobarbital sodium of 15 mg/kg intravenously according to the " Guidelines for Animals Experiment in Kobe University School of Medicine ". The animals were heparinized systemically with an intravenous bolus injection of 100 units/kg . The grafts of 2cm long were provided 3mm in diameter for the carotid and the femoral arteries and 6mm in diameter for the abdominal aorta (**Fig. 3a**). The target artery was resected and interposed with the polyurethane graft by continuous suture using 7-0 monofilament polypropylene suture material (**Fig.3b,3c,3d**). Hemostasis was easily obtained after the initial woozing through the graft at declamping .

To assess the patency of the grafts , Duplex scanning was carried out everyday (**Fig. 4a**). All grafts were also patent on arteriogram 4 and 8 weeks after grafting (**Fig. 4b,4c,4d**). At the examination, the catheter (4Fr) was inserted into the right brachial artery , and contrast medium was injected when the catheter was placed in the carotid artery , the femoral artery and the abdominal aorta , respectively .

The Type III grafts was removed 1, 2, 4 and 8 weeks after grafting and inspected macro- and microscopically .

[Results]

Patency of the grafts

All of Type I and Type II grafts were occuluded within 1 week after grafting . In contrast , all of Type III grafts were patent though one infected graft was occuluded 11 days after grafting . An excellent healing was observed around the grafts at 2 weeks after implantation .

Macroscopic findings

The Type III grafts removed one week after implantation were as soft and pliable as

the native artery , and showed no aneurysmal changes. The inner surfaces of the grafts were red , glistening and smooth , and showed no thrombus formation (**Fig.5a**). The grafts removed 2 weeks after implantation were firmly covered with a large amount of connective tissue , and were also as soft and pliable as the native artery without aneurysmal changes . The inner surfaces became less redish , and persisted glistening and smooth with no thrombus formation (**Fig.5b**). The grafts removed 4 weeks after implantation were also as soft and pliable as the native artery without aneurysmal changes .The inner surfaces became yellow and showed shiny white at the neighboring area of the proximal and distal suture lines (**Fig.5c**). The grafts removed 8 weeks after implantation were also as soft and pliable as the native artery without aneurysmal changes . The inner surfaces persisted smooth and glistening , and showed the shiny white area extending towards the center of the graft (**Fig.5d**).

Microscopic findings

In the graft removed one week after grafting , the inner surface was covered with the thin pseudointima consisting of fibrin and clot . Minimal inflammatory reaction was observed around both sites of anastomotses (**Fig.6**). In the graft removed 2 weeks after grafting , neointima was observed at the both sites of anastomoses , and the inner surface was covered with pseudointima (**Fig.7**). In the graft removed 4 weeks after grafting , the inner surface was almost coverded with matured fibril membrane , and endotherial cells extended several millimeters long from the suture lines towards the center of the graft . In the outer surface of the graft , numerous capillaries were observed invading the wall of the graft (**Fig.8**). In the graft removed 8 weeks after grafting, the inner surface was covered with endothelrial cells not accompanying intimal hyperplasia throughout the graft. The outer surface was covered with

connective tissue which contained a lot of capillaries , and numerous capillaries were also observed in the neointima (**Fig.9**).

[Discussion]

Much attention has been paid to an ideal small-caliber vascular prosthesis for coronary artery bypass or peripheral artery bypass[6.7.8.9.10.11.12.] . A lot of pilot studies have been performed for small-caliber vascular reconstruction using the prosthetic grafts or biografts , but the satisfactory results have not been obtained . The segmented polyurethane has been already used for diaphragm of artificial heart and balloon of intraaortic pump because of its antithrombogenecity[13.] . Recently , a variety of polyurethane grafts has been developed for small-caliber vascular prosthesis . For long-term patency of the prosthesis, microporous structure which enhances tissue ingrowth is mandatory . In this study to give a microporous structure to the polyurethane vascular prosthesis microporosity , the tubes made up from mixed solution of segmented polyurethane and calcium carbonate were placed into the hydrochrolic acid .The hydraulic permeability of the grafts proved to be well correlated with quantity of calcium carbonate mixed with polyurethane .

In addition , three types of grafts were provided according to the porosity of 0 , 20 and 30 ml/min/cm^2 , and were implanted in the femoral arteries of the dogs . The patency rate was obviously higher in the grafts with porosity of 30 ml/min/cm^2 than porosity of 0 or 20 ml/min/cm^2 .This type of grafts with high porosity showed execellent endthelrialization in a short duration of 2 months after implantation . This result suggested that the porosity of at least 30 ml/min/cm^2 , which was nearly equal to that of e-PTFE graft was necessary for excellent endotherialzation[14.].

Our technique produced foamlike wall structure which exhibited rough inner surface .

This structure can afford to make the pseudointima firmly attached to the graft wall and induced neointima smoothly . In this microscopic study , pseudointima was gradually matured without thickening and induced neointima . This might be because that numerous capillaries which were observed in the inner and outer surfaces of the graft made a contribution to stabilization of pseudointima .

The previous studies indicated that the compliance mismatch might cause flow and flow separation at the anastomotic sites[15.16.] . This hydrodynamic consequence can lead to thrombus formation and continual endothelrial injury stimulating chronic tissue proliferation . Therefore , our grafts with the compliance similar to the host vessels might provide a long-term patency . In addition , intimal hyperplasia was not observed at the suture lines on the arteriograms and macroscopical findings and infiltration of the smooth muscle cells was little seen in the neointima microscopically .

[Conclusion]

We developed a new method to give microporosity to vascular prosthesis produced by polyurethane. This microporous polyurethane graft might provide a potentiality for small-caliber prosthesis .

[References]

1) Boretos J W: Segmented polyurethane : A polyeter polymer. J Biomed Mater Res 1978; 2 : 121 ~ 130

2) Nyilas E, Ward Jr R: Developement of blood compatible elastomers. V. surface structure and blood compatibility of Avcothane elastomers. J Biomed Mater Res 1977; 8 : 69 ~ 84

3) Ookoshi T, Noishiki Y, Egoh Y, et al : Microporous polyurethane small diameter vascular prostheses with hydraulic permeability. Jpn J Artif Organs 1996; 25 : 193 ~ 196

4) Association for the advancement of medical instrumentation : Cardiovascular implants - Vascular prostheses. American national standard 1994

5) Kobarai Y, Takano Y, Nagai H, et al : The development of the plasmin-treated fibrin coated vascular prosthesis. Jpn J Artif Organs 1994; 23 : 810 ~ 813

6) Hiromichi M, Takehisa M: An integrated approach to the design and engineering of hybrid arterial prostheses. J Vasc Surg 1994; 19 : 658 ~ 667

7) Miralem P, Warhen MG, Berhard O, et al : Seeding with omental cells prevents late intimal hyperplasia in small - diameter dacron grafts. Circulation 1995; 92 : 2605 ~ 2616

8) John LG, Stevens SK, Gregory CZ, et al : FGF-1 affication stimulats e-PTFE endothelialization without intimal hyperplasia. J Surg Res 1994; 57: 596 ~ 612

9) Noishiki Y, Tomizawa Y, Yamana Y, et al : Autocrine angiogenic vascular prosthesis with bone marrow transplantation. Nat Med 1996; 2 : 90 ~ 93

10) Noishiki Y, Miyata T, Kodama K: Development of a small vascular graft by a new crosslinking method incorporating slow heparin release collagen and natural

tissue compliance. Trans Am Soc Artif Intern Organs 1986; 32 :114 ~ 119

11) Doi K, Nakayama Y, Oka T, Matsuda T: A new microporous polyurethane vascular graft prepared by an excimer laser ablation technique. ASAIO J 1995; 41: 608 ~ 611

12) Doi K, Nakayama Y, Matsuda T: Novel compliant and tissue - permeable microporous polyurethane vascular prosthesis fabricated using an excimer laser ablation technique. J Biomed Mater Res 1996; 31 : 27 ~ 33

13) Frazier OH, Rose EA, Macmanus Q, et al : Multicenter clinical evaluation of the Heart Mate 1000 IP left ventricular assist device. Ann Thorac Surg 1992; 53:1080 ~ 1090 , 1992

14) Clowes AW, Kirkman TR, Reidy MA: Mechanisms of arterial graft healing : Rapid transmural capillary ingrowth provides a source of intimal endothelialium and smooth muscle in porous PTFE prostheses. Am J Pathol 1986; 123 : 220

15) Lyman DJ, Fazzio FJ, Voorhess H,et al : Compliance as a factor effecting the patency of a copolyurethane vascular graft. J Biomed Mater Res 1978; 12 : 337

16) Shan - hui H, Helen K: On matching compliance between canine carotid arteries and polyurethane grafts. Artif Organs 1997; 21 : 1247 ~ 1254

[Legends]

Fig. 1 Water permeability of the polyurethane graft.

The polyurethane graft was provided with calcium carbonate to polyurethane ratio of 1:1 , 4:1 , 6:1 , respectively . Porosity of polyurethane graft was 1.2 ± 1.0 ml/min/cm^2 (1:1) , 21.5 ± 3.4 ml/min/cm^2 (4:1) , and 34.4 ± 2.7 ml/min/cm^2 (6:1) .

Fig. 2 The relationship between the intraluminal pressure and the time .

As the compliance under a pressure of 100mmHg, the canine jugular vein was 5.06 %/mmHg , the polyurethane graft was 1.16 %/mmHg ,and the e-PTFE graft was 0.08 %/mmHg . The polyurethane graft was more similar to the juglar vein than the e-PTFE graft in elasticity .

Fig. 3a The microporous polyurethane graft which we provided . This graft was white , pliable , and elastic .

Fig. 3b Implantation into the abdominal aorta .

Fig. 3c Implantation into the carotid artery .

Fig. 3d Implantation into the femoral artery .

Fig. 4a Douplex scanning of the graft .

Fig. 4b Arteriogram of the abdominal aorta 8 weeks after grafting . No anastomotic stenosis and no aneurysmal change was observed .

Fig. 4c Arteriogram of the carotid artery 8 weeks after grafting . No anastomotic stenosis and no aneurysmal changes were observed .

Fig. 4d Arteriogram of the femoral artery 8 weeks after grafting . No anastomotic stenosis and no aneurysmal change was observed .

Fig. 5a The inner surface of the graft removed one week after grafting . The inner surface was red , glistening and smooth with no thrombus deposition .

Fig. 5b The innersurface of the graft removed 2 weeks after grafting . The inner surface became less redish , and persisted smooth and glistening .

Fig. 5c The inner surface of the graft removed 4 weeks after grafting . The inner surface became yellow and showed the shiny white at the neighboring area of the proximal and diatal suture lines .

Fig. 5d The inner surface of the graft removed 8 weeks after grafting . The inner surface persisted smooth and glitening , and showed the shiny white area extending towards the center of the graft .

Fig. 6 Histologic section of the graft after one week implantation . Longitudinal section at the anastomosis stained with hematoxylin-eosin . Pseudointima consisting of fibrin and clot extended from the host vessel to the surface of the graft . (× 40)

Fig. 7 Histologic section of the graft after 2 weeks implantation . Longitudinal section at the anastomosis stained with hematoxylin-eosin . Neointima was observed at the site of anastomosis .The inner surface of the graft was covered with pseudointima . (× 40)

Fig. 8 Histologic section of the graft after 4 weeks implantation .

(a, b) Longitudinal section at the anastomosis stained with hematoxylin-eosin .

Endotherial cells extended several milimeters long from the suture line towards the center of the graft . Section of the inner surface was almost covered with matured fibril membrane . (a × 40 , b×100)

(c, d) Section of the graft wall stained with hematoxylin-eosin . Numerous capillaries invaded the graft wall . (c× 200 , b×400)

Fig. 9 Histologic section of the graft after 8 weeks implantation .

(a, b) Longitudinal section at the anastomosis stained with hematoxylin-eosin . the inner surface was covered with endotherial cells not accompanying intimal hyperplasia throughout the graft. (a × 40 , b×100)

(c) Section of the outer surface of the graft stained with hematoxylin-eosin . The outer surface was covered with connective tissue which contained numerous capillaries .

(d) Section of the neointima of the graft stained with hematoxylin-eosin . In the neointima , numerous capillaries were observed .

Fig. 1

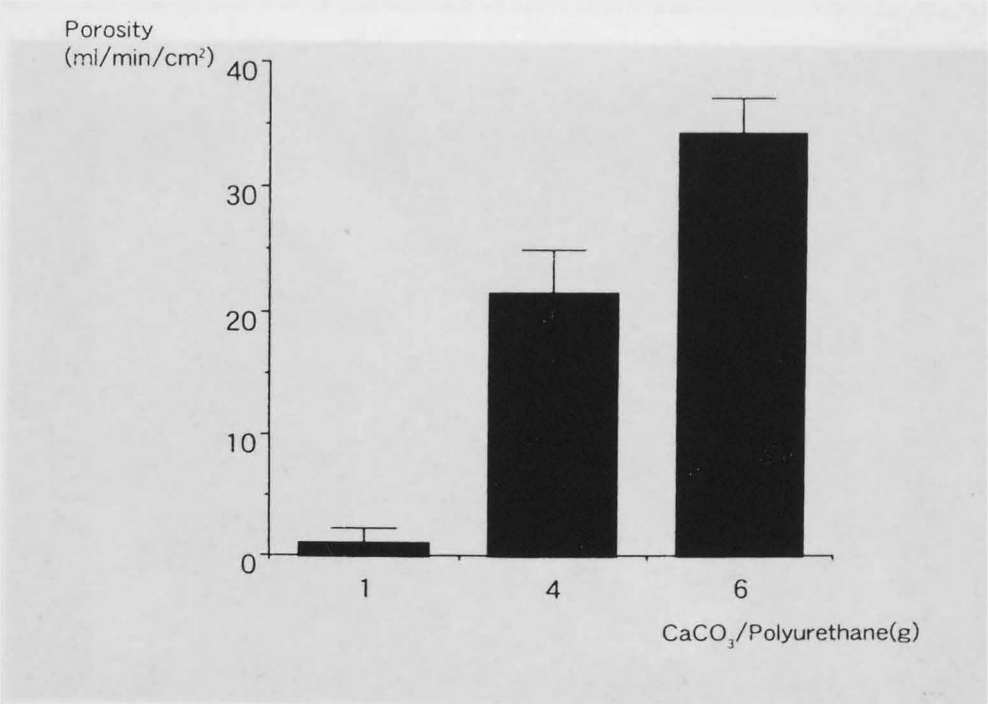
Porosity
(ml/min/cm²)
40
30
20
10
0
1
4
6
CaCO₃/Polyurethane(g)

Fig. 2

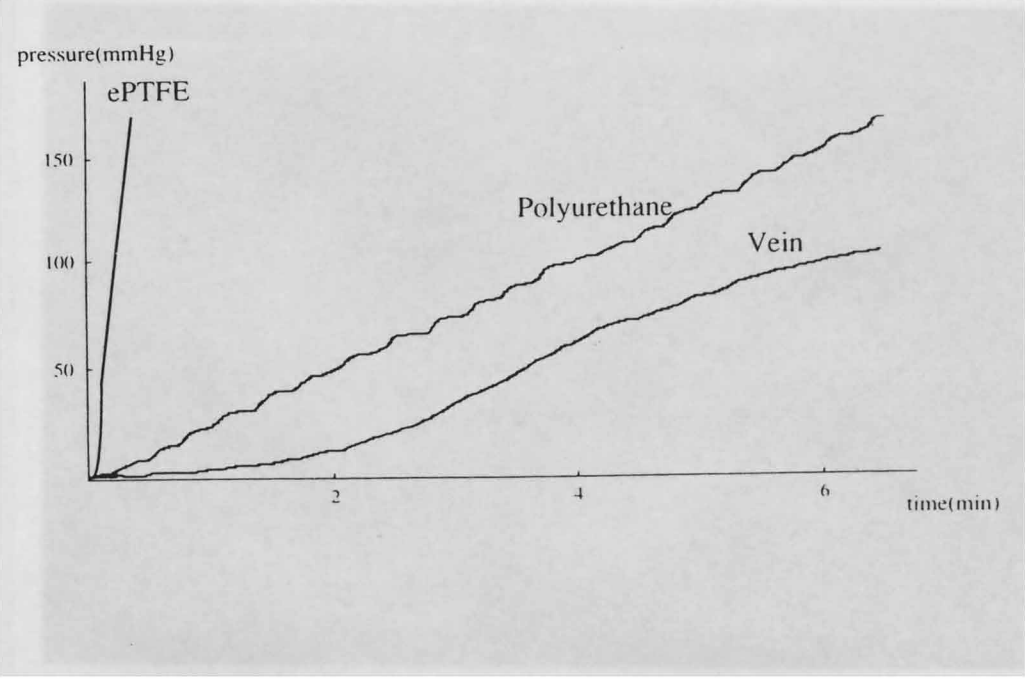
pressure(mmHg)
ePTFE
150
100
50
Polyurethane
Vein
2
4
6
time(min)

Fig. 3a

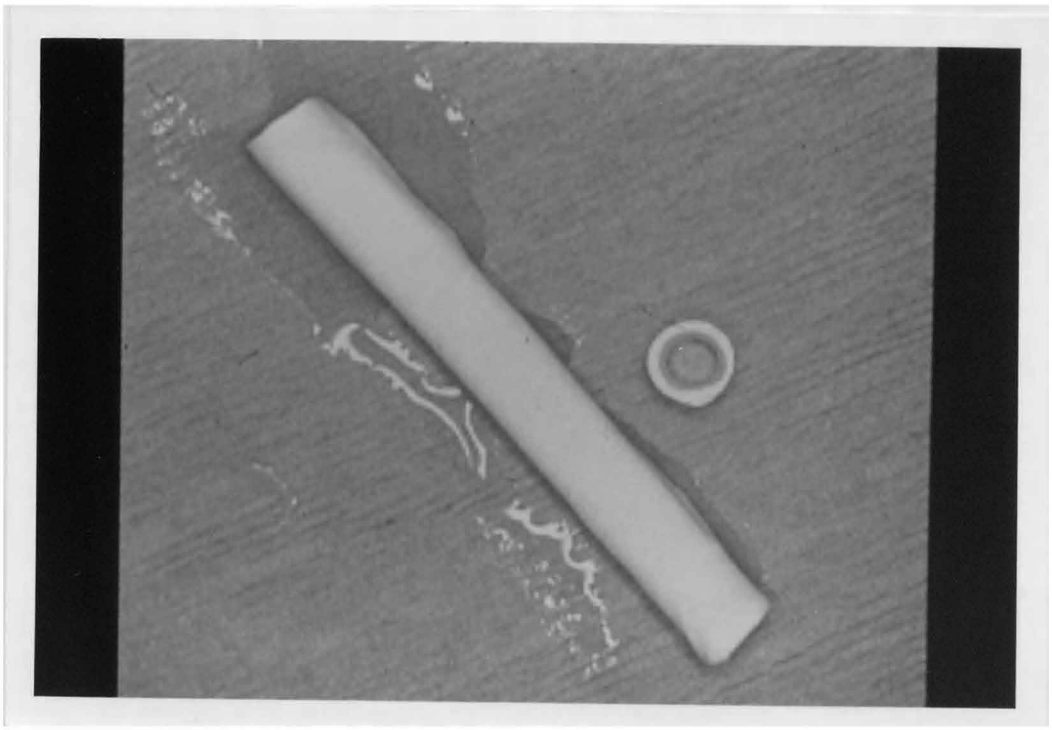

Fig. 3b

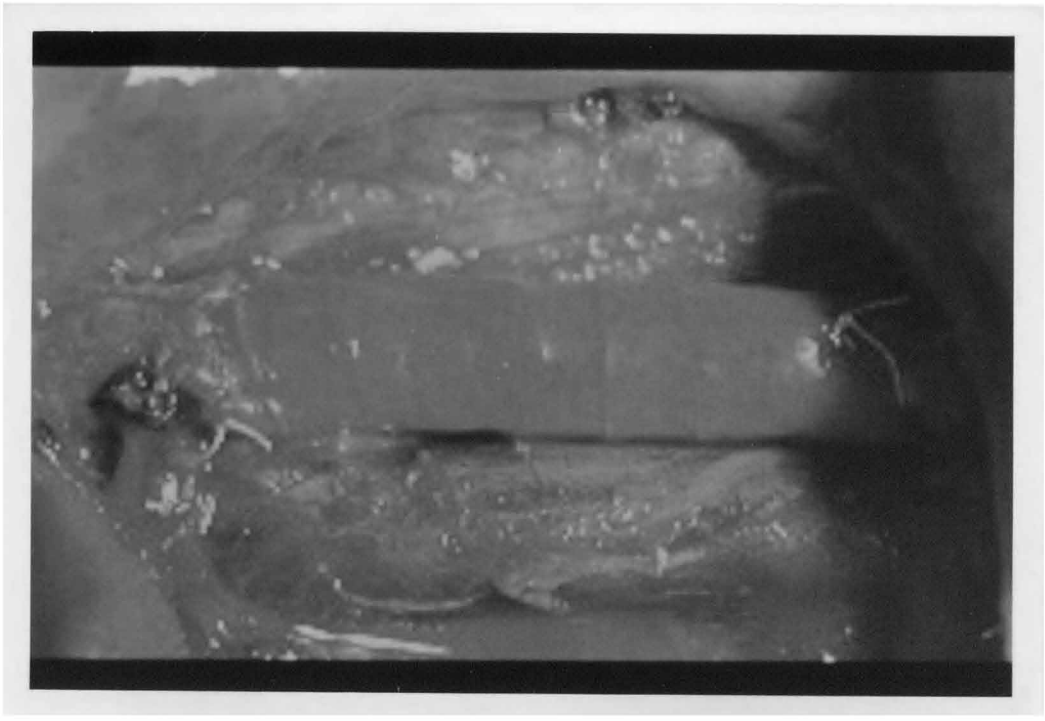

Fig. 3c

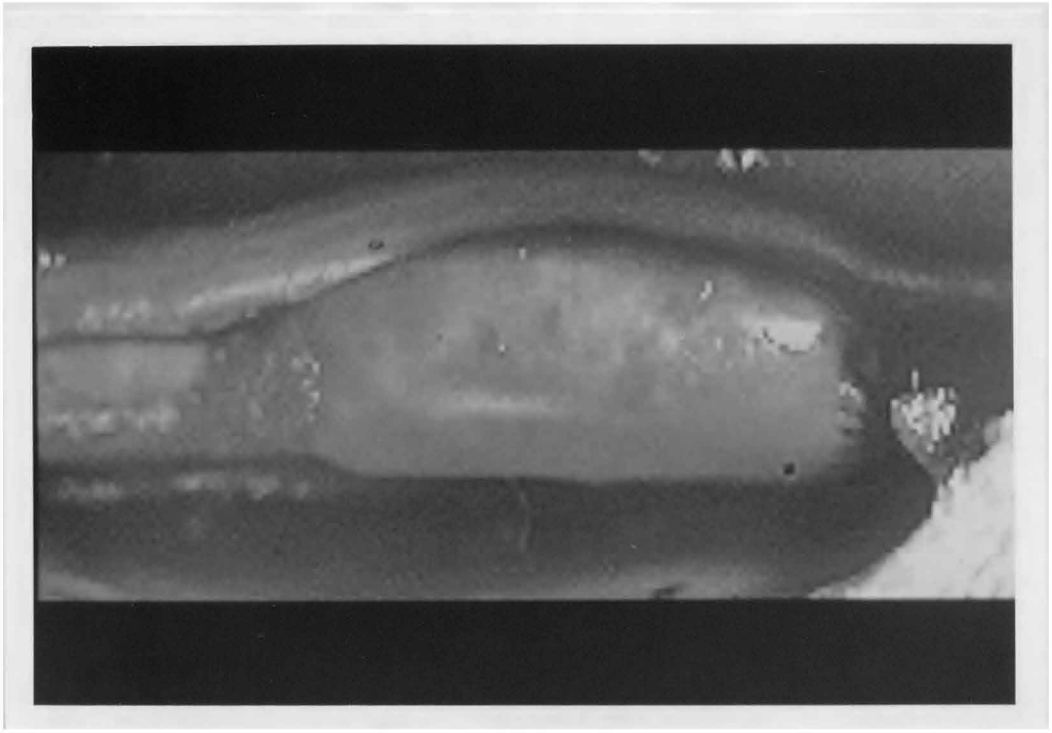

Fig. 3d

Fig. 4a

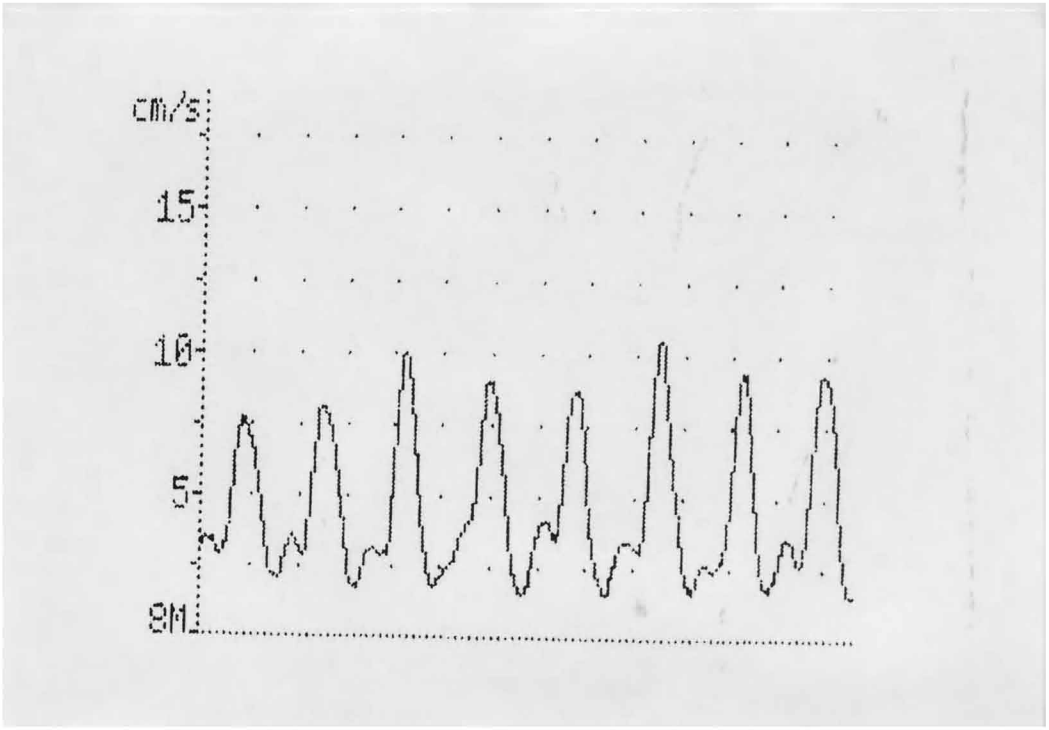

Fig. 4b

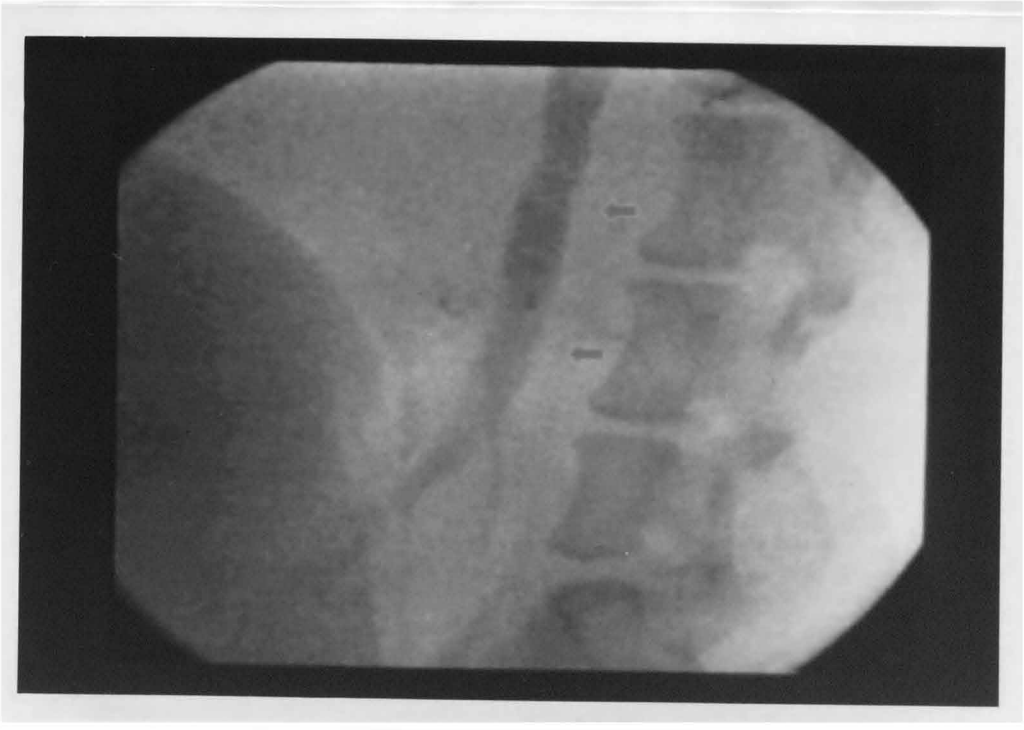

Fig. 4c

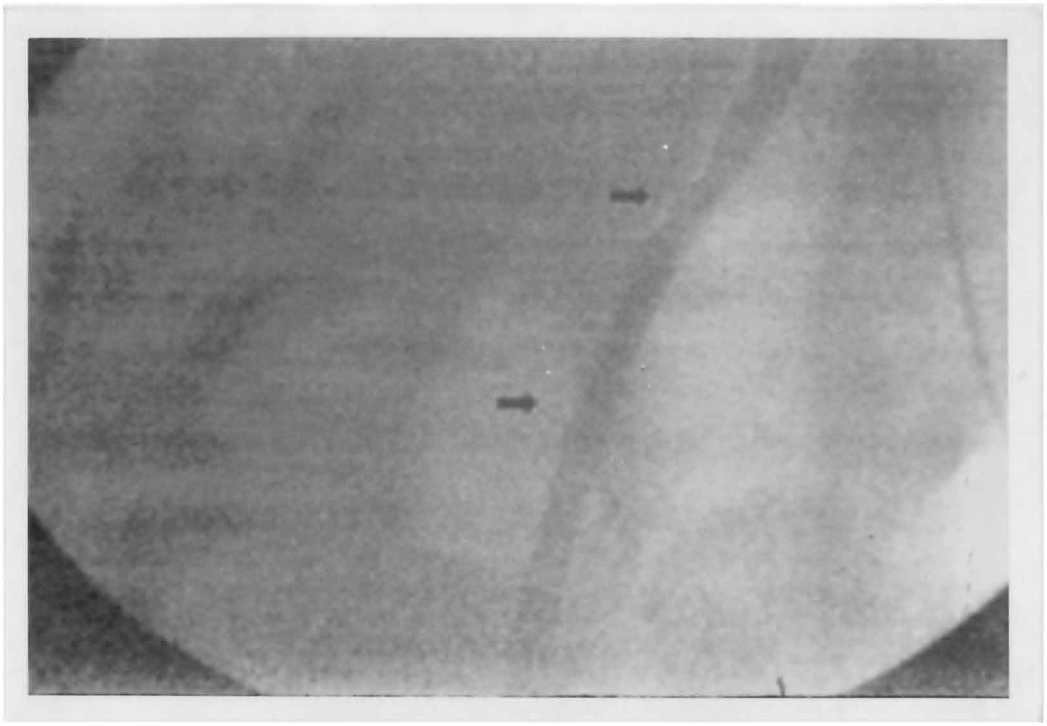

Fig. 4d

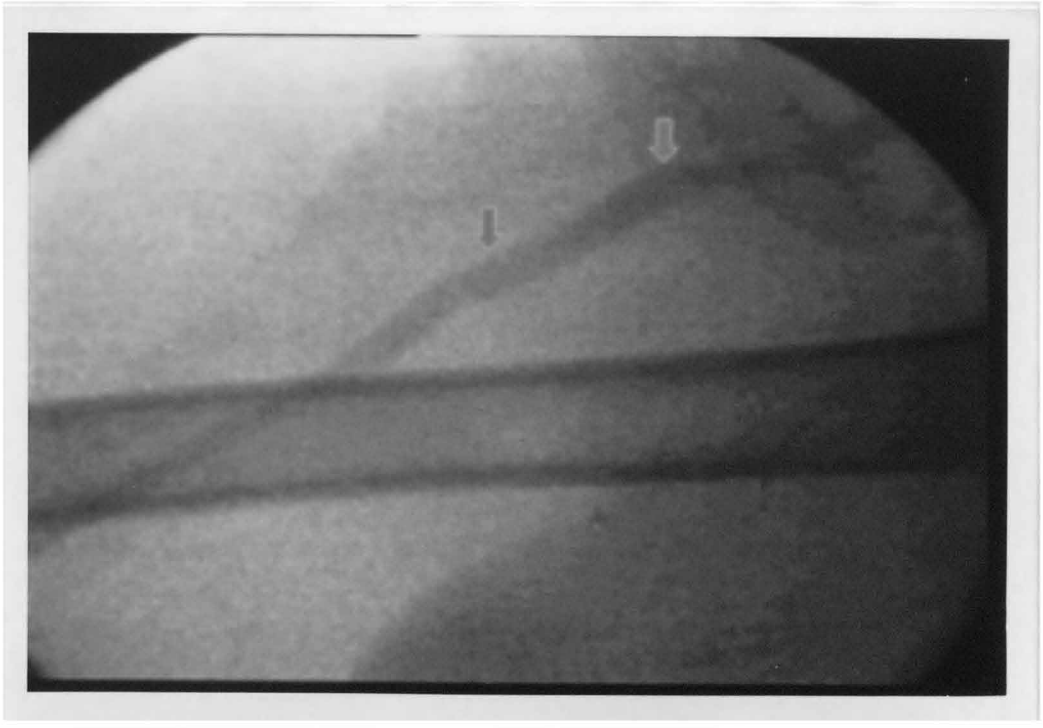

Fig. 5a

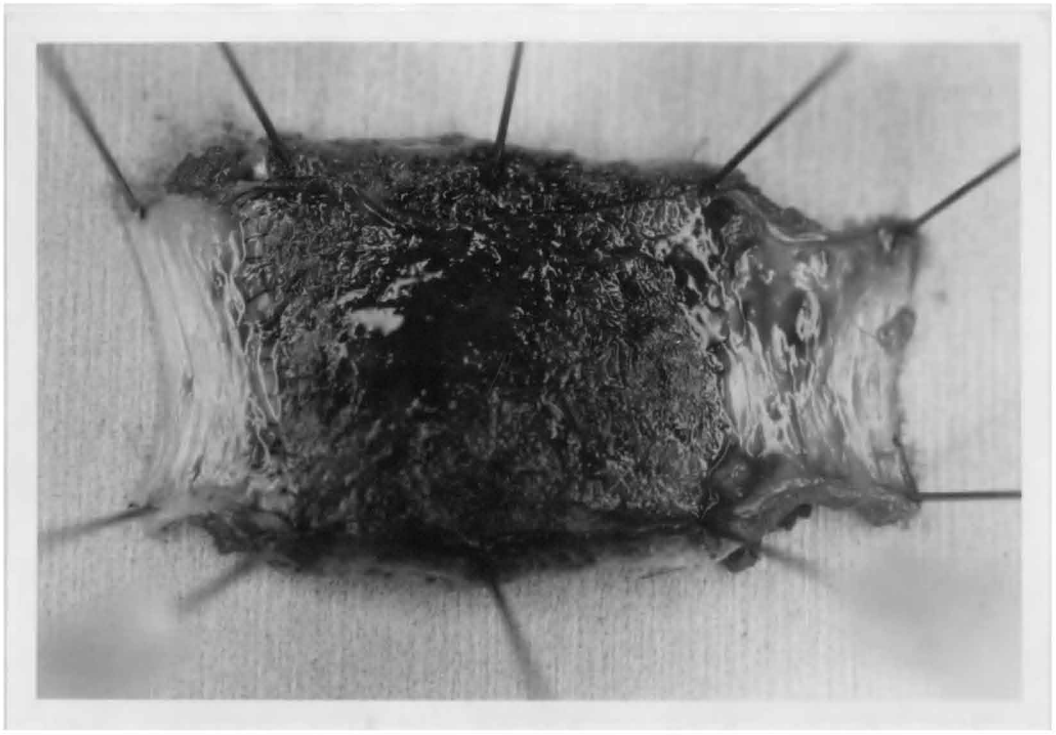

Fig. 5b

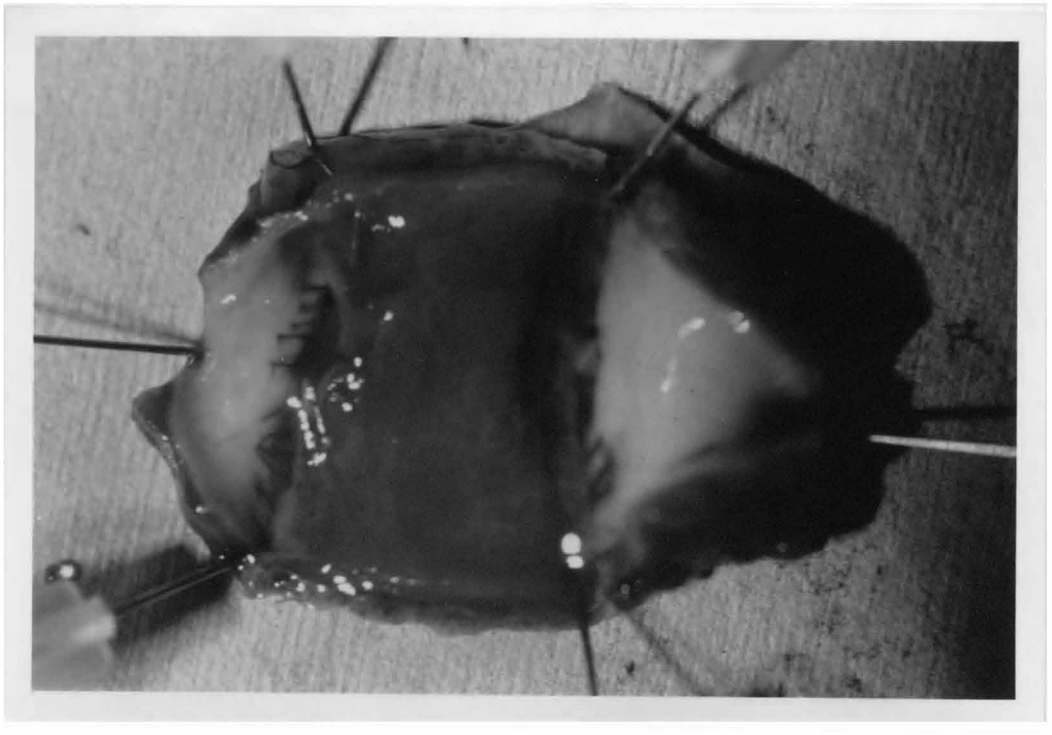

Fig. 5c

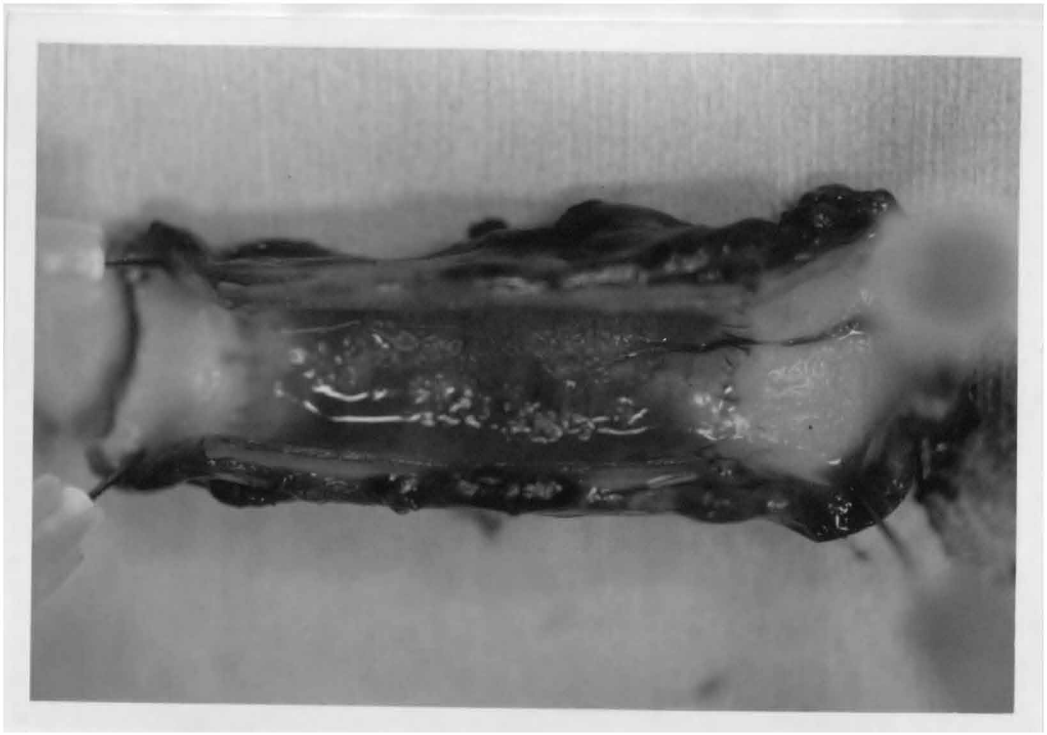

Fig. 5d

Fig. 6

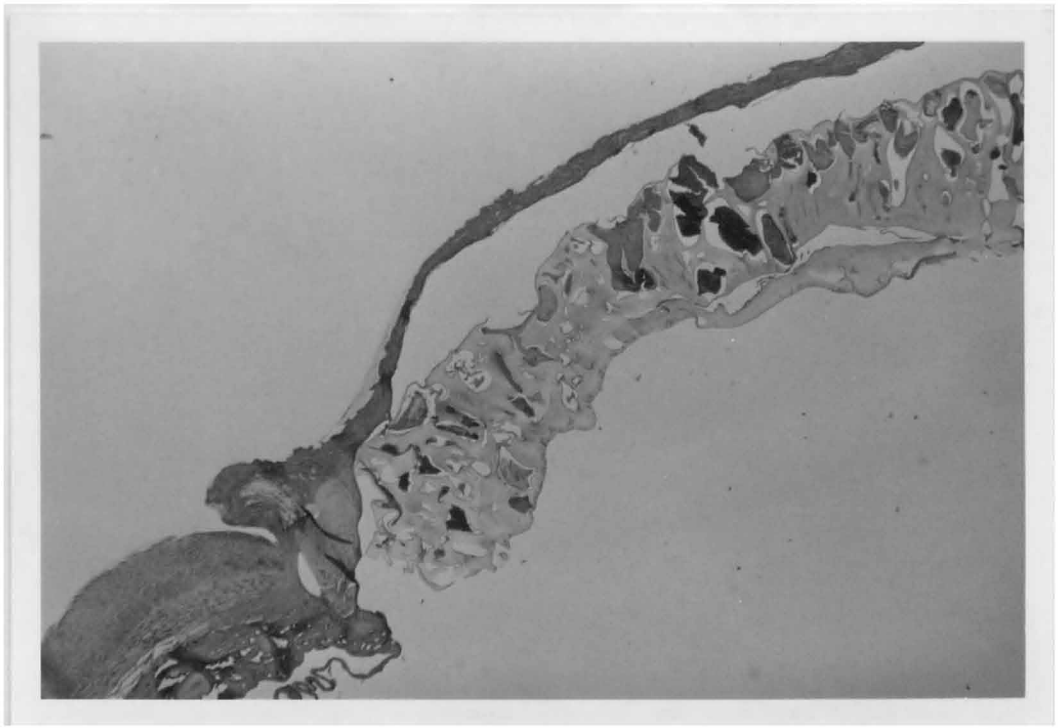

Fig. 7

Fig. 8a

Fig. 8b

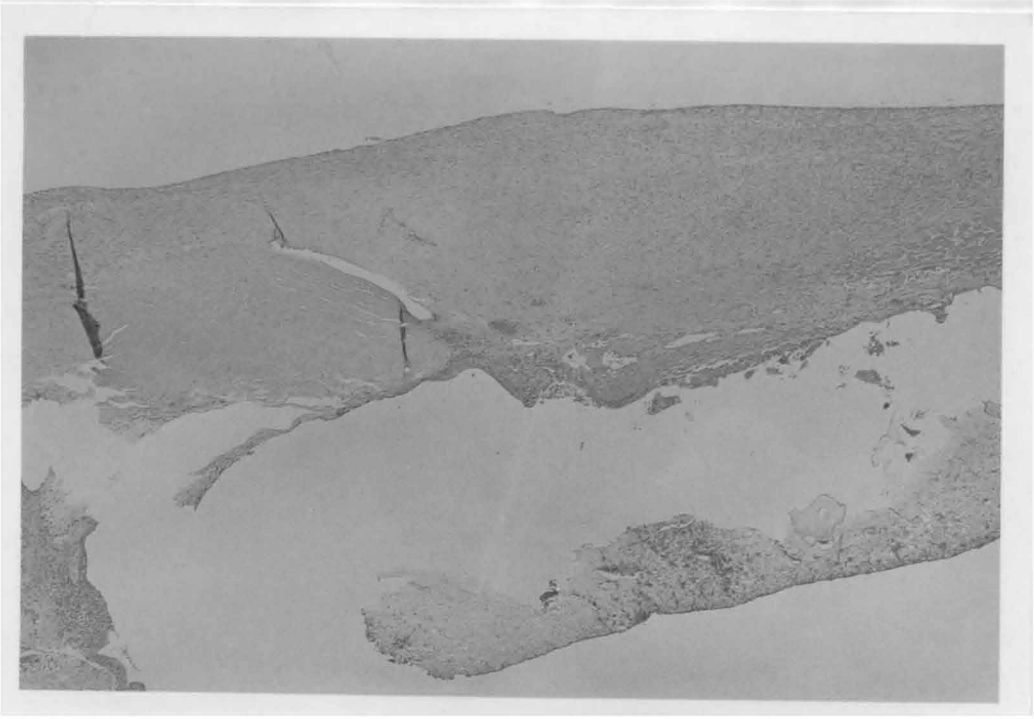

Fig. 8c

Fig. 8d

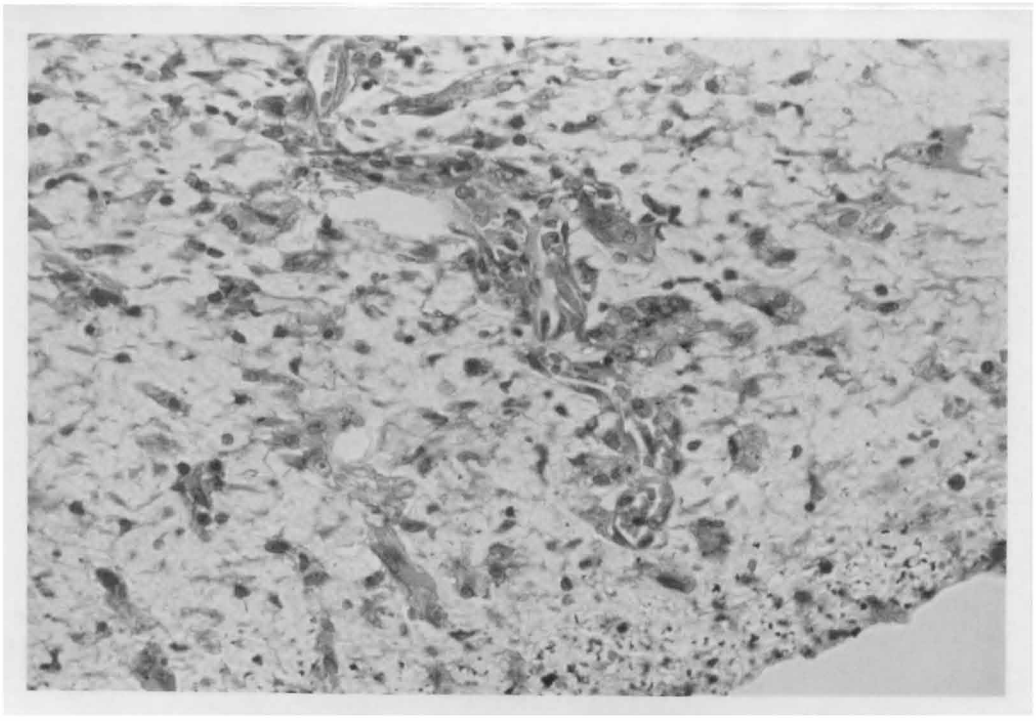

Fig. 9a

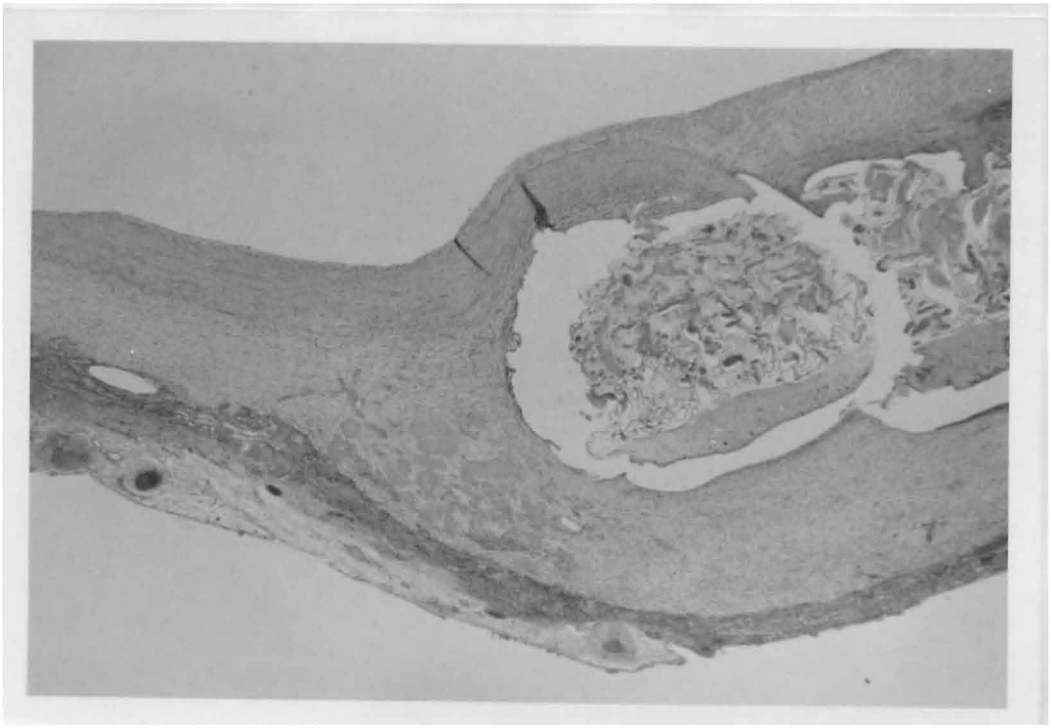

Fig. 9b

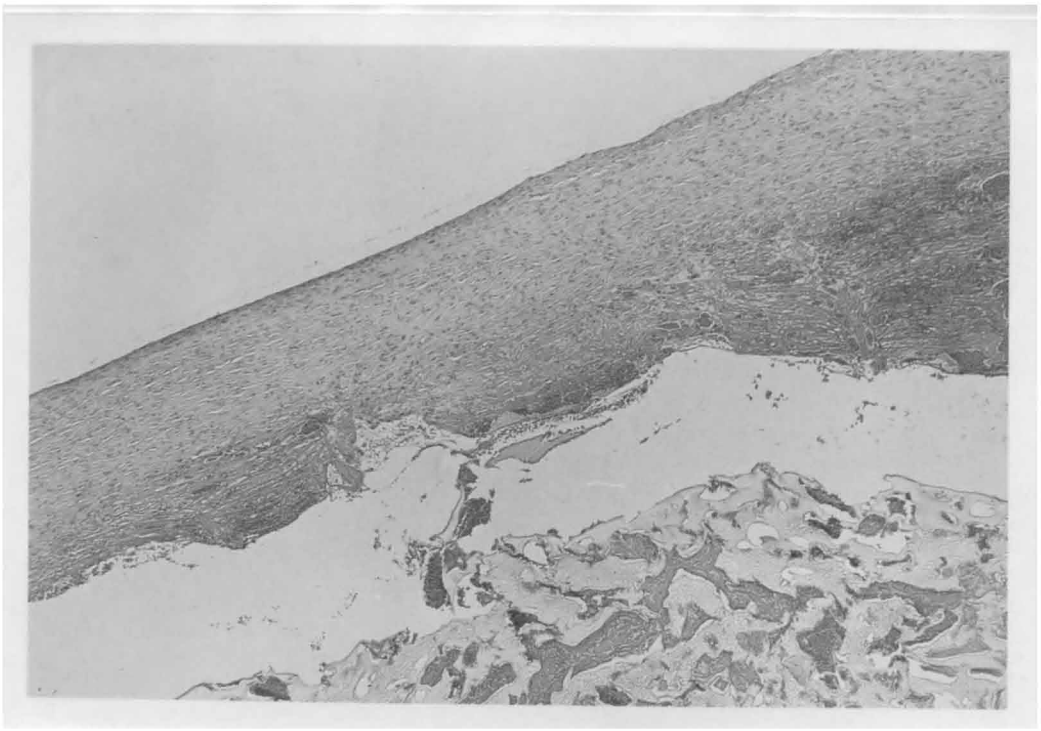

Fig. 9c

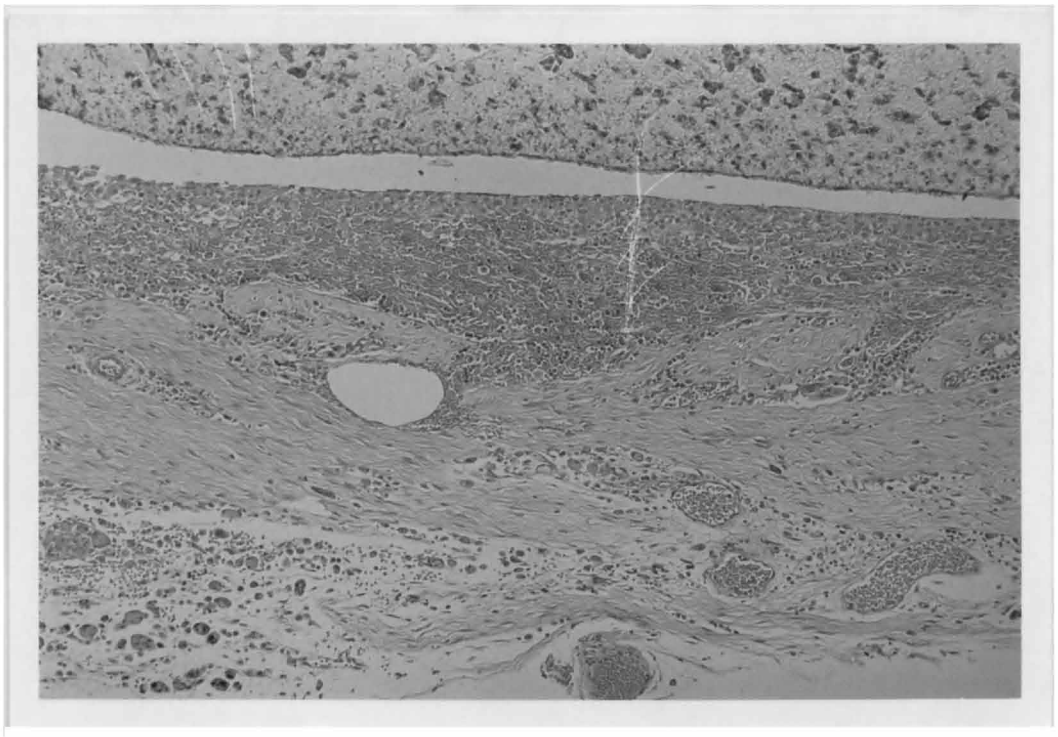

Fig. 9d