

Bioresistant Surface Modification of Implantable Materials

Application

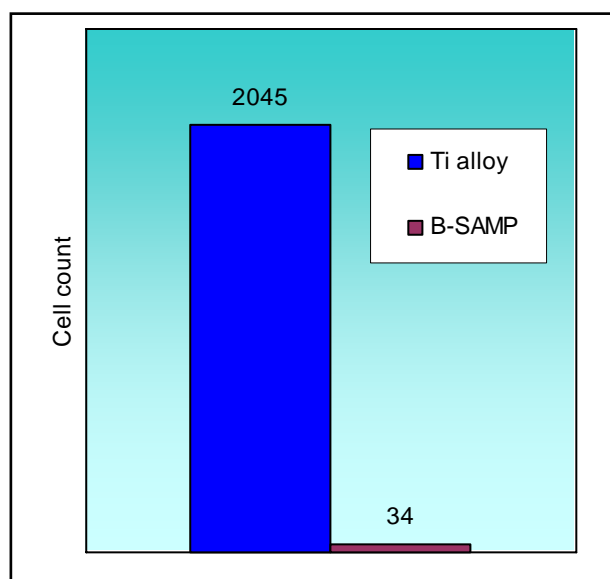
Bioresistant Surface Modification of metal or polymer implantable medical and dental devices to create protein- and cell-resistant surfaces for materials used in medical implants.

Why Bioresistant Medical Devices?

Bioresistant devices are desirable in orthopaedic, dental, cardiovascular and general surgery applications where limiting tissue integration, platelet aggregation, or protein build up is beneficial to patient outcomes.

The Orthobond Bioresistant Self-Assembled Monolayer Phosphonate (B-SAMP) Surface Modification is one molecule thick and is covalently bound to the surfaces of implantable materials. Covalent bonding creates an exceptionally strong attachment between the surface treatment and the material to which it is applied.¹ Because SAMP is one molecule thick, it completely covers the material to which it is applied and assures total implant coverage regardless of the type or texture of the implant material. The B-SAMP surface treatment makes materials resistant to the body's natural physiological response, i.e., tissue attachment and integration (Figures 1 & 2).²

FIGURE 1. FIBROBLAST ADHESION AT 24 HOURS



Orthopaedics: Tissue integration into some permanent orthopaedic implants could lead to impaired function. For example, tissue adhesions in hand implants could lead to reduced range of motion or increased pain. Surgeons also have sought to limit tissue ingrowth into spine and joint arthroplasty prostheses, which has been a leading failure mode following these procedures. The Orthobond bioresistant technology can address these issues by limiting soft-tissue adhesion.

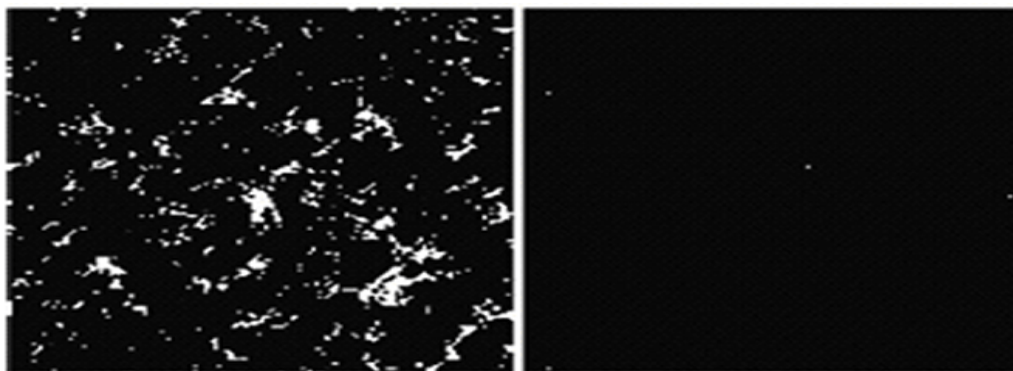
Cardiovascular: Bioresistant materials could create a protein-resistant surface that would limit platelet aggregation or soft tissue integration, thus avoiding early occlusion of stents or grafts. This could help to prevent thrombosis in patients with coronary stents, thus reducing postoperative morbidity.

General Surgery: Bioresistant catheters, shunts, and biliary stents with diminished adhesion of biomolecules provide the benefits of reducing early occlusion and possible device failure. Additionally, B-SAMP-treated materials could afford easier removal of implants.

Clinical Benefits

- **Cell-growth resistance:** Unwanted tissue does not grow on or into the implant and therefore does not interfere with the device's desired function.
- **Easier implant removal:** Because bioresistant implants can be designed not to integrate with the host tissue, temporary implants and devices can be removed with minimal patient morbidity.
- **Protein resistance:** Unwanted proteins do not aggregate on the implant surface; thus, undesirable physiological responses are not triggered, such as aseptic loosening or implant rejection from host tissue.

Figure 2. COMPARISON OF CELL ADHESION TO TREATED AND UNTREATED TITANIUM AT 24 HOURS



Ti Alloy
No Surface Modification

B-SAMP
Bioresistant Surface Treatment

Benefits for Medical Device Innovators

- **Increased material choices:** The B-SAMP surface modification can make virtually any material more bioresistant, creating innovative options that can improve clinical outcomes.^{3,4}
- **Non-biologic option:** The Orthobond B-SAMP surface treatment does not leach from its material host so there is no undesirable secondary result.²
- **Conforming nanoscale coverage:** Due to its nanometer scale, the Orthobond surface treatment does not interfere with desired mechanical surface features that may be critical to the function of an implant; the treatment does not change the texture, look, or cosmetic aspects of the implant surface in any way.
- **Safe:** Pre-clinical studies have shown no adverse effects from the surface treatment.⁵
- **Tailored duration:** The Orthobond bioresistant surface treatments can be tailored to last from a week to several weeks.

Processing

Processing can be integrated into the manufacturing of any implant. The process can be scaled to the size of any operation and can be done on implants of any size or shape. Surface modification can be completed during primary manufacturing or at an off-site location. The treatment may replace the need for metal passivation.

Research & Testing

In Vitro Testing

- The Orthobond SAMP surface modification has been tested for durability on a variety of materials, including stainless steel, titanium, nylons, polyurethanes and PEEK.
- Evaluation of the bioresistant surface treatment against plain Ti alloy: less than 2% of that of plain Ti alloy at 24 hours (Figure 3).

On-Going

- Long-term (more than 8 weeks) evaluation of bioresistant surfaces.
- Stability under gamma sterilization.
- Shelf life of SAMP surface treatment.
- ISO 10993 testing for cytotoxicity, sensitization, irritation, systemic toxicity, pyrogenicity, endotoxin, and hemolysis testing are on-going.

Regulatory Considerations

The Company believes that the addition of the Orthobond B-SAMP to Class II medical devices can be cleared through a 510(k) regulatory path and Class III devices may require a PMA Supplement. Orthobond is prepared to assist in the preparation and filing of the required regulatory submissions.

¹ Schwartz, J., et al., *Mat. Sci. Engr. C.*, **2003**, 23, 395-400.

² Schwartz, J., et al., Manuscript in preparation.

³ Midwood, K. M., et al., *Langmuir*, **2004**, 20, 5501-5505.

⁴ Dennes, J. D., Schwartz, J., *Soft. Matter*, **2008**, 4, 86-89.

⁵ Hejink, A.; et al., *Clin. Orthoped. Rel. Res.*, **2008**, 466, 977-984