

The Effect of Cathodic Voltage-Controlled Electrical Stimulation on the Bone-Titanium Interface
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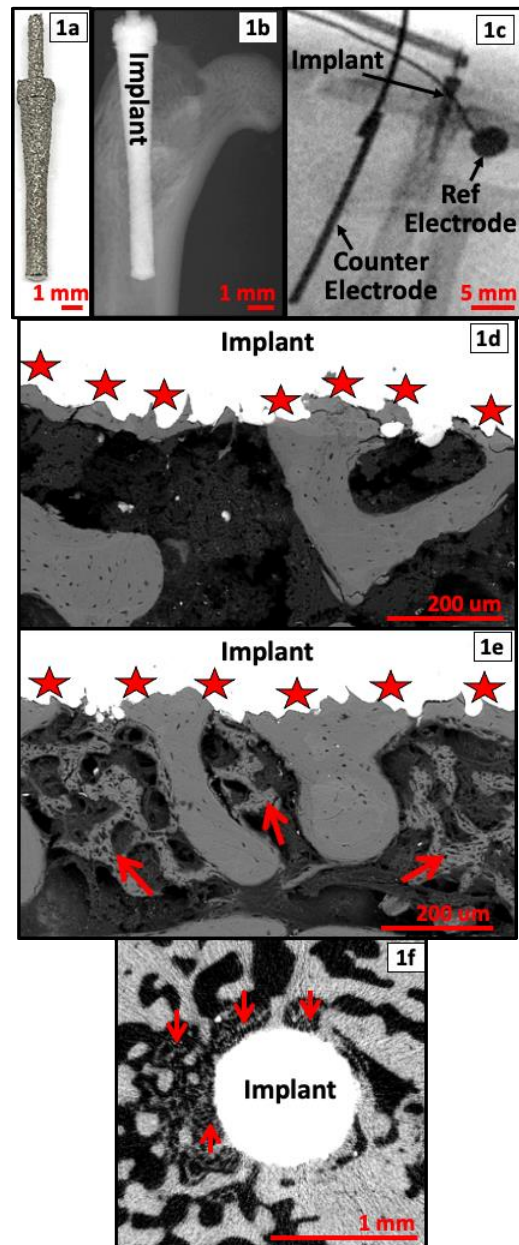
Introduction: Previous studies have shown that cathodic voltage-controlled electrical stimulation (CVCES) of titanium (Ti) implants is an effective and broad-spectrum antimicrobial treatment for implant-associated infections (IAI) [1-2]. The purpose of this study was to evaluate how the application of CVCES to an osseointegrated titanium implant subsequently effects the quality and quantity of bone tissue contacting, or immediately adjacent to, the implant interface.

Methods: Under IACUC approval, custom Ti implants (Fig1a) were press-fit into the medullary canal of Long-Evans rats (Fig1b). The animals were randomly assigned into a treatment group (n=4) or a control group (n=4). On post-op day 42 (POD42) animals in the treatment group received CVCES of -1.8V vs. Ag/AgCl for 1 hour applied to the Ti implant via a three-electrode potentiostatic configuration (Fig1c). A sham procedure (electrodes placed but no CVCES treatment delivered) was performed on POD42 in the control group. All electrodes were disconnected and removed, and the animals were then returned to their cages for 1 week. On POD49 the femur (with implant intact) was harvested and imaged with micro-CT to calculate %bone area immediately adjacent to the implant. Subsequently, a longitudinal section at the mid-sagittal plane of the implant was imaged with a scanning electron microscope (SEM) and analyzed to quantify the %bone-implant contact (%BIC).

Results: The control group had %bone area of $61.9\% \pm 8.2\%$ and the treatment group had an increased %bone area of $65.7\% \pm 6.5\%$. The control group had a %BIC of $42.4\% \pm 0.8\%$ while the treatment group had an increased %BIC of $50.7\% \pm 6.1\%$. These differences in the %bone area and %BIC were not statistically significantly different. SEM images showed that tight integration of bone tissue with the implant was present in the control samples (stars in Fig1d) and in treatment samples (stars in Fig1e). Furthermore, all CVCES samples showed the presence of additional woven bone formation (arrows in Fig1e) in the recessed spaces between the struts of mature bone contacting the implant. This additional woven bone was not present in any control samples. The woven bone was also present in the cross-sections obtained from micro-CT images (arrows in Fig1f) of the CVCES samples.

Conclusions: Osseointegration of the titanium implants is maintained 1 week after application of CVCES of -1.8V vs Ag/AgCl for 1 hour. This pilot study showed the mean values of the %bone area and %BIC were higher for the CVCES treatment group as compared to the control group. These differences were not statistically different. However, analysis of this pilot study data indicated it was underpowered and a sample size of 6 animals would be needed to detect statistical differences in these data sets. Nevertheless, this data indicates that CVCES does not have a deleterious effect on the bone tissue directly in contact with the stimulated implant. Furthermore, the CVCES

appears to promote new, woven bone formation in the recessed spaces adjacent to the stimulated implant. Additional studies are ongoing to increase sample size, and evaluate additional timepoints further out from the CVCES treatment. These findings of enhanced bone growth are encouraging and in combination with the proven antimicrobial effects, indicate that CVCES holds promise for potentially treating infections while promoting new bone growth and enhanced osseointegration.



References:

1. Ehrensberger, M et al. *Biomaterials*. 2015;41:97-105.
2. Nodzo, S et al. *Clin Orthop Rel Res*. 2016;474(7): 1668-75.