Highly Manufacturable Anti-Fouling Surface Modification of Vascular Access Catheters

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Statement of Purpose: The CDC estimates that two million US citizens contract hospital acquired infections annually, resulting in approximately 90,000 preventable deaths, the majority of which are associated with medical devices (1). Additionally, vascular access catheters are often at risk of occlusion from thrombosis leading to delayed therapy, high clinical management costs and complications associated with the utilization of anticoagulants such as heparin.

Semprus is developing a single surface modification that is designed to simultaneously reduce microbial adhesion and thrombus formation over multiple months of exposure to blood. Current technologies address these complications separately and suffer from limited duration, potential toxicity, and risk of generating drug resistant strains. Our previous work has demonstrated the unique ability of betaine polymers to simultaneously reduce microbial adhesion and thrombus accumulation on a variety of substrates (2). The dual reduced-microbial adhesion and anti-thrombogenic properties are maintained after clinically relevant stresses, including prolonged (>30 d) challenges in serum and plasma; demonstrating robustness crucial for the prolonged reduction of medical device complications. The goal of this work was to translate the earlier proof-of-concept anti-fouling surface modification to full length catheters.

Methods: Using proprietary polybetaine grafting technology, various medical-grade substrates were modified. These materials included: polyurethanes (Tecoflex®, Tecothane®, and Carbothane®), silicones, and polyvinylchloride. Characterization of the surfaces included: ATR-IR to verify the chemical composition of the modification, SEM on the sample cross-section to determine modification thickness and conformality, and a radio-labeled assay to quantify fibrinogen adsorption. Anti-thrombogenic performance was assessed in an *ex vivo* flow loop model of thrombosis, performed at the Medical Device Evaluation Center (MDEC) using fresh bovine blood. After 2 hours of blood circulation in the flow loop simulating placement of catheters in a vein, catheters were removed, inspected visually for thrombus formation, and the adhered platelets were quantified using a Gamma counter.

Results: Because of the different performance/geometric requirements of their constituent parts, vascular access catheters are generally constructed from a combination of materials. Polybetaine grafted across a collection of medical grade substrates had reductions in protein fouling of at least 99% from unmodified substrates.

Single Surface Modification Applied to Full Product

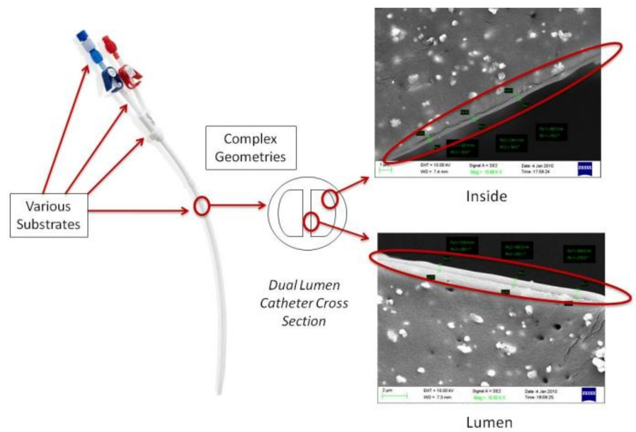

Figure 1. Vascular access catheter with "hub to tip" coverage, inside and out: SEM cross-section images of betaine modified dual lumen vascular access catheter.

The modification was adapted to a double-lumen catheter where both outer surfaces and intra-luminal surfaces, including the septum, were homogenously modified. Modified catheters showed a 99% reduction in platelet adherence when compared with unmodified catheters.

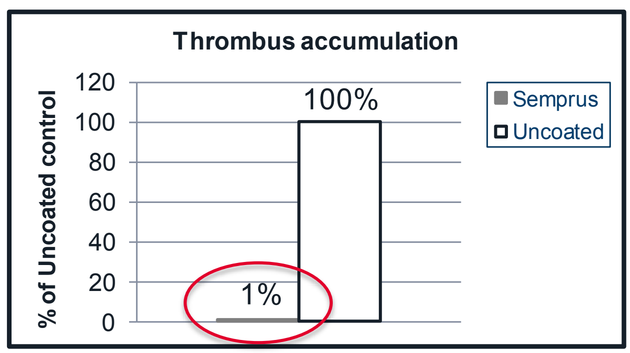

Figure 2. Semprus modified vascular access catheter demonstrates reduced thrombus accumulation.

Conclusions: The surface modification can be applied with a single manufacturing process to produce catheters that are highly resistant to protein fouling and thrombus accumulation. These devices will be assessed in clinical trials, targeting the reduction in vascular access catheter-related complications over a chronic time period.

References: 1. Public Health Reports, 2002:160-166.
2. Z. Zhang, et al., Annual Meeting of the Society for Biomaterials; 2010 Apr 21-24; Seattle, WA.

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