Self-assembled Surfaces Enable the Evaluation of Tissue Response to Implants with Precisely Controlled Feature Sizes

Adam S. Hacking, Ph.D., 1 Jing Wang, MD/Ph.D., 1 Benjamin Hatton, Ph.D., 2 Jue Wang, MD, 3 Brandon A. Berger, BSc., 1 Joanna Aizenberg, Ph.D., 3

1Massachusetts General Hospital, Boston, MA, USA, 2University of Toronto, Toronto, ON, Canada, 3Harvard University, Boston, MA, USA.

Disclosures: 

Introduction: The ability to control and direct cell and tissue response is beneficial for the function of many implanted devices and tissue engineered scaffolds. For many cell types, surfaces with features at the micro- and nano-scales are an effective tool for directing cell activity and behavior[1-7]. As a result, a fundamental tool for understanding cell-surface interactions is the generation of high fidelity surfaces with micro and nano-scale features.

On planar substrates, top down directed techniques like lithography can reliably generate micron-sized features and direct write e-beam techniques can reliably pattern nano-sized features. These patterning techniques are poorly adaptable to surfaces of implanted devices that possess large surface areas with complex and non-planar geometries. A major barrier to advancing the understanding of the effects of topography on cell behavior and tissue response is the inherent difficulty of generating repeatable topographical features at the nano- and micro-scale on an implant surface[8].

Self-assembly describes a process where complex structures are formed from pre-existing components without external direction. Colloidal co-assembly is a useful method to deposit continuous, highly-ordered nano-porous layers, onto non-planar surfaces[9].

The purpose of this study was to demonstrate the utility of the colloidal self-assembly technique by determining the tissue response to implants covered with surfaces of highly ordered nano-scale pores or random surface features.

Methods: Four groups of grade 5 titanium alloy rods (1.0mm in diameter and 20mm long) were prepared for this study. Two groups had a highly polished surface while the remaining 2 groups had an irregular surface created by acid etching. A nanoporous SiO2 coating, consisting of multiple layers of 300 nm pores was deposited on rods in one of the polished and one of the etched groups[9]. The remaining groups were masked with a layer of SiO2. 24 male Sprague-Dawley rats underwent bilateral femoral implantation. Implants were retrieved after 6 or 9 weeks and processed for undecalcified thin section histology. 8 sections were generated from each of the 48 femurs and the percentage of bone apposition for each implant was determined by backscatter electron microscopy and computer aided image analysis.

Results: In general, apposition differed with surface coating and implantation time. At 6 weeks, bone apposition was greatest to the SiO2 masked and etched surface. Apposition to the nano-porous coating on the polished surface was 41.8 ± 8.7%, to the nano-porous coating on the etched surface was 34.1 ± 13.4%, to the SiO2 masked polished surface was 36.8 ± 11.8% and 47.4 ± 8.7% to the SiO2 masked etched surface. Bone apposition to the etched surface + SiO2 mask was significantly greater than apposition to the etched surface + nano-porous coating (p=0.04).

At 9 weeks, bone apposition to the nano-porous coating on the polished surface was 53.8 ± 15.4%, to the nano-porous coating on the etched surface was 28.6 ± 15.7%, to the SiO2 masked polished surface was 37.0 ± 18.1% and 36.5 ± 12.6% to the SiO2 masked etched surface. Bone apposition to the nano-porous coating on the polished surface was significantly greater than the etched and SiO2 masked surface (p < 0.03).Bone apposition to the nano-porous coating on the polished surface was significantly greater at 9 weeks (53.8 ± 15.4%) than at 6 weeks (41.8 ± 8.7%, p=0.05). Bone apposition to the SiO2 masked etched groups was less at 9 weeks than 6 weeks.

Discussion: In this study the tissue response to femoral implants with a homogeneous and precise pore size was determined. Using a colloidal self-assembly technique, an implant surface consisting of a regular array of highly ordered pores, 300nm in diameter was produced over both non-planar (rods) and irregular (etched) implant surfaces. It is important to recognize that while self-assembly has been used to produce molecular (chemical) coatings on implants, this is the first study that describes the use of a colloidal self-assembly technique to produce a highly ordered topography at the sub-micron scale.

A distinct advantage of the colloidal self-assembly technique is the broad range of pore sizes, from 100-3000nm in diameter, that can be generated by simply changing the diameter of the PMMA spheres used.

The use of novel coating technologies can generate surfaces with distinct morphological and chemical characteristics. In cases where fabrication from the same material is not feasible (or practical) masking techniques can be of great benefit. By masking control implants with a layer (~150nm) of SiO2, the effects of surface chemistry were controlled and the effects of surface morphology on tissue response were investigated[13].
In conclusion, this study demonstrated that colloidal co-assembly offers an entirely new method to coat large non-planar implants with highly ordered surfaces of precisely controlled nano-scale porosity.

**Significance:** This study demonstrated that colloidal co-assembly is a facile method to produce surfaces of controlled topography over large areas and is a new and important tool for studying interactions at the implant tissue interface.

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**References:**

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