A new titanium fiber mesh-cuffed peritoneal dialysis catheter: An experimental animal study

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CAPD catheters are associated with infectious complications. To solve this problem, we developed a new catheter. In our design, sintered titanium fiber mesh material replaced the Dacron® cuffs, as used in standard Tenckhoff catheters. The purpose of the current study was to compare the tissue response to new titanium-cuffed vs. Dacron®-cuffed catheters.

Experimental and standard Tenckhoff catheters were inserted intraperiotoneally in 12 goats, using a so-called two-stage surgical technique. In the first surgical session, the catheters were implanted. However, the percutaneous part of the catheter was buried subcutaneous. After 3–5 weeks, the percutaneous part of the catheter was exteriorized. After 14 weeks of implantation, all implants with surrounding tissue were retrieved and prepared for histological evaluation. Subsequently, we quantified: the characteristics of the fibrous tissue capsule surrounding the cuffs, the tissue inside the cuff porosity, and the epidermal downgrowth.

Histologic and histomorphometric evaluation showed that titanium mesh evoked a lesser inflammatory response inside the cuff porosity compared with Dacron® cuffs. Besides, the fibrous tissue capsule surrounding the titanium cuffs was significantly thinner.

Supported by the obtained results, we conclude that the use of titanium fiber mesh has a great potential for application in percutaneous devices.

Introduction

Peritoneal dialysis (PD) has some important advantages compared to conventional dialyzing methods, like hemodialysis. On the other hand, permanent percutaneous access devices, as has to be used for PD, are associated with numerous clinical problems. Frequently observed complications are exit-site infections and peritonitis. To solve this problem, we developed a new catheter. In our design, sintered titanium fiber mesh material replaces the Dacron® cuffs, as used in standard so-called Tenckhoff catheters. Further, we use a so-called two-stage surgical procedure for installation of the devices.

The purpose of the current study was to compare the tissue response to new titanium-cuffed vs. Dacron®-cuffed catheters.

Materials and methods

Percutaneous catheters

Two different types of percutaneous catheters were used in the study (Fig. 1). One of the catheters was the commercially available Tenckhoff catheter that consists of a silicone tube with two polyethylene terephthalate Dacron® cuffs attached to it.

The other catheter used consisted of a similar silicone rubber tube as used in the Tenckhoff catheter. In contrast, this tube was provided with two cuffs made of titanium fiber mesh. The mesh had a fiber diameter of 40 μm, a volumetric porosity of about 90%, and a weight of $600\,g\,m^{-2}$. The titanium cuffs were provided at their inner side with titanium foil and were attached to the silicone tube with medical grade silicone glue.

Surgical procedure

Experimental and standard Tenckhoff catheters were inserted intraperitoneally in 12 goats, using a so-called two-stage surgical technique. Each goat received both catheter types.

During the first surgical session, distal to the costal ridge, a semi-circular incision of about 10 cm was made through the skin and a subcutaneous pocket was created. Subsequently, the various muscle layers were incised. On

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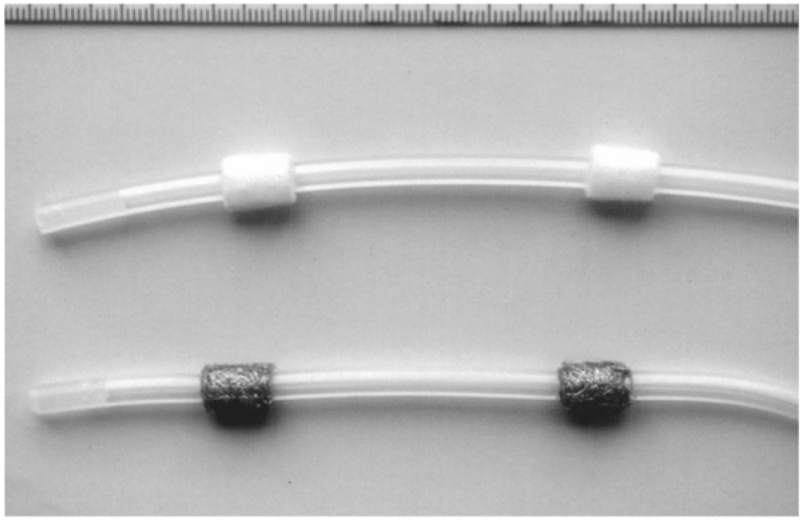

Figure 1 The titanium- and Dacron®-cuffed catheter, that were used in the experiment (scale bar in cm).

reaching the peritoneum, this was opened and the perforated part of the catheter was inserted in the abdominal cavity. Then, the pre-peritoneal cuff was fixed with a purse string suture that also closed the peritoneum around the catheter. Thereafter, by means of a blunt dissection with scissors, a tunnel was created from the peritoneum, in between the various muscle layers towards the top of the subcutaneous pocket. Hereafter, the catheter was pulled through the tunnel and the superficial cuff and percutaneous part of the catheter were positioned in the subcutaneous pocket. Eventually, all incisions were closed by means of vicryl sutures. A total of 24 catheters were placed: 12 catheters provided with two cuffs of titanium fiber mesh, and 12 implants with the Dacron® velour cuffs. After an intervening healing period of four weeks, the percutaneous part of the catheter was exteriorized.

The catheters were left *in situ* for 14 weeks after creating the percutaneous exit-site. During this period, the animals were stabled together in a separate room. The heads of the goats were fixed between two vertical bars to prevent the animal's from manipulating the percutaneous catheter part.

Histological evaluation techniques

At the end of the experiment the goats were sacrificed using an overdose of Nembutal®. The catheters with their surrounding tissues were excised immediately and fixed in 4% buffered formalin solution. Subsequently, the tissue specimens were embedded in methylmethacrylate using standard histological preparation procedures. After polymerization, thin (10 μm) histological sections were prepared using a modified diamond-blade sawing microtome technique. The sections were stained with methylene blue and basic fuchsin and investigated by light microscopy.

To assess the soft tissue response to the cuffs, both histologic and histomorphometric evaluations were

TABLE I Histologic grading scale for percutaneous implant cuffs

	Response	Score
Capsule quantitatively	Thickness rating:	
	1–4 fibroblasts	4
	5–9 fibroblasts	3
	10–30 fibroblasts	2
	> 30 fibroblasts	1
	Not applicable	0
Capsule qualitatively	Capsule tissue is fibrous, mature, not dense, resembling connective or fat tissue in the non-injured regions	4
	Capsule tissue is fibrous but immature, showing fibroblasts and little collagen	3
	Capsule tissue is granulous and dense, containing both fibroblasts and many inflammatory cells	2
	Capsule consists of masses of inflammatory cells with little or no signs of connective tissue organization	1
	Cannot be evaluated because of infection or other factors not necessarily related to the material	0
Interstitium qualitatively	Tissue in interstitium is fibrous, mature, not dense, resembling connective or fat tissue in the non-injured regions	4
	Tissue in interstitium shows blood vessels and young fibroblasts invading the spaces; few macrophages may be present	3
	Tissue in interstitium shows giant cells and other inflammatory cells in abundance but connective tissue components in between	2
	Tissue in interstitium is dense and exclusively of inflammatory type	1
	Implant cannot be evaluated because of problems not related to the material tested	0

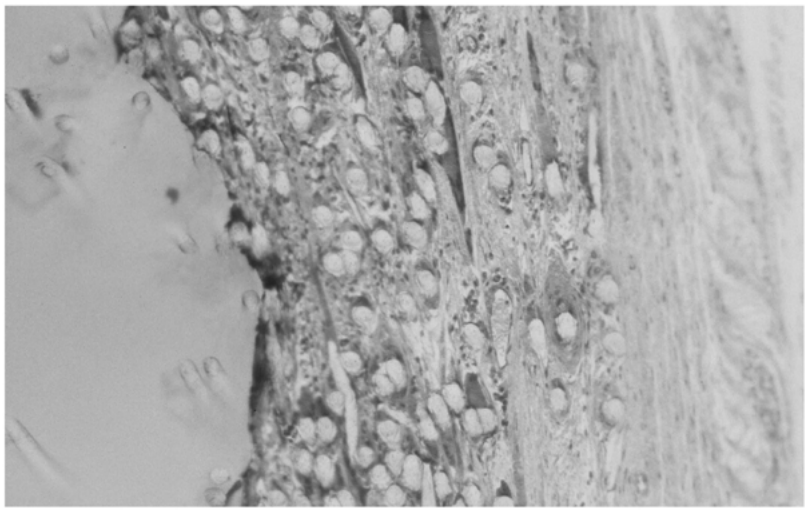

Figure 2 At a high magnification, it can clearly be observed that the interstitium of Dacron® velour cuffs exhibit an abundance of inflammatory cells (original magnification 40×).

performed. Therefore, the following approaches were used:

1. The characteristics of the capsule surrounding the implant were rated according to a method that already has been described extensively by Jansen *et al*. [1] (Table I).
2. The interstitial tissue response was quantified by numerical rating of the tissue morphology and cellularity (Table I).
3. The epidermal downgrowth was determined.

Results

Histologic and histomorphometric evaluation

The histologic and histomorphometric results of the capsule and interstitium are shown in Figs 2–5. Statistical testing, using a Student's *t*-test, revealed that:

1. The fibrous capsule surrounding the subcutaneous titanium-cuff was quantitatively as well as qualitatively better compared to the subcutaneous Dacron®-cuff (Figs 5a, b, $p < 0.05$).
2. The quality of the interstitial tissue inside the subcutaneous titanium-cuff was better compared to the subcutaneous Dacron®-cuff (Fig. 5c; $p < 0.05$).
3. The quality of the tissue inside the pre-peritoneal titanium-cuff was better compared to the pre-peritoneal Dacron®-cuff (Fig. 5c; $p < 0.05$).
4. The capsule and interstitial tissue response between the subcutaneous and pre-peritoneal cuffs was not significantly different for both titanium and Dacron® (Figs 5a–c; $p > 0.05$).

The evaluation of the epidermal downgrowth revealed that:

1. Around four Dacron®-cuffed catheters, the epidermis had migrated to below the subcutaneous cuff;
2. Around eight Dacron®-cuffed catheters, the epidermis had migrated to the subcutaneous cuff;
3. Around all the titanium-cuffed catheters, the epidermis had migrated to the subcutaneous cuff.

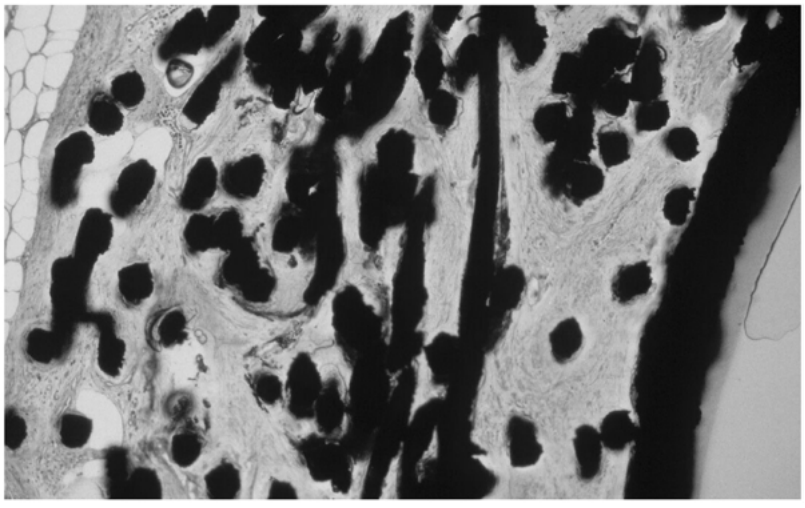

Figure 3 The interstitium of a titanium cuff, showing the mild interstitial reaction, and the formation of a thin fibrous capsule (original magnification 40×).

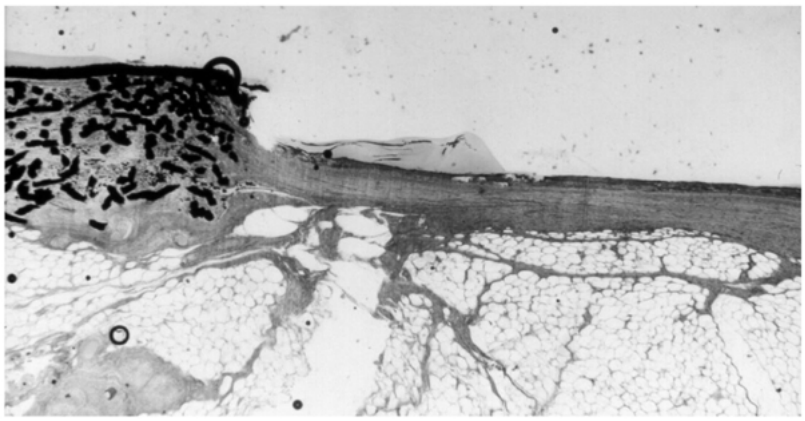

Figure 4 Longitudinal section through a titanium cuff. Sinus tract formation can be observed as a lining with epithelial cells and keratin (original magnification 5×).

Discussion and conclusion

Many researchers have been intrigued by the failure of percutaneous catheters. Consequently, a lot of approaches were followed to improve catheter design, for instance by applying silver coatings and rings, various surface treatments, or surface micro-texturing [2–4]. Next to alterations in the catheter design, a lot of efforts were directed at implantation techniques, profilactic antibiotics, and exit-site care [5]. Unfortunately, with all these novel techniques still no consistent favorable result was achieved.

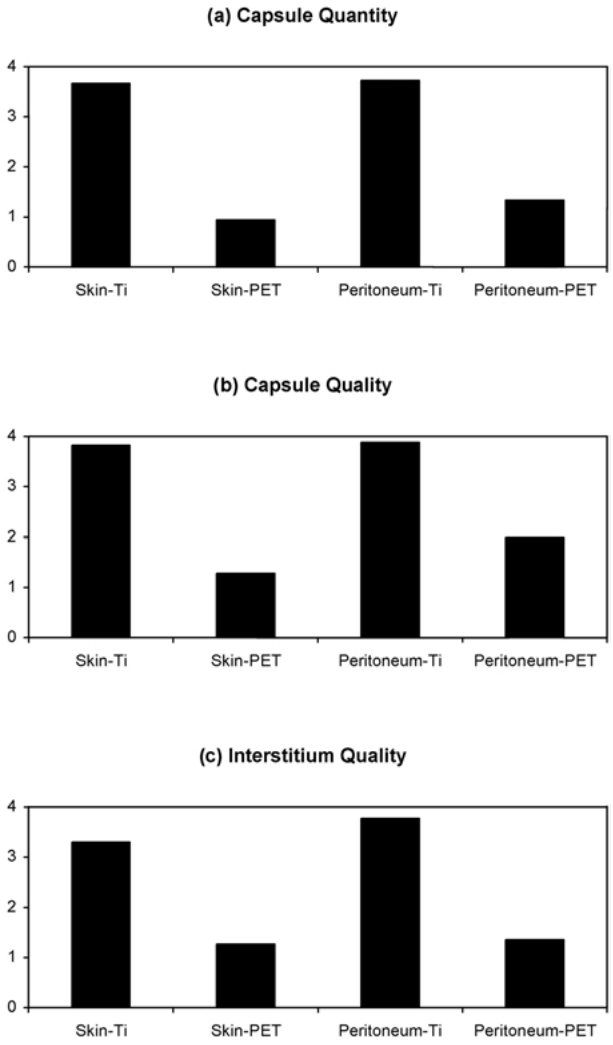

Figure 5 Graphs of the histomorphometric evaluations of (a) capsule quantity, (b) capsule quality, and (c) interstitium quality. The bars are averages over all 12 animals for the Dacron® (PET) cuff equipped catheter, and the titanium (Ti) cuff equipped catheter. Skin means the cuff that was located on the skin side, peritoneum means the pre-peritoneal catheter cuff.

During the last decade, our laboratory has focused on the use of titanium fiber mesh to create a failure-free percutaneous passage. The current experiment is the last one in a consecutive series of studies. The presented results confirm again that titanium fiber mesh cuffs are able to improve the clinical behavior of indwelling skin-penetrating catheters.

In view of the above-mentioned, the light microscopical analysis revealed a number of differences in tissue behavior between Dacron® and titanium cuffs. Most importantly, the titanium fibers evoked a lesser inflammatory response. This difference in tissue behavior of course can explain the better clinical performance of the newly-developed catheter.

One of the other evident results of our study was that the capsule surrounding the titanium cuffs was significantly thinner. Wound healing around implants usually starts with an accumulation of polymorphonuclear leukocytes and macrophages, which can develop in foreign body giant cells. Later, fibroblast-like cells arrive. Usually, when the material is ''inert'', the wound healing around the implant will result in the formation of a fibrous tissue capsule. Within this capsule lies the implant, then further 'ignored' by the body. The thickness of this capsule is determined by the rate of agitation. For instance, if there is a constant mechanical stimulus evoked by the implant, the capsule will be thick in measure. A toxic material, or a material that degrades slowly leaving foreign degradation products, also will result in a thick and inflammated capsule. Agitation of a capsule will result in capsule contraction, often leading to implant damage. Similarly, the thickness of the capsule around a fibrous mesh is determined by the mobility of the implant, and by the tissue reaction towards the interstitium. Apparently the titanium evokes no or hardly any inflammatory response in the mesh interstitium, and therefore hardly capsule formation is present [6]. This confirms with our earlier reports about the favorable integration of titanium with the surrounding tissue [7, 8].

In summary, we conclude that titanium fiber mesh has

a great potential for application in percutaneous catheters. Consequently, the start of human clinical trials with this new type of peritoneal dialysis-catheters appears to be justified.

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