Morpheus™
MOLDABLE
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Morpheus™ MOLDABLE

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Morpheus Product Features and Pre-clinical Evaluation

Figure 1. *Morpheus extruded from syringe and molded.*

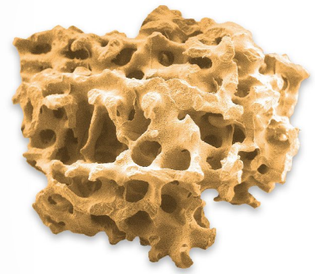

Figure 2. *Magnified image of osteoSPAN granule.*

Biogennix Morpheus was found substantially equivalent to osteoSPAN™ granules for use in the extremities and pelvis (FDA # K132377) and additionally as a bone graft extender in the posterolateral spine (K142828).

Morpheus is a moldable form of the original osteoSPAN granule product. It is composed of 1-2mm osteoSPAN granules suspended in a rapidly resorbable organic binder to facilitate placement and containment of the implant. Once this binder is resorbed in-situ, only the osteoSPAN granules are left behind without affecting their natural osteoconductive or resorbable properties.

The synthetic polymer binder added to the osteoSPAN granules in Morpheus provides improved intraoperative handling characteristics over granules alone and does not interfere with the osteoconductive properties of the osteoSPAN granules. This family of polymers has been used in countless pharmaceutical formulations and medical applications for decades, including bone graft substitutes classified in FDA product code MQV by Allosource (K071849 & K103036), Apatech (Actifuse products K071206 & K080736), Integra (K103742), Isotis Orthobiologics (K040419, K050642, K050690 & K070751), Therics (K053228) and others.

All osteoSPAN products are resorbable osteoconductive scaffolds for use in bone reconstruction. They are a calcium phosphate and calcium carbonate composite with interconnected pores of approximately 500 microns and 65% porosity. All surfaces in the interconnected porosity of osteoSPAN products are completely coated with a thin layer (approximately 4 microns) of calcium phosphate, the primary mineral content of bone.

This composite is biocompatible, osteoconductive, resorbable, and radiographically opaque. Once implanted next to viable bone and stabilized, new bone and soft connective tissue will begin to grow throughout the pores of the device. Within months osteoclasts dissolve the calcium phosphate surface layer to expose the more rapidly resorbable calcium carbonate base material while osteoblasts replace the implant material with new bone. This implant biodegradability is a key attribute of all osteoSPAN products and plays an important role in tissue engineering applications. Through normal physiological remodeling processes osteoSPAN's radio-opacity is systematically decreased as new bone density is increased.

Bone scaffolds that are designed to degrade over time in synchrony with tissue regrowth rates may provide a more effective therapy than materials that do not degrade.[1] Clinical outcomes are much easier to assess using standard x-ray and CT analysis methods when biodegradable materials are used since these types of materials gradually disappear over time and do not mask the progression of natural tissues.

The phase purity, phase composition and crystallinity of osteoSPAN materials have been compared to Actifuse granules using x-ray powder diffraction methods. All osteoSPAN products are more than 95% crystalline and nominally contain 8% calcium phosphate with the remaining balance being calcium carbonate; conversely, Actifuse granules are also more than 95% crystalline but are almost entirely hydroxyapatite (95%), making them much less likely to degrade over time.

Blinded side by side studies using Morpheus and Actifuse ABX were completed in critically sized tibial bone defects and posterolateral spines of skeletally mature rabbits.[2] Figure 3 illustrates resorption and osteoconduction of an osteoSPAN granule in Morpheus at twelve weeks in the posterolateral spine. The false color images are non-decalcified histology, viewed under a scanning electron microscope with backscatter electron emission (SEM-BSE). The thin white, wave shaped line starting in the lower left corner of the 100µm image is the calcium phosphate layer (approximately 4 microns thick) that covers all osteoSPAN surfaces. As can be seen here, a small breach in the calcium phosphate coating near the apex of the wave shape has already allowed bone to rapidly replace a large section of the calcium carbonate base material.

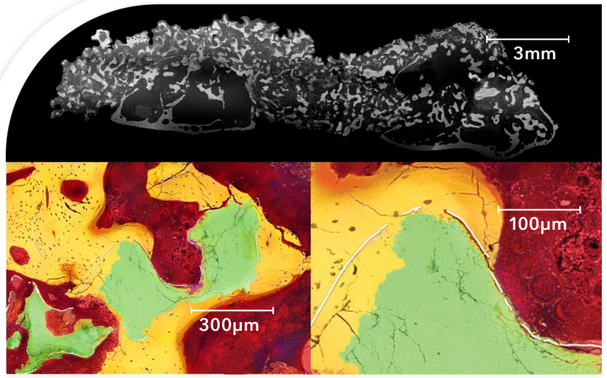

Figure 3. *SEM-BSE image of Morpheus in a spine application.*

- *= Bone*
- *= Calcium Carbonate*
- = Calcium phosphate
- *= Soft Tissue*

Figure 4. *False colored Isometric Micro-CT view of Morpheus in rabbit posterolateral spine.*

Additionally, Morpheus has been qualitatively judged to have excellent handling characteristics during pre-clinical studies and actual clinical usage. Morpheus easily integrates autogenous materials without losing its molding and handling capabilities. Also, the binder in Morpheus leaves less residual material on surgical gloves, making it easier for the surgeon to hold surgical instruments.

Multivariable assessments were conducted in each preclinical study using Morpheus to fully assess study outcomes.[2] Morpheus passed biocompatibility tests for cytotoxicity, endotoxicity, genotoxicity, acute systemic injection, intramuscular implantation, long term implantation and intracutaneous reactivity. Manual palpation scoring of fusion masses in all posterolateral spine studies showed Morpheus performed equivalently to Actifuse ABX and osteoSPAN granules at both six and twelve week study intervals. At twelve weeks Morpheus consistently showed signs of resorption on micro-CT images when compared to Actifuse ABX. Figure 5 contains exemplary images of a transverse micro-CT view of each implant in the posterolateral spine. The ovoid shaped segments on both ends of the fusion mass in each image are adjacent transverse processes that have been connected by a bridge of implant material. The Actifuse ABX implant (bottom) has distinctly more pronounced radio-opacity than Morpheus, providing a clear indication that Morpheus is gradually being remodeled and replaced by natural tissue.

Figure 6 contains coronal micro-CT images of the critical sized tibia defect at six weeks. These images illustrate how the entire transcortical defect and intramedullary canal were packed with implant materials. The image on the top shows new bone has almost entirely replaced the Morpheus implant along the cortical surface; conversely, the lower image demonstrates how difficult it is to see any cortical regeneration in the Actifuse ABX implant at the same time interval.

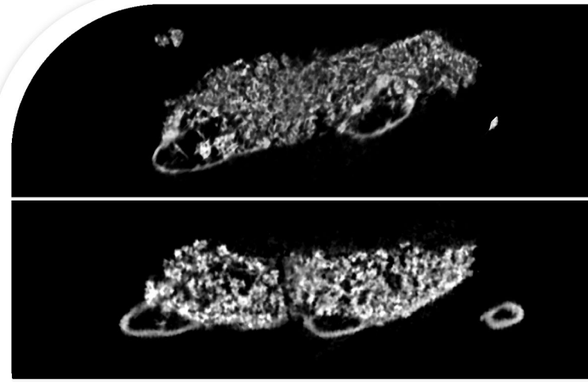

Figure 5. *Micro-CT Images (100 µm resolution) of Morpheus (top) and Actifuse ABX (bottom) at 12 Weeks in Posterolateral Spine.*

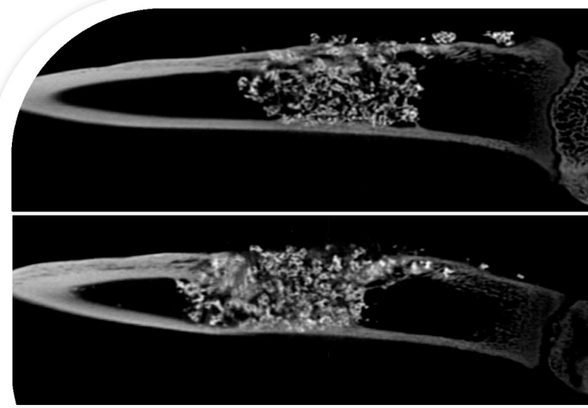

Figure 6. *Micro-CT Images (100 µm resolution) of Morpheus (top) and Actifuse ABX (bottom) at 6 Weeks in a Critically Sized Tibial Defect.*

[1]Ericka M. Bueno and Julie Glowacki. 2011. Biologic Foundations for Skeletal Tissue Engineering (Synthesis Lectures on Tissue Engineering). Morgan & Claypool Publishers. [2] Data on file at Biogennix.