Preliminary Comparison of Titanium Mesh and Dacron Cuffs in Subcutaneous and Percutaneous Rabbit Models

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Statement of Purpose: Percutaneous fixation of tunneled central venous catheters for hemodialysis is currently dependent on integral Dacron cuffs. These cuffs must be surgically removed during catheter repositioning or exchanges for infection or fibrin sheath formation. The Ported Vascular Access System (PVAS^{TM}) has been developed to allow ease of exchange and reposition, without necessitating repeated surgical insults, which leave the patient vulnerable to infection during the resulting cuff ingrowth period. The PVAS employs a novel titanium mesh tissue-ingrowth cuff, which remains fixed in the skin during catheter repositioning and exchanges. This preliminary study in 2 rabbits compared the tissue reaction to phantoms of the PVAS device and Dacron-cuffed catheters in subcutaneous and percutaneous models at 28 days.

Methods: *Subcutaneous test phantoms* were constructed of Ti4AlV6 conduits, coated with commercially pure (c.p.) titanium mesh using proprietary brazing technology, surrounding a 3" length of polyurethane hemodialysis catheter (MedComp, 14.5Fr Hemoflow) that had been filled with room temperature vulcanizing (RTV) silicone. *Subcutaneous control phantoms* consisted of 3" sections of the same catheter, with the bonded Dacron cuff centrally located (Figure 1). *Percutaneous test phantoms* were constructed of Ti4AlV6 posts coated with c.p. titanium mesh, with a reinforced silicone suture anchor. *Percutaneous control phantoms* consisted of the same post and silicone anchor, with a section of catheter and its adherent cuff bonded to the post (Figure 1).

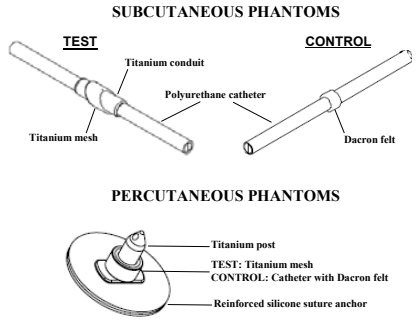

Figure 1

In vivo procedures were approved by the Testing Facility's IACUC for compliance with regulatory guidelines concerning the care and use of animals. Two New Zealand white rabbits (F, 3-5kg) were maintained on a closed circuit ventilator with general isofluorane anesthesia. Eight incisions were made perpendicular to the midline of the dorsum of 1 rabbit. Six subcutaneous test (N=3) and control (N=3) phantoms were implanted parallel to the midline and secured with absorbable sutures. In the remaining rabbit, 3 pairs of pockets were created to the right and left of the midline of the dorsum. A small hole was created in the center of the skin overlying each pocket, and six percutaneous test (N=3) and control (N=3) phantoms were inserted into each pocket, with the tip of the post passing through the skin. Absorbable sutures secured the subcutaneous anchor to the skin. Both animals were allowed to recover. At 28 days, animals were sedated and euthanized with an overdose of sodium pentobarbital. The phantoms with surrounding tissue were removed *en bloc*, fixed in 10% neutral buffered formalin, and embedded in methyl methacrylate. Longitudinal and transverse sections were glued to slides, polished to an optical finish, and stained with hematoxylin & eosin or Wasatch trichrome with aniline blue counterstain. The implants were histopathologically evaluated for percent connective tissue ingrowth, capsule thickness, and tissue response and inflammation. In addition, all implants were graded for capsule qualities & thickness, and interstitial tissue quality using the scoring system of ten Hallers *et al* 2007.

Results: At 28 days, all implants were stably implanted with no signs of infection. The subcutaneous test phantoms had similar connective tissue ingrowth (100% vs. 79.3 ± 1%, respectively, P=0.1), interstitial quality (scores of 3.0 vs. 2.0, P=0.1) and capsule quality (scores of 3.0 for both) and thickness (0.52 ± 0.3 mm vs. 0.22 ± 0.1mm, P=0.11; scores of 2.67 ± 1.2 vs 3, P=0.7). Percutaneous test and control phantoms had similar connective tissue ingrowth (100% vs. 63.3 ± 3%, respectively, P=0.1), interstitial quality (scores of 3.0 vs. 2.0, P=0.1) and capsule quality (scores of 3.0 vs. 2.33 ± 0.6, P=0.2) and thickness (0.18mm vs. 0.32mm, P=0.441; scores of 3 for both). The fibrovascular stroma was more mature, had more vascularization, and less inflammatory cell infiltration in the subcutaneous and percutaneous test phantoms than in the corresponding control phantoms. The percutaneous test phantoms also exhibited less epidermal downgrowth than the control phantoms. The trichrome stain indicated that there was minimal to no collagen production by the fibrous connective tissue and the fibroblasts within the fibrous biomaterials of all the implants after 28 days of implantation.

Conclusions: The tissue reaction, as described by connective tissue and capsule quantity and qualities, to the test titanium mesh and control Dacron fibrous biomaterials was similar in rabbits following 28 days of subcutaneous and percutaneous implantation. These preliminary experiments also indicated that there was greater vascularization and less inflammation in the test material. These results support further long-term, sufficiently powered *in vivo* investigations of the replacement of Dacron cuffed catheters with titanium mesh coated percutaneous conduits.

References:

1. E.J. ten Hallers, J.A. Jansen, H.A. Marres, G. Rakhorst, G.J. Verkerke. Histological assessment of titanium and polypropylene fiber mesh implantation with and without fibrin tissue glue. *J Biomed Mater Res A* **80**(2):372-80.