

## Osteoconductive Surface Modification to Implantable Materials

### Application

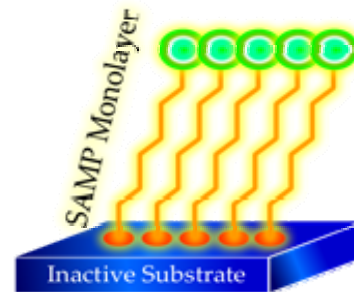
Osteoconductive surface modification of metal or polymer implantable devices to accelerate and strengthen bone incorporation.

### Why Osteoconductive Surface Modifications?

Biocompatible materials have been traditionally selected for dental and orthopedic implants based on their mechanical properties. These materials do not integrate well with the surrounding bony tissue due to the low bioactivity of their surfaces. These surfaces do not encourage comprehensive bone growth (osteoconductivity) onto the implant itself, which is the leading cause of implant failures causing loosening at the device-bone interface.

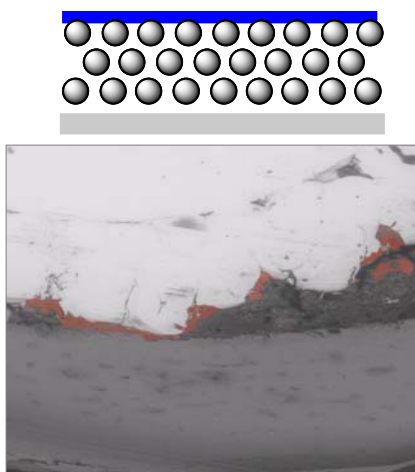
The Orthobond Osteoconductive Self-Assembled Monolayer of Phosphonate (O-SAMP) Surface Modification is one molecule thick and covalently bound to the surfaces of implantable materials (Figure1)<sup>1</sup> Because O-SAMP is one molecule thick, it permeates all of the interstices of the material to which it is applied, assuring total implant coverage regardless of the type or texture of the implant material (Figure 2). The O-SAMP surface treatment makes inorganic implant materials illicit a response similar to that of a biologic but without using a biologic.

FIGURE 1. COVALENT BONDING OF O-SAMP

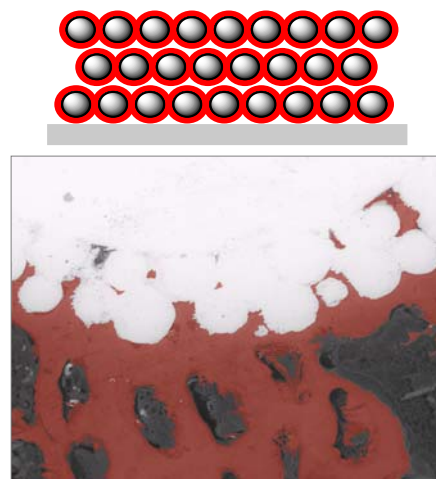


The Orthobond O-SAMP treatment rapidly recruits osteoblasts to the surface of the implant;<sup>2,3</sup> there, the osteoblasts experience enhanced proliferation, differentiate into bone and mineralize the surface. This is the first step in the biologic process of attaining adhesion between implants and the host bone, with the final result being direct integration. This surface modification increases the fixation between the implant and the bone at a rapid rate.

FIGURE 2. POROUS PERMEATION



Hydroxyapatite occludes pores, preventing bone growth into a beaded implant (shown in red).



The Orthobond O-SAMP encourages bone growth into and around beaded surfaces, allowing full tissue penetration.

## Clinical Benefits

- **Rapid fixation of implants within host bone:** Studies show rapid recruitment, enhanced proliferation and mineralization of osteoblasts and the deposition of bone on O-SAMP.<sup>4</sup> This can lead to the improved healing and integration between the host bone and implant(s).<sup>5</sup>
- **Cementless arthroplasty procedures:** The Orthobond osteoconductive technology may eliminate the need for implant cementing by expediting the process of bone-to-implant integration.
- **Options for osteoporotic patients:** Implants processed with the Orthobond osteoconductive treatment may give patients with poor bone quality better outcomes by increasing the quantity and quality of bone growth to an implant.

## Benefits for Medical Device Innovators

- **Increased material choices:** O-SAMP may make any material more osteoconductive, creating options for design innovations that can improve clinical outcomes<sup>4</sup>, e.g., PEEK implants<sup>6</sup>.
- **Permanent and robust non-biologic option:** O-SAMP is covalently bound to the implant surface and highly stable under physiological conditions. It does not leach from its material host.<sup>4</sup>
- **Conforming nanoscale coverage:** Due to its nanometer scale, the Orthobond surface treatment does not interfere with current surface features that may be critical to the design of an implant. Cosmetic features are also unaffected.<sup>1</sup>
- **Safe:** Pre-clinical studies have shown no adverse effects associated with O-SAMP.<sup>5</sup>

## 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 osteoconductive treatment may replace the need for passivation, currently a necessary step in the processing of metal implants.

## Research & Testing

### *In Vitro Testing*

- O-SAMP surface treatment has been tested for durability on metals such as stainless steel, titanium, titanium alloy, and cobalt chrome, and polymers such as nylon, polyurethanes, and PEEK.
- O-SAMP surface treatment has been tested on titanium alloy (Figure 3) and PEEK<sup>6</sup> (Figure 4) for osteoblast attachment, proliferation, and differentiation into bone cells.

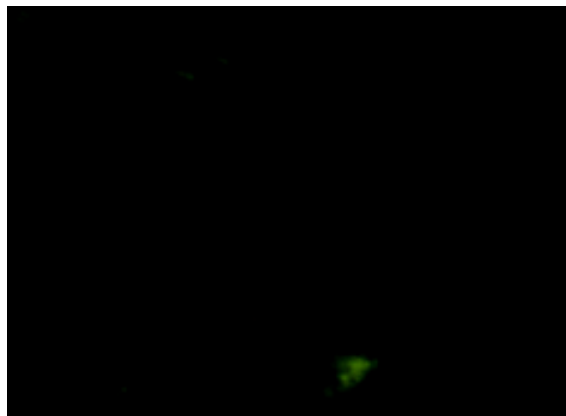
### *In Vivo Testing - Rabbit Study*

A Hospital for Special Surgery rabbit study showed extensive new bone ingrowth on SAMP-treated pins when compared to hydroxyapatite

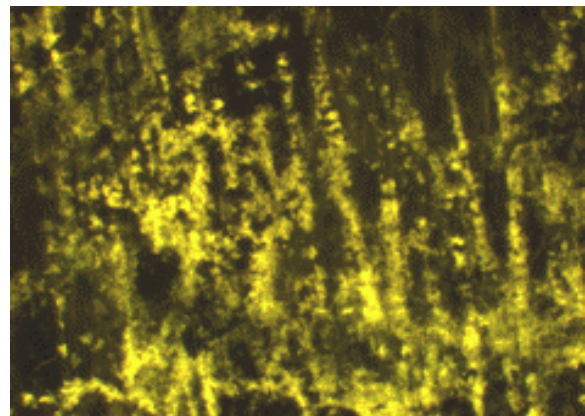
### **On-Going Research & Testing**

- Stability under gamma sterilization.
- Endurance under multiple autoclaving cycles.
- Shelf life of O-SAMP surface modified implants
- Preclinical study to examine benefits in a threaded implant model.

FIGURE 3. OSTEOBLAST MINERALIZATION OF TI ALLOY AT 7 DAYS

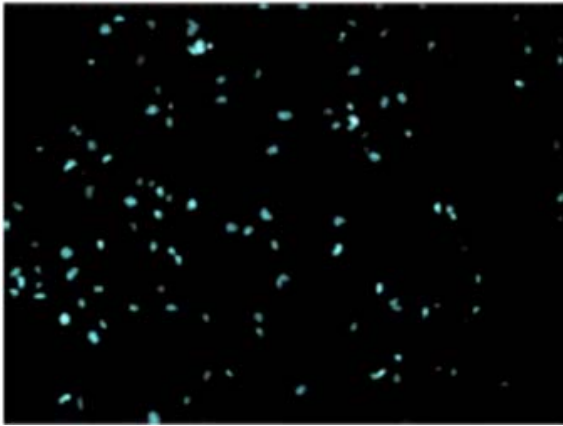


**Non-Treated Ti Alloy**  
Untreated titanium alloy  
shows no signs of mineralization

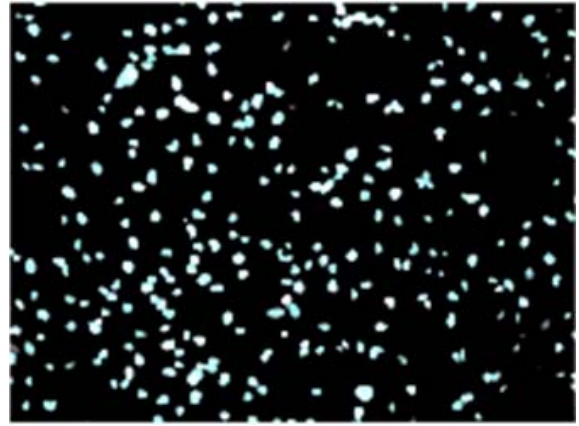


**SAMP Treated Ti Alloy**  
Titanium alloy treated with Orthobond's O-SAMP  
technology shows significant mineralization

FIGURE 4. OSTEOBLAST PROLIFERATION ON PEEK AT 24 HOURS



**Non-Treated PEEK polymer**  
Untreated PEEK shows weak attachment,  
little evidence of cell spreading



**SAMP Treated PEEK Polymer**  
PEEK treated with Orthobond's O-SAMP  
technology shows significant attachment  
and cell spreading

#### ISO 10993 Testing

- Orthobond has not yet conducted ISO 10993 testing. However, 16-week long rabbit studies showed no adverse effects.
- Treated implants must satisfy biocompatibility requirements for permanent tissue or bone contact.
- Cytotoxicity, sensitization, irritation, acute systemic toxicity, rabbit pyrogenicity, endotoxin, and indirect hemolysis testing are on-going.

- The Orthobond O-SAMP treatments are stable under ETO and repetitive autoclaving sterilization.

#### Regulatory Considerations

The Company believes that the addition of the Orthobond O-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 regulatory submissions.

<sup>1</sup> Gawalt, E. S., et al., *Langmuir*, **2001**, *17*, 5736-5738.

<sup>2</sup> Schwartz, J., et al., *Materials Science and Engineering C*, **2003**, *23*, 395-400.

<sup>3</sup> Gawalt, E. S.; et al., *Langmuir*, **2003**, *19*, 200-204.

<sup>4</sup> Midwood, K. S., et al., *Langmuir*, **2004**, *20*, 5501-5505.

<sup>5</sup> Hejink, A., et al., *J. Clin. Orthop. Relat. Res.*, **2008**, *466*, 977-984.

<sup>6</sup> Dennes, J., Schwartz, J., *J. Am. Chem. Soc.*, **2009**, *131:10*, 3456-3457.