Dermal Integration Cuff Improves Resistance to Exit Site Infections in Porcine Bacterial Challenge

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Introduction: Patients who require percutaneous devices such as catheters are at high risk to acquire life-threatening infections. Despite surgical advances and improvements in device design and materials, a patient catheterized for four months has >50% probability of infection. One third to one half of these infections occur via the breach of the skin barrier due to inadequate sealing of the exit site between the device and the surrounding skin, especially with longer term uses. We investigated the ability of a new exit site cuff to protect against exit site infection. STARcuff™ (Healionics, Seattle, WA) takes advantage of precisely selected pore geometry to form an integrated skin seal.

Methods: STARcuff test articles were given a macrotextextured microporous biointerface layer by fragmenting sphere-templated silicone with 35-µm pores (as described in US Pat. App. 2008/0075752) into porous granules (300-500 µm) and applying a monolayer of granules to silicone tubing with a dip-coated silicone adhesion layer. In each of three 35-kg domestic pigs, 8-cm segments of 3-mm diameter silicone tubing were implanted percutaneously in the dorsum, with the exterior end sealed to prevent bacterial entry through the lumen. Six implants per pig contained a STARcuff biointerface layer positioned at the skinline, six were 'NoCuff' controls with no antimicrobial cuff at or near the skinline, and another six (in 2 of 3 pigs) included a VitaCuff™ silver ion loaded antimicrobial cuff (Bard Access Systems, Salt Lake City, UT). All three types of test articles included a subcutaneously positioned Dacron felt cuff (Bard's SureCuff™ or equivalent) to restrict motion by encouraging ingrowth of fibrous scar tissue. The test sites on both animals were sprayed with chlorhexidine antiseptic on days 0, 3, 7, and 14 and protected by gauze bandages. On day 27, the wound sites on 2 of the 3 pigs were inoculated by placing a porous polycarbonate ring loaded with *S. aureus* (10^6 to 10^8 CFU) onto the skin around the implant. The rings were removed on Day 28. Digital photos and infrared thermography images were taken at days 0, 3, 7, 14, 21, 27, 28, 29, 30, and 31. The animals were euthanized on Day 31. All samples were harvested and submitted for histological analysis, with a 5-mm subcutaneous segment of tubing between 1 and 1.5 cm from the exit site and surrounding tissue excised from each sample for quantitative bacterial culture.

Results: From gross observations, 58% (7 of 12) of challenged NoCuff control exit site wounds showed mild signs of infection (purulent discharge and/or thicker pericatheter crust), compared to 33% (4 of 12) of VitaCuff controls and %0 of STARcuff exit sites. All NoCuff controls and 92% of VitaCuff controls showed signs of a sliding interface with increased inflammatory response, while all STARcuff exit sites appeared relatively healthy and tightly integrated with surrounding tissue. Quantitative culture results (summarized in Fig. 1) revealed viable CFUs in 58% of NoCuff controls, 42% of VitaCuff controls, and 17% of STARcuff exit sites, with arithmetic mean *S. aureus* log CFU counts of 5.1, 5.1, and 2.3 respectively.

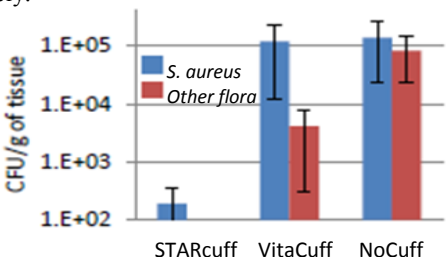
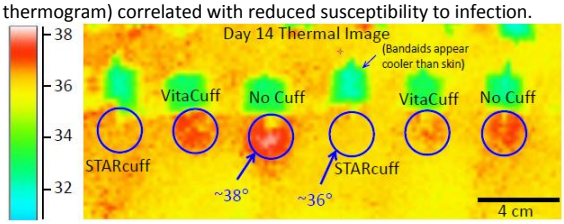


Figure 1. STARcuff exit sites showed reduced CFUs 4 days after challenge (error bars = arithmetic mean ± SEM.

IR thermography results (exemplified in Fig. 2) showed that increased susceptibility to infection (defined as positive *S. aureus* culture at Day 31) correlated with elevated exit site skin temperature at Day 14 ($p = 0.0003$) and Day 21 ($p = 0.0002$).

Figure 2. Reduced inflammation at STARcuff exit sites (as evidenced by thermogram) correlated with reduced susceptibility to infection.



Preliminary histology of NoCuff and VitaCuff exit sites showed epidermal downgrowth several mm along the wall of the tubing; beyond the edge of the epidermis, the implant-tissue interface contained dense granuloma, with a robust biofilm populated by gram-positive cocci evident in some cases. In contrast, STARcuff exit sites were characterized by vascularized dermal ingrowth into the pore structure, minimal epidermal downgrowth, reduced inflammatory response, and no biofilm.

Conclusions: STARcuff implants resulted in better-sealed, healthier exit sites than controls. Evidence from gross observations, quantitative culture, IR thermography, and histological analysis indicate that STARcuff improves resistance to exit site infection. VitaCuff did not show a significant effect on infection resistance when challenged 27 days post-implant, suggesting that its antimicrobial activity was depleted by the time of the challenge. Since STARcuff's effectiveness does not depend on release of an antimicrobial agent, we hypothesize that it provides protection indefinitely. Planned future work will investigate both longer-term and shorter-term efficacy. This approach can potentially pave the way for an improved standard of care for any percutaneous devices used for an extended duration, including dialysis catheters, abutments for prosthetics, ventricular assist devices, and others.

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