Innovations to Resist Catheter-Related Complications: Bio-Inspired Zwitterionic Surface Treatment for Indwelling Catheters
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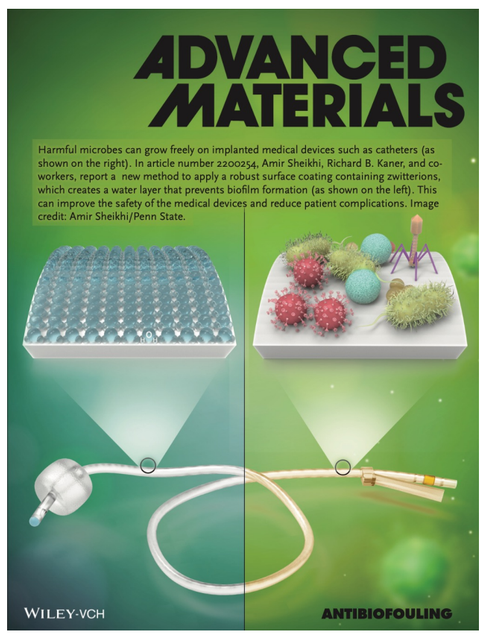
Brian McVerry[1], Ethan Rao[1], Min Kyu Lee[1], Suzy Matinyan[1], Alexandra Polasko[2], Yi-Wei Chen[1], Na He[1], Ivy Kwok[1], Evgeniy Kreydin[3], Glenn Werneburg[4], Howard Goldman[4], Ana Flores-Mireles[5], Hung Ton-That[1], Shaily Mahendra[1], Richard Kaner[1]

[1]University of California, Los Angeles, [2]Stanford University, [3]University of Southern California, [4]Cleveland Clinic, [5]Notre Dame University

Introduction:

Indwelling urinary catheters (IUCs) are one of the most used implantable medical devices. Catheter-associated urinary tract infections (CAUTIs) are the most common of any hospital acquired infection, occurring in over 1 million cases in the United States annually[1]. Latex and silicone-coated latex materials used for conventional IUCs create a perfect nidus for biofilm growth, attract organic material to the catheter surface, and initiate biofilm formation within minutes[2]. Insertion of these tacky materials also cause microtrauma to the urothelial tissue lining the bladder walls and urinary tract, inducing inflammation[3]. As inflammatory factors are secreted in response to catheter placement, pathogenic microbes can use these factors as "scaffolding" to strengthen the biofilm, causing pathogens within biofilms to be approximately 1,000 times more resistant to antibiotics than non-biofilm pathogens[4].

Zwitterion chemistry has long been recognized as one of the most powerful technologies to resist the deposition of organic materials on synthetic surfaces. Zwitterionic polymers bind to water electrostatically to create an extremely thin hydration layer on the surface of materials, enabling resistance to biofilm adherence, inflammation/foreign-body response, and blood coagulation[5-7]. However, due to the complexity and high-cost, utilization of zwitterionic coatings has been previously constrained. Recently, coordinated research among material scientists, chemists, microbiologists, and biomedical engineers has led to the development of a scalable manufacturing process that enables the broad-based use of zwitterionic chemistry on foley catheters[8].



The platform technology used on the zwitterion surface treated catheters was originally published in *Advanced Materials* in 2022[8]

Objectives:

The aim of the study is to investigate the clinical improvement of zwitterion-treated silicone catheters. In addition to in-vitro and in-vivo experiments, two randomized clinical studies are being conducted on long-term catheterized patients measuring biofilm presence and encrustation on explanted catheters, as well as UTIs, patient quality of life, and complications rates in catheterized patients enrolled in the study.

In-Vitro Results:

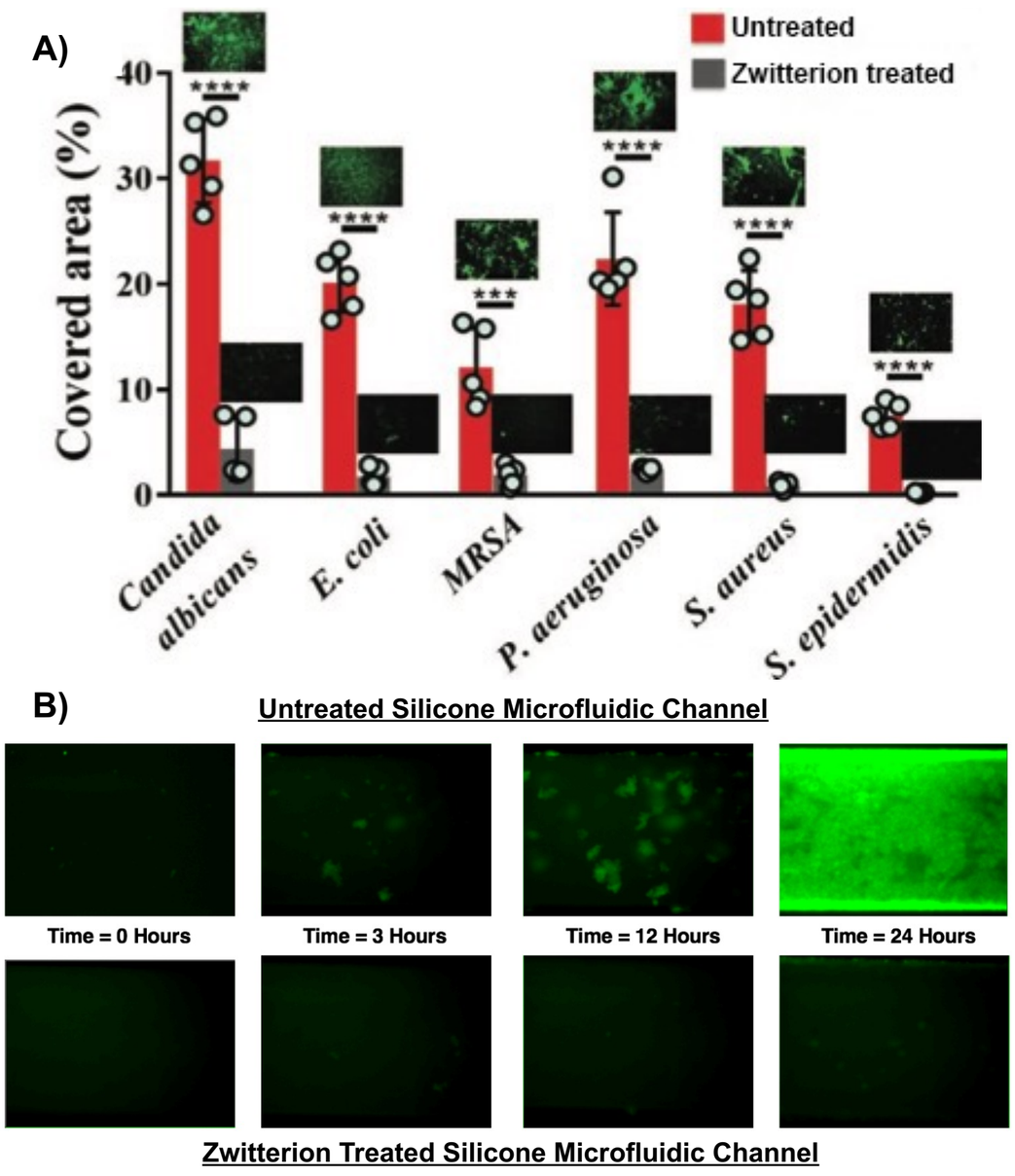


Figure 1: A proof-of-concept assessment of microbial adhesion to zwitterion treated silicone substrates. **A)** Static adhesion of an array of microbes shown to be responsible for hospital acquired infections. **B)** Images of the interior of a silicone microfluidic channel with a fluorescent *E. coli* solution under constant flow conditions

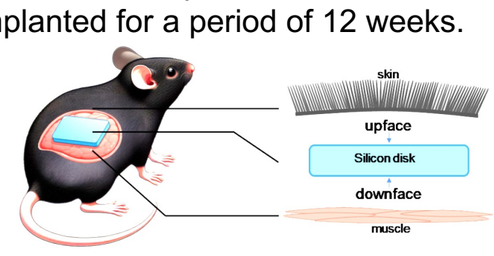
Comparison of Endotoxins Extracted from Commercial Foley Catheters:

Figure 2: In addition to completing all testing requirements listed in ISO 20696 *Sterile Urethral Catheters for Single Use,* zwitterion-treated silicone catheters were tested for pyrogenicity per FDA guidelines along with several other commercially available catheters. The results demonstrate that latex catheters contain substantially increased levels of endotoxins compared to silicone catheters as supported by peer reviewed literature[9]

In Vivo Results:

To demonstrate the in-vivo potential of the zwitterionic surface treatment in mitigating foreign body response, a known contributor to catheter associated urinary tract infections, we utilized a subcutaneous implantation murine model of treated and untreated silicone discs implanted for a period of 12 weeks.

Six silicone implants from each group were evaluated. Following explanation, the surrounding tissue upface and downface of the implants were imaged using a trichrome stain as shown below.



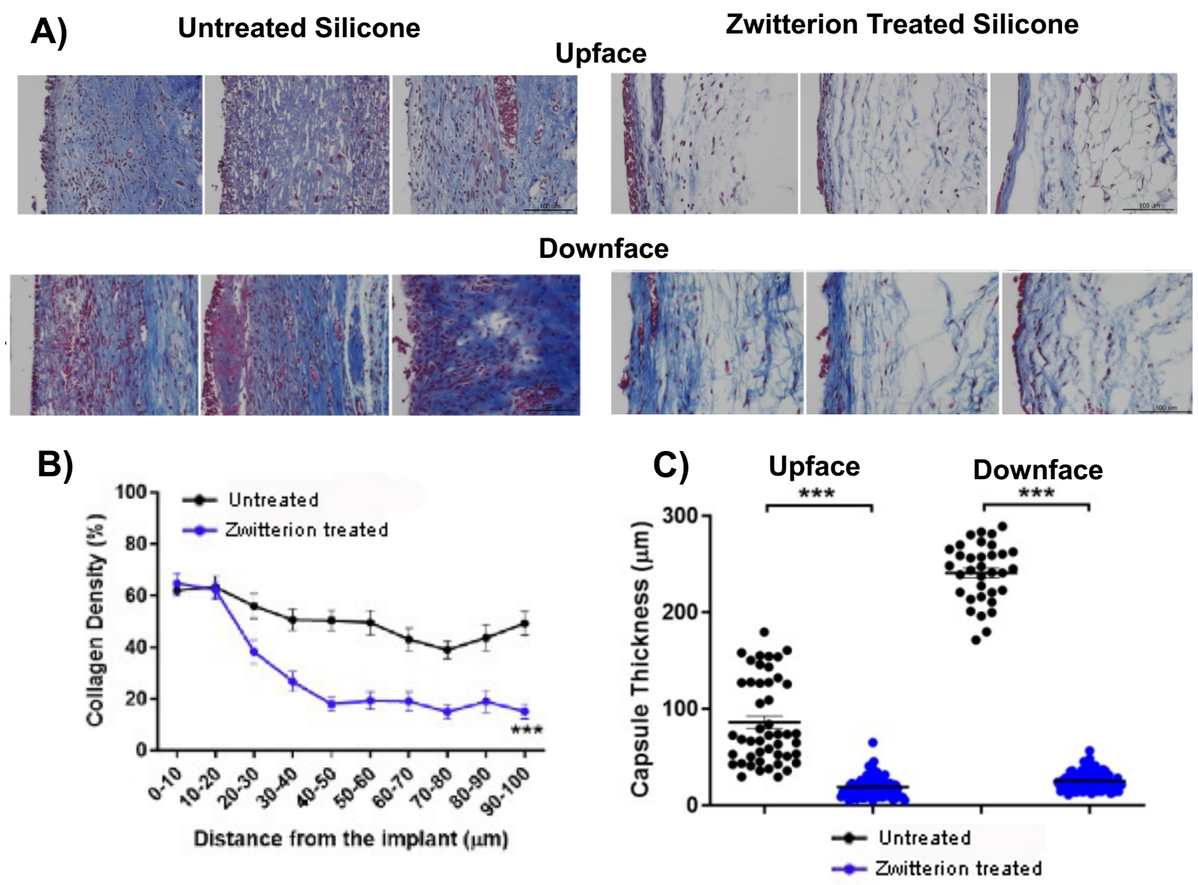


Figure 3: (A) The trichrome stain showing collagen (in blue) of the capsule formation surrounding the implanted silicone disk after 12 weeks post of implantation. **(B)** Analysis of the average collagen density of the capsule around the implantation in each experimental group. **(C)** Analysis of the collagen thickness of the capsule around the implantation.

Clinical Results of Zwitterion Treated Foley Catheters:

NCT04841226:

Catheter Type	Patients	Avg Mass of ATP on Explanted Catheter Surface (ng/in)
Silicone Coated	38	337.29
Silver Coated	40	316.80
Zwitterion Treated	36	137.07

A prospective, randomized, multi-center, post-market study in subjects that require a long-term indwelling Foley catheter. 114 patients were implanted with a study catheter for up to 30 days. Explanted catheters were sent to a 3rd party laboratory and subject to a the BacTiter-Glo Microbial Cell Viability Assay, a well characterized method for quantifying active biomass and biofilm.

NCT05931887 (In Progress):

Catheter Type	Patient Visits	Catheter Infections	Avg Mass of Encrustation (mg)
Standard of Care	130	22 (16.9%)	169.2
Zwitterion Treated	131	7 (5.3%)	53.4

*As of 9/3/24, **24 out of 25 patients (96%)** given study exit questionnaire have selected the zwitterion treated catheter as their preferred type.

A prospective, randomized, multi-center, post-market study designed to compare the incidence of catheter-related complications between the Zwitterion treated catheter and the current standard of care catheter is bring performed. Patients compare their experience with the zwitterion treated catheter against their standard of care catheter, using each type for 3 months in a randomized order. All catheter related complications are tracked throughout the study and explanted catheters are also analyzed for the presence of encrustation on catheter surface.

Conclusion:

Our study presents the potential benefits of using a zwitterion treated silicone catheter. *In-vitro* results of microbial adhesion reduction of a result of a zwitterionic treatment are supported by the observed reduction in cellular activity on the surface of explanted catheters (NCT04841226). Early results of the randomized crossover study (NCT05931887) indicate that the use of the zwitterion-treated catheter can reduce UTI and encrustation by 68.2% and 68.4%, respectively, in comparison of standard of care catheters. We believe that improvement in patient QoL is due to the reduced biofilm, endotoxin content, and the foreign body response properties of zwitterion-treated silicone catheters.

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