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Tissue reaction to Dacron® velour and titanium fibre mesh used for anchorage of percutaneous devices

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Dacron® velour is often used to anchor a percutaneous device, like the catheter used in peritoneal dialysis. However, exit-site infections complicate this method of dialysis and are supposed to be related to the design of the catheter. In animal experiments, a percutaneous device provided with a titanium fibre mesh to anchor the implant was not affected by infectious complications. The purpose of this study was to compare the differences in soft tissue reaction to Dacron velour and titanium fibre mesh under the same experimental conditions. Therefore, we placed implants, provided with either Dacron or titanium mesh, subcutaneously in the dorsum of goats. The implants were left *in situ* for 4 months. Histological and histomorphological evaluations were performed. It was found that the soft tissue response inside the Dacron was mainly inflammatory, while the titanium mesh evoked good biocompatible behaviour. We concluded that the limited fibrous tissue ingrowth into the Dacron cuff has to be the reason for the observed high failure incidence of a percutaneous device.

Keywords: Titanium, fibre mesh, percutaneous device, polyethylene terephthalate, soft tissue

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As reported earlier[1,2], peritoneal dialysis has some important advantages compared to more conventional dialysing methods, like haemodialysis. For example, peritoneal dialysis is more convenient to the patient, considering the positive social and medical implications of this method. Peritoneal dialysis is also relatively cheap and simple.

The method of peritoneal dialysis is based on the capacity of the peritoneum to exchange fluid and metabolic products. Therefore, dialysis fluid has to be instilled in the abdominal cavity through a permanent percutaneous access device. Most of the currently used catheters for peritoneal dialysis consist of a silicone tube with porous polyethylene terephthalate (Dacron®) cuffs attached to it. Unfortunately, access-related complications, such as exit-site infections, occur. A retrospective and prospective study, as performed in our hospital, showed that 35% of the standard catheters had to be removed because of infectious complications[2]. In addition, a strong correlation was observed between the appearance of exit-site infections and recurrent peritonitis[2,3].

Though it is known that the design of the dialysis catheter is of influence on the incidence of complications, an ideal peritoneal catheter is still not available. Much research has already been performed to develop a percutaneous device that can be maintained functional for long periods[4–16]. The purpose of these considerable research efforts was to obtain a tight skin seal in the percutaneous area which can prevent the downward migration of epidermis and the influx of bacteria. To achieve this, the devices were provided with a micro- or macroporous anchor, often made of Dacron velour. Despite the disappointing results as described above, this material is still used for the currently available peritoneal dialysis catheters. Therefore, Gokal *et al.*[17] recently emphasized the necessity of new improved access devices. This research should be focussed on (1) the application of more biocompatible materials to avoid foreign body response and (2) the design of the subcutaneous anchor to diminish motion at the exit-site and reduce the number of exit-site infections.

During the last decade in our laboratory, research was directed toward a better understanding of percutaneous implant failures and the development of more successful percutaneous devices[18–22]. These experiments have resulted in a percutaneous device provided with a subcutaneous flange made of a porous sintered titanium fibre mesh structure[23]. Various animal experiments have already shown the efficacy of our device. For example, it has been proven that: (1) ingrowth of connective tissue into the pores of the fibre mesh took place, (2) no, or only very limited,

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epidermal downgrowth was present after 6 months of implantation and (3) no percutaneous exit-site infections occurred. However, no comparative studies were performed between the titanium fibre mesh and the Dacron velour as used in the original Tenckhoff catheter. Consequently, the purpose of this study was to compare the differences in soft tissue reaction to Dacron velour and titanium fibre mesh under the same experimental conditions.

MATERIALS AND METHODS

Implant materials

We used two different types of implants in the experiments. One of the implants is shown in *Figure 1*. This implant is a section of the commercially available Tenckhoff catheter (Quinton®, Seattle, WA, USA). It consists of a silicone tube with a polyethylene terephthalate Dacron cuff attached to it by means of Silastic medical Silicone A adhesive. The length of the silicone tube is 7 cm. To avoid ingrowth of tissue, both endings of the silicone tube are sealed with medical grade silicone glue.

Figure 2 shows the other implant used. The device consists of two elements: (1) a flange-shaped component and (2) a holding element connected to a silicone tube. The flange-shaped part is composed of a mesh sheet of commercially pure sintered titanium fibres. The mesh was fabricated by interengaging and intertwining a multiplicity of commercially pure titanium fibres. After compression, the fibre structures were sintered to bond the fibres at their points of contact. The fibre diameter was 50 μm. The volumetric porosity was 86% and the weight of the mesh sheet was 600 g m^{-2}. The fibre mesh measured 3 cm in diameter and the length of the silicone tube was 5 cm. The holding element was composed of polychlortrifluoroethylene (PCTFE, a copolymer of ethylene and chlortrifluorethylene). To avoid tissue ingrowth, the holding element was closed with a small plug and the silicone tube was sealed with medical grade silicon glue.

Before insertion the implants were sterilized in an autoclave.

Implantation procedure

Fourteen healthy, adult (2–3 years of age), female Dutch goats weighing about 60 kg were used in the experiments. In each goat, four implants were inserted, two on the left and two on the right side of the spinal column in the soft tissue of the abdominal wall. The implants were left *in situ* for 4 months.

Surgery was performed under general anaesthesia, induced by intravenous injection of 25 mg kg^{-1} penthobarbital and atropine (0.5 mg per animal). After oro-tracheal intubation, anaesthesia was maintained by 2–3% ethrane through a constant volume ventilator. To reduce perioperative infection risk, the prophylactic antibiotic Albipen® was administered for 3 days starting 1 h postoperatively.

For the insertion of the implants, the animal was immobilized and the region distal to the costal ridge was shaved, washed and disinfected with povidone-iodine. A longitudinal incision was made parallel to the spinal column. Lateral to this incision a subcutaneous pocket was created by blunt dissection with scissors between the subcutaneous fat layer and the musculus obliquus abdominis externus. Centrally in the subcutaneous pocket, the muscle was cleft parallel to the muscle fibres over a distance of about 0.5 cm and a small tunnel was created by blunt dissection. Then, the silicone tube was inserted in this tunnel until either the titanium fibre mesh or the Dacron cuff was situated on top of the muscle layer. Thereafter, the wound was closed using resorbable vicryl 2-0 sutures. A total of 56 implants were placed, 28 implants provided with the titanium fibre mesh and 28 implants with the Dacron velour cuff.

To assure complete randomization, the position of the various implants into the back was based on a split plot design. Balancing was done by Latin Square to exclude experimental influences.

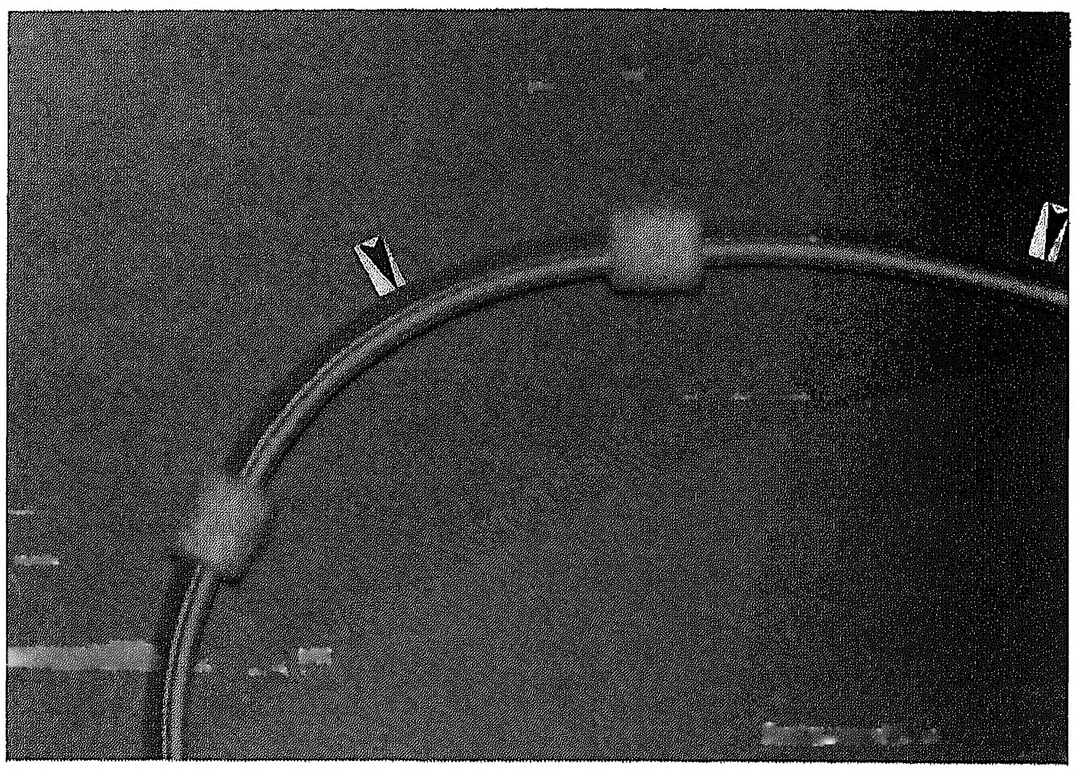

Figure 1 Part of the commercially available Tenckhoff catheter. Both Dacron® velour cuffs together with the silicone tube are visible. The arrows mark the area of the implant used for the experiment.

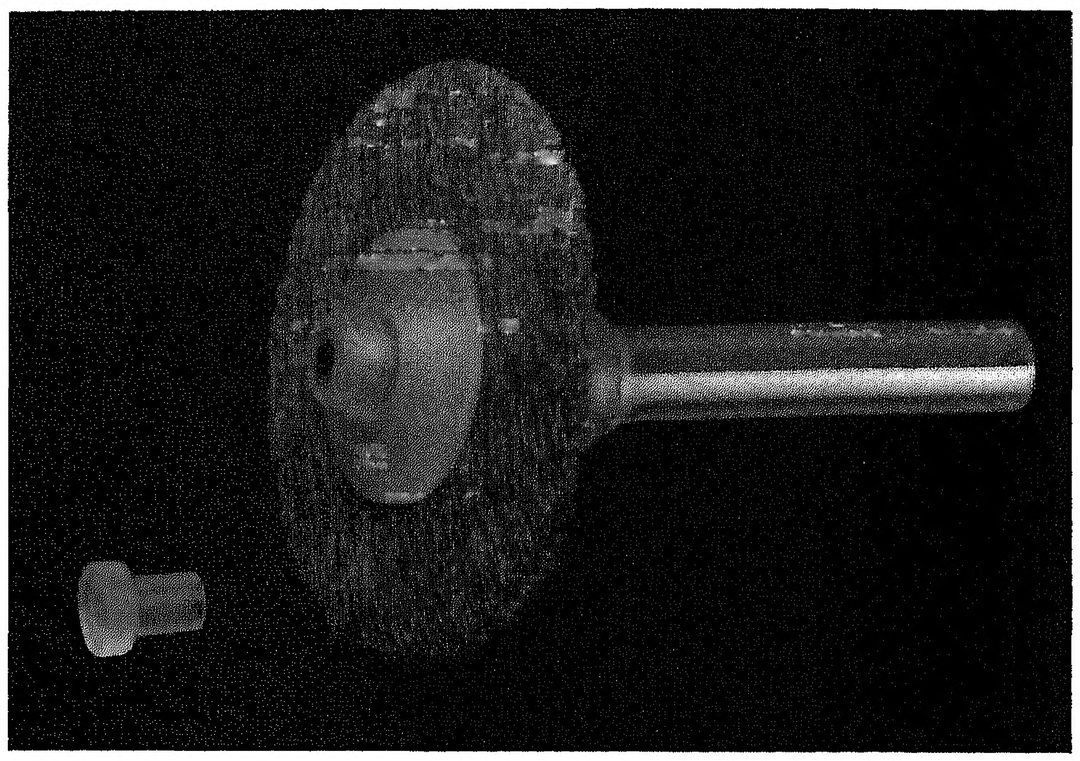

Figure 2 The implant consists of a flange-shaped titanium fibre mesh, a polychlortrifluoroethylene holding element and a silicone tube. The small plug seals the holding element.

Histological evaluation techniques

After 4 months, the animals were killed using an overdose of Nembutal®. After killing the animals, the implants with their surrounding tissues were excised immediately. Following fixation in 10% buffered formalin solution, the specimens were dehydrated by alcohol series. Subsequently, the tissue specimens were trimmed to remove excess tissue and embedded in methyl methacrylate. After polymerization, thin (10 μm) histological sections were prepared using a modified diamond-blade sawing microtome technique[24]. The sections, containing the implants and the surrounding tissues attached to them, were stained with Methylene Blue and basic fuchsin and examined by light microscopy.

To assess the soft tissue response to the implants, both histological and histomorphometric evaluations were performed. The histological evaluation consisted of thorough description of the observed tissue reaction. For the histomorphometric evaluation:

1. The mean distance between the individual fibres of either the Dacron velour or the titanium mesh was measured.
2. The fraction of either Dacron or titanium fibres with associated foreign body giant cells was determined according to a method described by Schreuders *et al.*[25]. For this purpose, the histological sections were examined at a total magnification of ×160 by light microscopy. In each section, the number of Dacron/titanium fibres with associated foreign body giant cells was counted inside four different, randomly chosen squares, measuring 500 × 500 μm. Then, this number was divided by the total number of Dacron/titanium fibres, as determined inside each square.
3. The tissue response was quantified by counting the number of nuclei of macrophages and foreign body giant cells in the interstitial tissue. This was performed at the four random spots described above, only for this histomorphometric analysis we used a square measuring 225 × 225 μm.
4. Earlier evaluations of retrieved human Tenckhoff catheters revealed that a large portion of the Dacron velour cuffs was filled with silicone glue. To confirm this observation, we measured the portion of Dacron velour available for tissue ingrowth and compared it to the part of Dacron velour filled with silicone glue (*Figure 3*).

All histomorphometric procedures were performed in five representative sections of each implant and done blindly by two different operators.

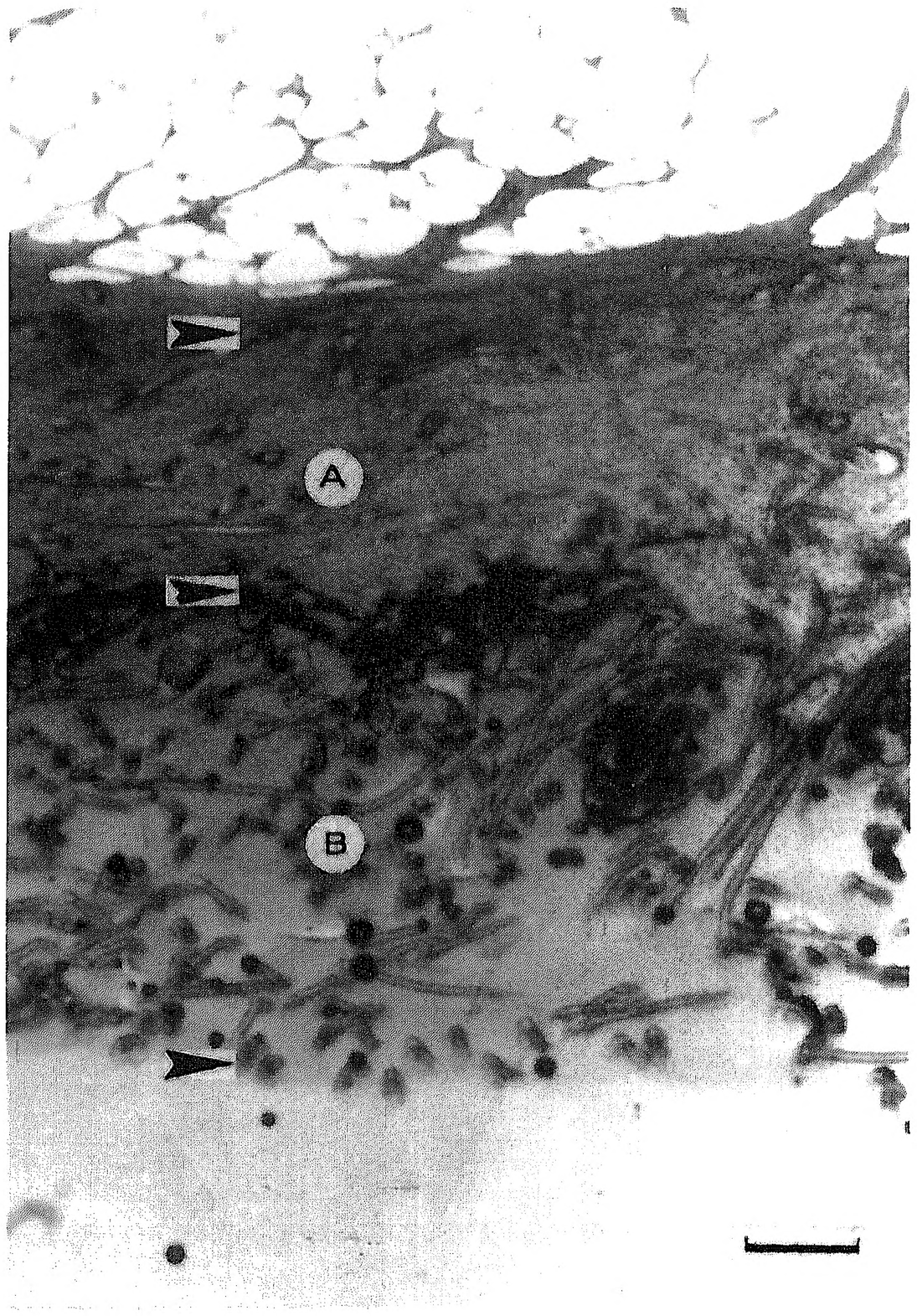

Figure 3 The portion of Dacron® velour available for tissue ingrowth (**A**) compared to the part of Dacron velour filled with silicone glue (**B**). In this figure, 35% of the cuff is available for tissue ingrowth. Original magnification ×12.5, bar = 244 μm.

RESULTS

Descriptive light microscopic evaluation

Dacron velour cuff

It appeared that the Dacron cuff was partially filled with silicone glue. Further evaluation of the prepared sections revealed that the tissue response to the silicone tube and the Dacron cuff was relatively uniform. The silicone tubes were surrounded by a thin to medium-thin fibrous tissue capsule measuring five to 15 layers of cells. The capsule was commonly free from inflammatory cells. Most of the Dacron cuffs were surrounded by a tissue capsule containing five up to 25 layers of fibroblasts (*Figure 4*). Closse to the Dacron fibres of the cuff, inflammatory cells were occasionally observed. Inside the velour cuff, almost all Dacron fibres were surrounded by a sleeve of macrophages and foreign body giant cells (*Figure 5*). Between the fibres the porosity was filled with immature fibrous connective tissue, but this was only the case where an appropriate distance between the individual Dacron fibres was present.

Titanium fibre mesh

The tissue response to the fibre mesh-provided implants was also relatively uniform. The silicone tube was again surrounded by five to 15 layers of fibroblasts, while the polymer (PCTFE) holding element was lined by a medium-thin fibrous tissue capsule measuring 10–25 layers of cells. The capsule was commonly free from inflammatory cells. Around the fibre mesh material we observed a thin to medium-thin capsule, containing 5 to 15 layers of fibroblasts (*Figure 6*). This capsule was free from inflammatory cells. Inside the porosity of the titanium mesh, more mature collagenous connective

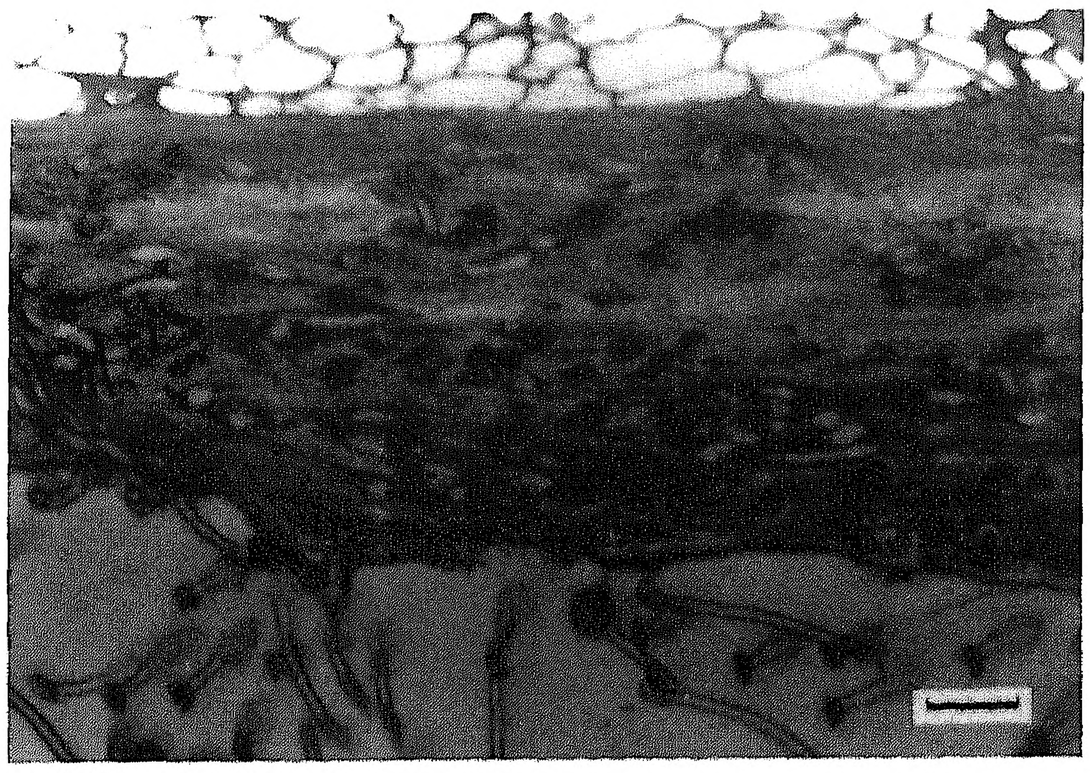

Figure 4 The Dacron® cuff is surrounded by a thin fibrous tissue capsule. Inside the porosity, strands of fibrous tissue are present where an appropriate distance between the individual fibres exists. Original magnification ×25, bar = 120 μm.

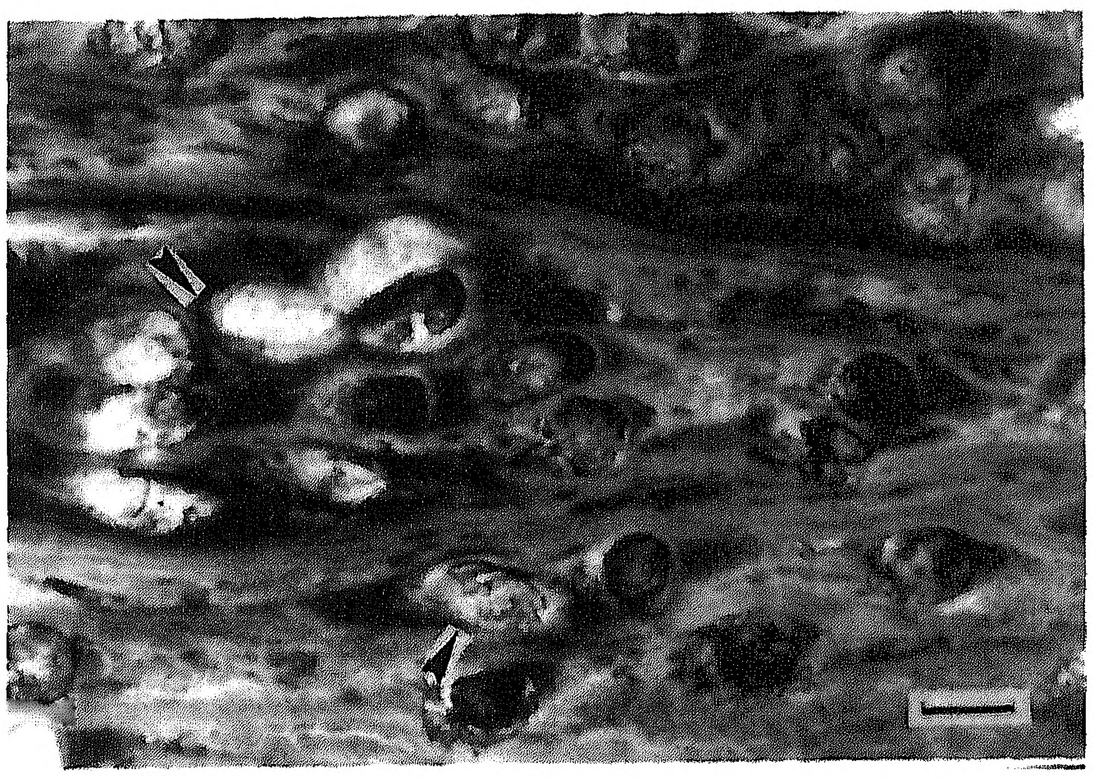

Figure 5 Almost all Dacron® fibres (arrows) are surrounded by a sleeve of macrophages and foreign body giants cells. Original magnification ×100, bar = 30 μm.

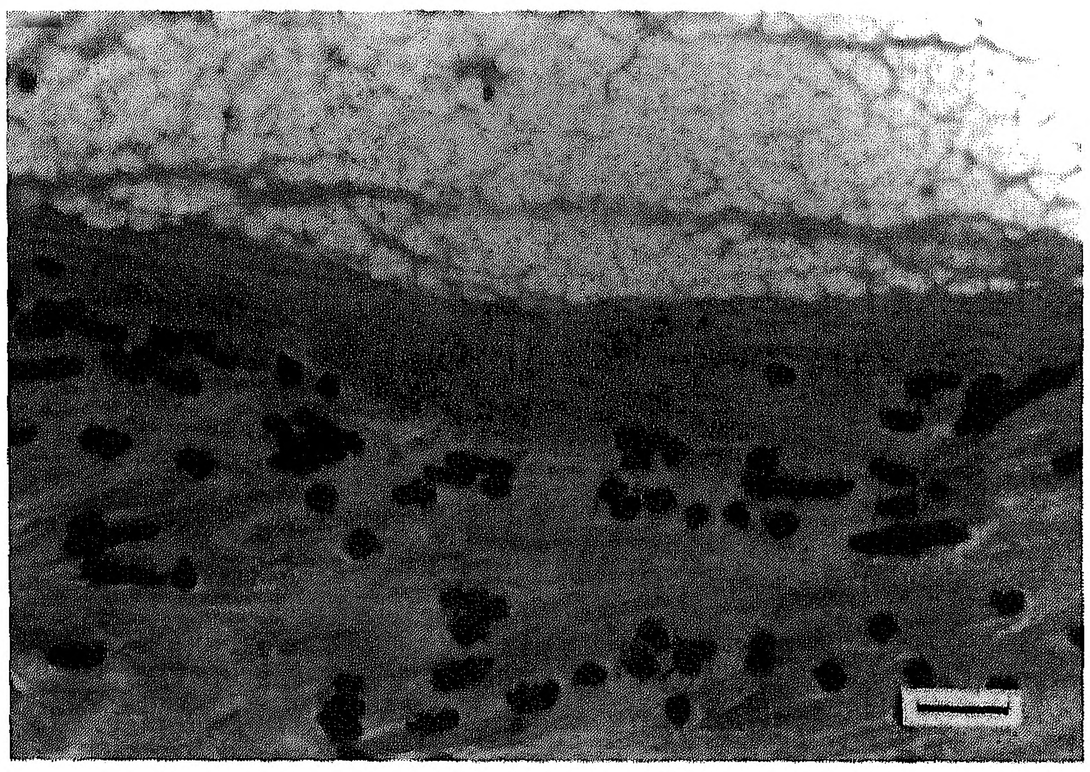

Figure 6 The titanium fibre mesh is surrounded by a thin to medium-thin fibrous tissue capsule. Original magnification ×10, bar = 303 μm.

tissue was found (*Figure 7*). Occasionally, macrophages were present in the interstitium and whenever foreign body giant cells were noticed, they were mostly lying on one side of the fibres.

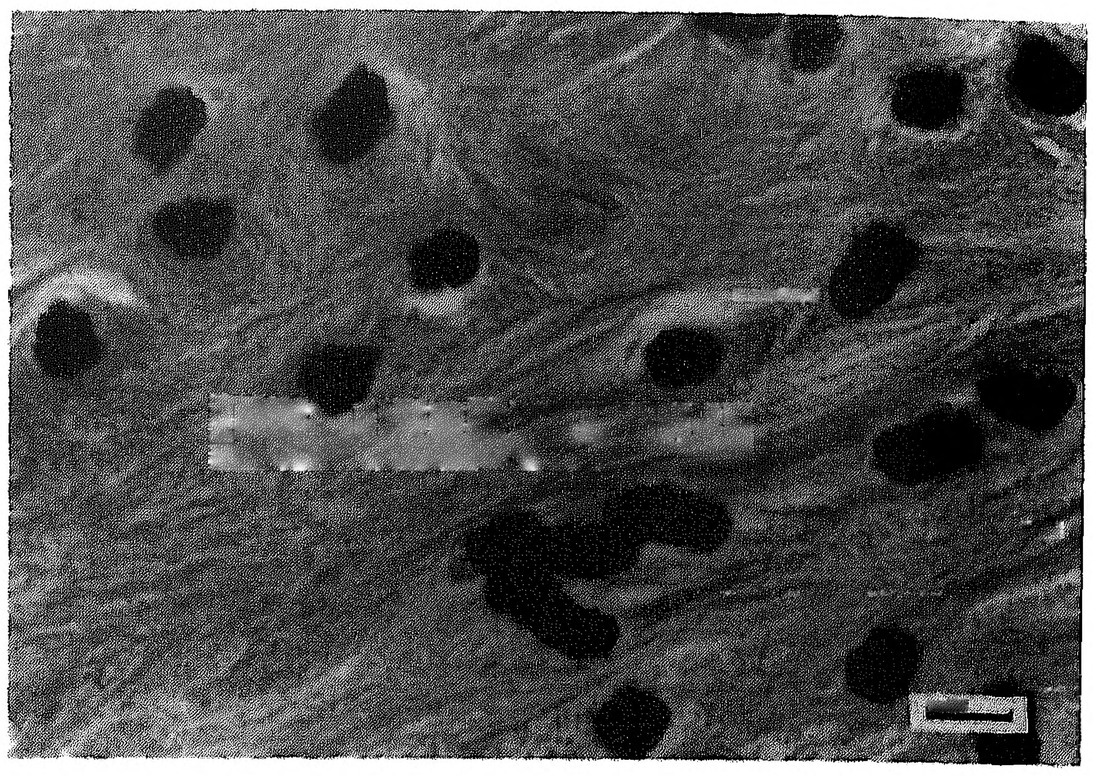

Figure 7 Inside the porosity of the titanium mesh, more mature collagenous connective tissue was found. Original magnification ×25, bar = 120 μm.

Histomorphometric evaluation

The mean distance between the individual fibres of the Dacron velour was 111.6 μm. Still, it has to be noted that the distance between the internal fibres was smaller compared to the peripheral part of the Dacron cuff. Inside the titanium fibre meshes, the mean distance between the individual fibres was 170.8 μm.

Second, we determined the ratio of fibres associated with foreign body giant cells compared to the total number of fibres in the indicated areas. It appeared that inside the Dacron velour 91 ± 4% of the fibres was associated with foreign body giant cells compared to only 23 ± 12% inside the titanium fibre mean structure. Statistical analysis of these data, using a non-parametric test according to Wilcoxon, revealed that significantly more fibres in the Dacron velour were associated with foreign body giant cells compared to the titanium mesh ($P < 0.001$).

Furthermore, we estimated the number of inflammatory cells inside the porosity of either the Dacron velour and the titanium fibre mesh by counting number of nuclei in the above described areas. Inside the Dacron velour 83.57 ± 29.50 nuclei and inside the titanium fibre mesh 27.50 ± 11.78 nuclei were counted in each area. Statistical analysis of these data, using a non-parametric test according to Wilcoxon, showed that this difference was significant ($P < 0.001$).

We also measured the part of the Dacron velour available for tissue ingrowth. It appeared that the part of the cuff filled with silicone glue as 51 ± 17%.

DISCUSSION AND CONCLUSIONS

The purpose of this study was to compare the differences in soft tissue reaction to Dacron velour and titanium fibre mesh, both materials used to anchor a percutaneous device.

The observed tissue reaction to the titanium fibre mesh was similar to our earlier experiments[1,21,22]. Inside the titanium mesh, the number of inflammatory cells and foreign body giant cells was significantly lower compared to the Dacron velour. In addition, more mature collagenous connective tissue was

observed. Two explanations can be given for this difference in tissue behaviour between Dacron and titanium. First, it can be related to differences in surface energetic properties. It is known that, in contrast to titanium, Dacron has a low surface tension. Biomaterials with low-energy surfaces are reported to be less biocompatible. Various *in vitro* and *in vivo* studies demonstrated the influence of this parameter on the foreign body host response[26–29]. It also appeared that radio frequency glow discharge treatment of implants, for instance, increases the wettability of these materials, resulting in an improved fibroblast behaviour to the implant surface. A second explanation is based on the findings of Steinemann and Mäusli[30], who described that the biocompatible behaviour of titanium occurs because the corrosion products are at saturation in living tissue and electroneutral. Therefore, an implant made of titanium will not effect a local tissue reaction.

In contrast to the difference in tissue reaction inside the porosity of the implants, the capsule thickness seems not to be influenced by the kind of implant material. This is in agreement with the observations reported earlier that the thickness of the fibrous tissue capsule is the result of the wound healing response to the surgical trauma and has no relation with the chemical compatibility of the implant material[31,32].

According to Tenckhoff, the Dacron cuff applied in dialysis catheters and situated in the subcutaneous area fulfils two functions: (1) promotion of fibrous tissue ingrowth for fixation of the catheter and (2) prevention of bacterial migration along the cuff into the subcutaneous area[33]. It is also known that the rate of epithelial migration alongside a percutaneous device appeared to be dependent on the degree of migration alongside a percutaneous device appeared to be dependent on the degree of connective tissue maturity inside the porosity of the implant[34]. However, as our evaluation shows, because of the production process one-half of the Dacron cuff is filled with silicone glue. Furthermore, the ingrowth of fibrous tissue is very limited. After 4 months implantation, the remainder of the cuff is mainly filled with inflammatory tissue. Despite a sufficient distance between the velour fibres to allow ingrowth, only some strands of fibrous connective tissue are present between the Dacron cuff fibres. These findings are confirmed by earlier studies on the tissue reaction of Dacron implants[25,34–38]. Combination of these observations with our earlier histological evaluation of experimental titanium mesh percutaneous devices placed in rabbits[22] can only lead to the conclusion that the limited fibrous tissue ingrowth into the Dacron cuff has to be the reason for the observed high failure incidence of this kind of device.

In summary, we assume that both designed functions of the Dacron cuff, i.e. fixation and percutaneous passage seal, will never be obtained in this material. As a consequence, exit-site infections and peritonitis will continue to be the major complications of peritoneal dialysis. In contrast, the tissue reaction to the titanium fibre mesh is significantly better. Therefore, a percutaneous device equipped with this material should be able to diminish the complication rates.

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REFERENCES

1 Paquay YCGJ, de Ruijter JE, van der Waerden JPCM, Jansen JA. Titanium fiber mesh anchoage for percutaneous devices applicable for peritoneal dialysis. *J Biomed Mater Res* 1994; **28**: 1321.

2 Paquay YCGJ, Jansen JA, Goris RJA, Hoitsma AJ. Long-term clinical experience with continuous ambulatory peritoneal dialysis. *J Invest Surg*, accepted.

3 Moncrief, JW, Popoich RP. Continuous ambulatory peritoneal dialysis (CAPD). In: Nolph KD, ed. *Peritoneal Dialysis*. Dordrecht, The Netherlands: Kluwer Academic, 1988: 152–168.

4 Amano I, Katoh T, Inagaki Y. Development of alumina ceramic transcutaneous connector to prevent skin exit site infections around CAPD catheter. *Trans Am Soc Artif Intern Organs* 1990; **36**: 94.

5 Bay WH, Vaccaro PS, Powell SL, Erlich LF. The Gore-Tex® peritoneal catheter: a clinical evaluation and comparison with the Tenckhoff catheter. *Am J Kidney Dis* 1984; **4**: 268.

6 Bessette RW, Cowper T, Natiella J, Menaghan M, Shatkin S, Schaaf N. Histological evaluation of pore size and shape in silicone implants in rhesus monkeys. *Ann Plast Surg* 1981; **7**: 447.

7 Calderaro V, Memoli B, Terracciano V, Ballotta MM, Genualdo R. A double chamber catheter for chronic ambulatory peritoneal dialysis (CAPD). *Proc Eur Dialysis Transplant Assoc* 1981; **18**: 297.

8 Chehroudi B, Gould, TRL, Brunette DM. The role of connective tissue in inhibiting epithelial downgrowth on titanium-coated percutaneous implants. *J Biomed Mater Res* 1992; **26**: 493.

9 Daly BDT, Dasse KA, Gould KE *et al.* A new percutaneous access device for peritoneal dialysis. *Trans Am Soc Artif Intern Organs* 1987; **23**: 664.

10 Grosse-Siestrup C, Affeld K. Design criteria for percutaneous devices. *J Biomed Mater Res* 1984; **18**: 357.

11 Hall CW, Cox PA, McFarland SR, Ghidoni JJ. Some factors that influence prolonged interfacial continuity. *J Biomed Mater Res* 1984; **18**: 383.

12 Heimke G. Percutaneous implants. *Adv Mater* 1991; **3**: 108.

13 Kantrowitz A, Daly BDT, Hermann VM, Twardowski ZJ, Cruz C. Development of a new long-term access device for continuous ambulatory peritoneal dialysis. *Trans Am Soc Artif Intern Organs* 1988; **34**: 930.

14 Thornhill JA, Hartman J, Boon GD, Riviere JE, Jacobs D, Ash SR. Support of an anephric dog for 54 days with ambulatory dialysis and a newly designed peritoneal catheter. *Am J Vet Res* 1984; **45**: 1156.

15 von Recum, AF, Park JB. Permanent percutaneous devices. *CRC Crit Rev Bioeng* 1981; **5**: 37.

16 Winter GD. Transcutaneous implants: reactions of the skin–implant interface. *J Biomed Mater Res Symp* 1974; **5**: 99.

17 Gokal R, Ash SR, Helfrichi GB *et al.* Peritoneal catheters and exit-site practices: toward optimum peritoneal access. *Perit Dial Int* 1993; **13**: 29.

18 Jansen JA, de Groot K. Guinea pig and rabbit model for the histological evaluation of permanent percutaneous implants. *Biomaterials* 1988; **9:** 268.

19 Jansen JA, van der Waerden JPCM, van der Lubbe HBM, de Groot K. Tissue response to percutaneous implants in rabbits. *J Biomed Mater Res* 1990; **24:** 295.

20 Jansen JA, van der Waerden JPCM, de Groot K. Wound-healing phenomena around percutaneous devices implanted in rabbits. *J Mater Sci: Mater Med* 1990; **1:** 192.

21 Jansen JA, van der Waerden JPCM, de Groot K. Development of a new percutaneous access device for implication in soft tissues. *J Biomed Mater Res* 1991; **25:** 1535.

22 Janssen JA, Paquay YCGJ, van der Waerden JPCM. Tissue reaction to soft-tissue anchored percutaneous implants in rabbits. *J Biomed Mater Res* 1994; **28:** 1047.

23 Ducheyne P, Martens M, de Meester P, Mullier JC. Titanium implants with porous structures for bone ingrowth: a general approach. In: *Titanium Alloys in Surgical Implants. ASTM STP 796.* Philadelphia, PA: American Society for Testing and Materials, 1983: 265–279.

24 Klein CAPT, Sauren YMHF, Modderman WE, van der Waerden JPCM. A new saw technique improves preparation of bone sections for light and electron microscopy. *J Appl Biomater* 1994; **5:** 369.

25 Schreuders PD, Salthouse TN, von Recum AF. Normal wound healing compared to healing within porous Dacron implants. *J Biomed Mater Res* 1988; **22:** 121.

26 Baier RE, Meyer AE. Implant surface preparation. *Int J Oral Maxillofac Implants* 1988; **3:** 9.

27 Jansen JA, van der Waerden JPCM, de Groot K. Fibroblast and epithelial cell interaction with surface treated implant materials. *Biomaterials* 1991; **12:** 25.

28 Johnson SD, Anderson JM, Marchant RE. Biocompatibility studies on plasma polymerized interface materials encompassing both hydrophobic and hydrophilic surfaces. *J Biomed Mater Res* 1992; **26:** 915.

29 Lemm W. *The Reference Materials of the European Communities.* Dordrecht, The Netherlands: Kluwer Academic, 1992.

30 Steinemann SG, Mäusli P-A. Titanium alloys for surgical implants—biocompatibility from physiochemical principles. *Sixth World Conference on Titanium,* 1988.

31 Coleman DL, King RN, Andrade JD. The foreign body reaction: a chronic inflammatory response. *J Biomed Mater Res* 1974; **8:** 199.

32 Jansen JA, von Recum AF, van der Waerden JPCM, de Groot K. Soft tissue response to different types of sintered metal fibre-web materials. *Biomaterials* 1992; **13:** 959.

33 Tenckhoff H, Schechter H. A bacteriologically safe peritoneal access device. *Trans Am Soc Artif Intern Organs* 1968; **14:** 181.

34 Gangjee T, Colaizzo R, von Recum AF. Species-related differences in percutaneous wound healing. *Ann Biomed Eng* 1985; **13:** 451.

35 von Recum AF. Applications and failure modes of percutaneous devices: a review. *J Biomed Mater Res* 1984; **18:** 323.

36 Yan JYJ, Cooke FW, Vaskelis PS and von Recum AF. Titanium-coated Dacron® velour: a study of interfacial connective tissue formation. *J Biomed Mater Res* 1989; **23:** 171.

37 Feldman DS, Hultman SM, Colaizzo RS, von Recum AF. Electron microscope investigation of soft tissue ingrowth into Dacron® velour with dogs. *Biomaterials* 1983; **4:** 105.

38 Feldman DS, von Recum AF. Non-epidermally induced failure modes of percutaneous devices. *Biomaterials* 1985; **6:** 352.