Microtextured Surface to Deter Biofilm Related Orthopedic Implant Infections – A Preliminary Study

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Statement of Purpose: Over 1 million total hip and knee replacements are performed yearly in the USA. Although total joint arthroplasties (TJA) will perform well for 15-20 years, infections rates of 5-10% in revision surgeries still occur [1]. It is estimated that the annual cost to treat ~4,000 patients who develop an infection after undergoing TJA is apprimately $200 million [5]. Infections in TJAs can occur soon after surgery or develop many years later. While acute infections may respond to antibiotics, chronic infections require a two-stage revision procedure to address the formation of biofilm on the implant surface. One option to prevent infection associated with these implants is to use materials/surfaces that deter biofilm formation.

Sharklet AF™, a surface patterning technology, has demonstrated anti-biofilm formation on such treated surfaces [2,3]. Additional studies have also shown that eukaryotic cellular adhesion is not deterred by these designs [2,4]. We hypothesized that if an optimized "Sharklet-like" pattern could be etched onto the surfaces of standard metallic materials utilized in orthopedic implants, such surfaces could prevent or limit biofilm formation while promoting osteoblast adsorption and the osseointegration of bone with orthopeadic implants. To test this hypothesis, sharklet-like patterns were fabricated onto silicone wafers/implants, coated them with pure titanium coating, and then assessed if fibroblast and osteoblast adhesion could occur while deterring biofilm formation.

Methods: Surface Topography Fabrication: Solidworks and L-edit CAD software was utilized to create microtextured designs of varying depths and widths similar to that of the Sharklet AF™. Patterns were etched onto a silicon wafer using established photolithography techniques and a 400 nm layer of titanium was evenly deposited over the etched silicon wafer using a multi-cathode sputtering system. The final product was gas sterilized with EtO.

Biofilm Adherence Study Using a modified CDC biofilm reactor (Surface Technologies Corp.), *Staphylococcus aureus* (Xen 36 strain; Caliper Life Sciences) was set up to grow biofilms on the sterilized microtextured wafers for 48 hours. Wafers were then washed in sterile water to remove planktonic cells. The IVIS Lumina II imaging system (Caliper Life Sciences) was used to visualize any hardy biofilm formation. Results were compared to a smooth, unpatterned wafer.

Cell Adherence Study Mouse 3T3 fibroblasts were seeded onto the sterilized microtextured wafer and grown in a desired medium over 2 hours. The cells on the wafers were fixed with formalin and imaged using scanning electron microscopy (SEM). The data was again compared to a smooth, unpatterned wafer.

Results: Initial data has demonstrated that metallic wafers with a patterned "Sharklet-like" design of ~11 µm/less in depth deterred biofilm formation (Fig. 1). Moreover, the fibroblasts were able to spread on these patterned metallic wafers at design depths between ~4 – 7.5 µm, suggesting there was an optimal depth that encouraged fibroblast adhesion (Fig. 2) while deterring biofilm formation. Bioluminescent images (Fig. 3) suggested that colonization of bacteria were limited in the patterned surfaces.

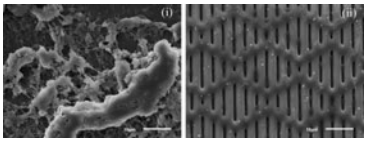

Figure 1: SEM demonstrating (i) exacerbated biofilm growth on the smooth wafer and (ii) absence of biofilm growth on the patterened wafer after an incubation period of 48-hours in the same biofilm reactor environment.

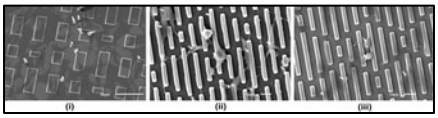

Figure 2: SEM depicting 3T3 mouse fibroblast adhesion and spread on microtextured wafers of varying depths and widths taken two hours after seeding. (i) design parameters of ~ 3 µm depth, 20 µm width; (ii) design of ~6 µm depth, 5 µm width; (iii) design of ~14 µm depth, 5 µm width. Designs (i) and (iii) prevented cells from spreading.

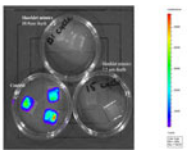

Figure 3: A representative set of IVIS images showing a high photon count of bioluminescent bacteria present in the smooth samples compared to the patterned samples.

Conclusions: The data has suggested there is an optimal topographical geometry that will deter biofilm formation while encouraging cellular attachment. Further *in vitro* studies are needed to optimize the geometrical design. This would help develop novel solutions to biofilm-related orthopaedic infections. Future studies will investigate the laser etching fabrication technique to create patterns on curved titanium surfaces. An early prosthetic infection model will also be created to test the ability of an intramedullary implant with the optimized microtextured surface to deter biofilm formation *in vivo* and, subsequently, prevent implant-related infections from occurring.

References:

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