

Electrical Stimulation Treatment of *Staphylococcus aureus* Biofilms on Titanium surfaces

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INTRODUCTION: Periprosthetic joint infection (PJI) is one of the most challenging complications of total joint arthroplasty. DAIR (Debridement, antibiotics, and implant retention) is an extensive debridement and removal of necrotic tissue, exchange of modular components, and irrigation of the infected joint [1] to treat PJI. During the DAIR procedure, an antibacterial wash (10% betadine) is used to disrupt the biofilm and treat the underlying infection, however its effectiveness varies widely. Previous research has concluded that cathodic voltage-controlled electrical stimulation (CVCES) is an effective method of treating biofilm infections [2-5]. Garwood Medical Devices has developed BioPrax™, a novel application of CVCES technology intended for clinical treatments. In this study, BioPrax is used to provide a CVCES treatment to determine its effectiveness at different voltages compared to 10% betadine on titanium surfaces without CVCES.

METHODS: Experiments were conducted with clinical orthopedic isolate strains MSSA (UAMS-1). Overnight cultures were prepared by inoculating one colony in 10mL of tryptic soy broth (TSB) and incubated overnight at 37°C. The culture was then used to inoculate sterile 3D printed Titanium (Ti) MAKO implants by covering them with TSB supplemented with 10% human plasma and 1% inoculum culture by volume. The implants were placed in an incubator for 18-24h to incubate. The inoculated implants were then rinsed with sterile PBS (Phosphate buffer saline) to remove loosely adherent bacteria and subjected to the treatment. The wash used in this experiment reflects a wash commonly used in the DAIR procedure: 10% Betadine. Following the growth incubation, all control and wash only samples were immediately harvested for CFU enumeration. Samples receiving a BioPrax treatment were placed in custom agar chamber and treated with BioPrax by utilizing a three-electrode system of a working (MAKO implant), counter (platinum), and reference electrode (Ag/AgCl). All samples that received a wash treatment were submerged in the respective wash for 3 minutes and rinsed in sterile PBS prior to BioPrax treatment or harvesting. The BioPrax treated samples were harvested after the 3h and 6h treatment at -1.5V, -1.8V, and -2.2V. Implants were washed with sterile PBS +0.1% saponin, sonicated, and dilution plated for CFU. A minimum samples size of n=2 was used. A one-way ANOVA followed by Tukey post-hoc compared log transformed CFU across experimental conditions.

RESULTS: Compared to the control group, there were 3 log reductions in washed samples and the samples treated with -1.5V 3h (p<0.001) and 6h and -1.8V for 3h. 3.5 and 4 log reduction was found in the sample treated with -1.8V for 6h (p<0.05) and -2.2V for 3 h (p<0.01), whereas no detectable colonies were found at -2.2V for 6h. A statistically significant difference was found (p<0.001) between the control and the -2.2V treated biofilm for 6h. In addition, -2.2V 6h treated biofilms were more efficient than 10% betadine with p<0.05. When comparing BioPrax treatment at different voltages, -2.2V 6h was more effective with no detectable colonies than any other voltages used. Furthermore, high charge transfer was correlated to no detectable CFU's with charge being 800 C at -2.2V 6h.

DISCUSSION: PJI infections are a detrimental complication of orthopedic procedures that can be extremely costly without an effective method of infection treatment. Through this study, we have shown that the antibacterial wash commonly used in the DAIR procedure is not always effective at creating a significant reduction in CFU. The outcomes of this work show that the application of a BioPrax results in a >99.99% reduction in biofilm CFU, an important milestone towards improving the patient standard of care. Future studies should focus on testing the BioPrax treatment on different bacteria strains and with different antibacterial washes, along with optimizing the BioPrax treatment time.

SIGNIFICANCE/CLINICAL RELEVANCE: Current methods for PJI treatments are often ineffective, and can result in reinfection, implant removal, amputation, or even death. The use of cathodic voltage controlled electrical stimulation has been shown to more effectively reduce biofilm associated infection levels and decrease the biofilm CFU levels much more significantly than antibacterial wash treatment alone.

REFERENCES: 1. Kuiper, J.W., et al. 2014, 2. Ehrensberger, Tobias et al. 2015, 3 Nodzo, Tobias et al. 2015, 4. Nodzo, Tobias et al. 2016, 5.Canty, Hansen et al. 2019

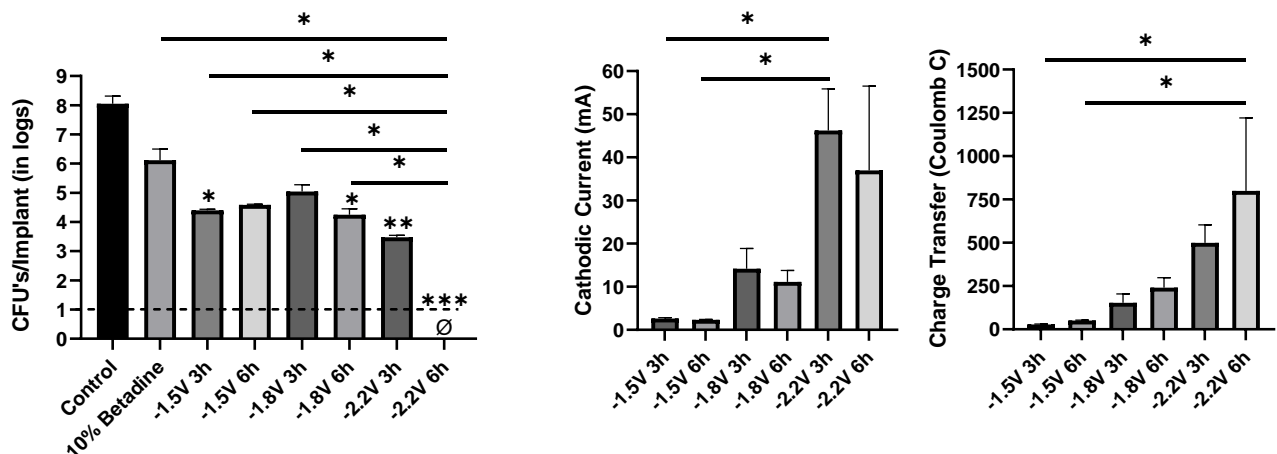


Figure 1: Colony forming units (CFU's) per implant of UAMS-1 biofilms enumerated from Ti implants for control, exposure to 10% betadine, and CVCES treatment at different voltages. ϕ represents zero CFU's. The limit of detection is denoted with a dashed line. Error bars indicate mean \pm SEM. *p<0.05, **p<0.01, ***p<0.001. The significant difference on top of the bars represent comparison with control

Figure 2: Average current (mA) (left) and charge transfer (Coulomb C) (right) measured following CVCES treatment. Error bars indicate mean \pm SEM. *p<0.05