OSSIO*fiber*™ Intelligent Bone Regeneration
Technology Overview

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Executive Summary

OBJECTIVE

This paper will discuss OSSIO*fiber*'s reinforced bio-integrative material composition and structural design, explaining how these two factors contribute to high strength and balanced material integration following orthopedic fixation. Additionally, the differentiated elements of OSSIO*fiber* compared to other fixation materials are discussed.

OSSIO*fiber* MATERIAL COMPOSITION

OSSIO*fiber* orthopedic implants are made from a reinforced bio-integrative material technology comprised of two distinct components, each derived from a regulatory-approved, proven family of biomaterials:

1. **~50% Continuous reinforcing natural mineral fibers**
2. **~50% Poly (L-lactide-co-D,L-lactide) (PLDLA)**

MICRO-ARCHITECTURE

Within each OSSIO*fiber* implant are thousands of continuous natural mineral fibers which are bundled and organized into layers. These are suspended in the polymer resin. These materials are combined into a reinforced matrix structure that supports both biomechanical performance and bone incorporation.

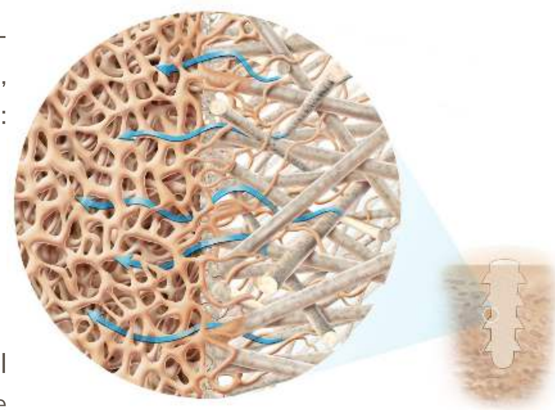


Figure 1: Illustration of OSSIO*fiber* (right) and bone (left) hybrid integration mechanism

HYBRID INTEGRATION MECHANISM

OSSIO*fiber* leverages the individual degradation mechanism of both material components and internal micro-architecture to achieve a hybrid integration mechanism (**Figure 1**). Incorporation to native anatomy is achieved through:

1. **OSSIO*fiber*'s high mineral content, supporting high mechanical strength and gradual bone integration.**
2. **A balanced pH environment, promoting a healthy environment for bone healing.**
3. **Channels of interconnected pores that gradually and progressively allow for fluid flow and clearance of degradation by-products from the local area of the implant.**

The combination results in a bio-integrative profile in which the implant is safely and predictably incorporated into the local bone environment.

Introduction: **Developing the Ideal Bone Fixation Material**

Developing an orthopedic material platform that enables complete restoration to native anatomy following fixation has the potential to greatly impact patient care and broader stakeholders of the healthcare system. There have been many attempts to achieve this goal through different material types including bio-resorbables, bio-composites, PEEK and allograft. However, these materials have well-documented limitations which limit their utilization and in-vivo performance. Metal fixation, therefore, continues to be the standard fixation material in orthopedics, despite its many shortcomings including unwanted removal surgeries, associated complications, and an unnatural healing environment for patients.[1-3]

The scientific community has developed a framework which characterizes the ideal bone fixation implant material. This is described in **Table 1**. The characteristics of an implants performance are impacted both by material choice and by internal architecture.

Designing a device that can achieve all of the stated elements requires a fundamental change in material choice and implant architecture, without compromising on proven surgical technique. Until now, the industry has fallen short on developing a non-permanent fixation material that is both strong and supports natural bone regeneration.

Through the material composition and internal architecture, OSSIO*fiber*™ is designed to provide both the mechanical strength required for insertion and secure fixation while having the ability to integrate into native bone without adverse inflammation. In doing so, OSSIO*fiber* Intelligent Bone Regeneration Technology creates a new category of fixation, called "bio-integratives".

Table 1: Characteristics of the Ideal Bone Fixation Implant

1. **Degradation of the material should be controlled and at the pace of the healing bone.**[4]
2. **The material should maintain "sufficient strength" during biological bone union.**[2 5]
3. **There should be no prolonged adverse inflammatory responses while the material is in the body.**[5]
4. **After full resorption of the material, the body should fully restore its native physiology as if there never was an implant.**[5]
5. **The material should be able to be manufactured into a wide variety of implant geometries.**[5]

Bio-Integrative Material Composition

OSSIO*fiber*™ orthopedic implants are made from a reinforced bio-integrative material technology comprised of two distinct components, each derived from a regulatory-approved, clinically proven family of biomaterials:

1. **Continuous reinforcing natural mineral fibers**
2. **Poly (L-lactide-co- D,L-lactide) (PLDLA)**

The percent volume by weight is ~50% continuous reinforcing mineral fibers and ~50% PLDLA (**Figure 3**). The continuous fibers provide the superior mechanical properties of the implant while the polymer resin binds the fibers together into a cohesive unit.

The combination provides high strength and promotes a favorable environment for bone in-growth and replacement following implantation.

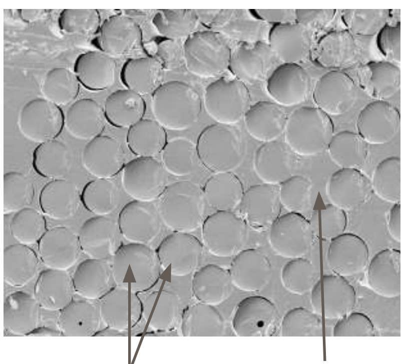


Figure 3: Scanning Electron Microscope (SEM) cross-section of OSSIO*fiber*, highlighting both material components.[a]

CONTINUOUS MINERAL FIBER COMPOSITION

The natural mineral fibers are comprised of a blend of elements found in native bone, that includes but not limited to calcium, silica, magnesium.[6-8] The reinforcing mineral fibers are composed of SiO_2, Na_2O, CaO, MgO, B_2O_3, and P_2O_5. OSSIO*fiber* is the first to combine a reinforced matrix architecture with the highest mineral content of any commercially available non-permanent implant material (**Figure 4**).

The mineral combination of OSSIO*fiber* is a key part of previously FDA-cleared osteoconductive bone graft products. In bone filler compositions, the minerals have been shown both in vitro and in vivo to be osteoconductive (promoting bone growth and regeneration).[9] In OSSIO*fiber*, this mineral blend is designed into continuous mineral fibers, enhancing mechanical performance, structural integrity, and bone in-growth.

This mineral content level within OSSIO*fiber* (~50%) is significantly greater than that of biocomposite implant products, which generally contain between 10-30% mineral content in the form of HA, ß-TCP, and CaS granules.[10][11] The higher mineral content contributes to a dramatic biomechanical advantage, while supporting the natural bone healing process, which is discussed in detail in the subsequent sections.

POLYMER MATERIAL COMPOSITION

The polymer ("biopolymer") resin component of OSSIO*fiber* is comprised of poly(L-lactide-co-D,L-lactide), (PLDLA), 70:30 L:DL ratio. This resin acts as binder for the fiber matrix comprised of the continuous natural mineral fibers.

Unlike previous biocomposites and bioresorbables, which rely solely on the polymer content for mechanical performance, OSSIO*fiber* leverages the biomechanical advantage of the natural mineral fiber matrix.

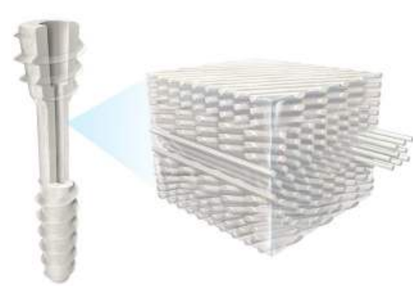


Figure 4: Illustration of matrix design. The matrix structure enhances mechanical performance and bone in-growth following implantation.

Structural Architecture

Traditional materials that have been used in orthopedic implants such as metals (Steel, Titanium, etc) and polymers (PGA, PLA, etc), are uniform in all mechanical axes (tensile, compression, shear, bending, torque). The mechanical properties of the implant depend solely on the composition of the material used (material properties) and on the geometry of the implant.

OSSIO's reinforced bio-integrative technology is unique in that the internal structure of each implant can be adapted to create the optimal biomechanical profile for the needs of the indication. This is achieved through designing implants that are comprised of thousands of continuous natural mineral fibers. The fibers are aligned into fiber bundles which are then built into an organized layer structure. Each fiber layer is oriented to provide mechanical properties (ie flexural or bending) in a different mechanical axis. These layers are combined into a matrix structure that can be uniquely tailored to ensure biomechanical properties unique to a specific clinical indication.

Within a single implant, there are tens or even hundreds of distinct oriented fiber layers that provide the mechanical properties for that implant. The biopolymer resin binds the fibers and layers together such that the mechanical contribution of each of the fibers and all the layers come together to create a biomechanically optimized implant (**Figure 5**).

> "...the internal structure of each implant can be adapted to create the optimal biomechanical profile..."

The SEM image on the right depicts:

I) **The individual continuous reinforcing fibers.** Thousands, or even millions, of these reinforcing fibers are combined to produce each implant.

II) **The distinct oriented fiber layers.** The orientation of each layer, thickness, and location within the implant determine the mechanical effect that the layer will contribute to the implant.

Figure 5: Oriented fiber layers as seen in a SEM image of an implant cross-section[a]

Restore. Regrow. Renew.

Hybrid Integration Mechanism

INDIVIDUAL MATERIAL INCORPORATION PROFILE

Continuous natural mineral fibers are integrated and replaced by bone. This process of bio-integration resembles the integration of synthetic bone filler products into the bone as the bone heals. The space that was filled with bone filler becomes renewed with healthy bone.

The polymer content of OSSIO*fiber* degrades by hydrolysis into alphahydroxy acids that are metabolized by the body. The low overall polymer content of OSSIO*fiber* ensures that the polymer degradation profile of the reinforced biocomposite is progressive and gradual. Thus, the biopolymer degradation products can be progressively cleared by body, avoiding the accumulation of polymer content and subsequent foreign body reactions during degradation of previous bioresorbables.[4]

BALANCED, FAVORABLE BONE REGENERATION ENVIRONMENT

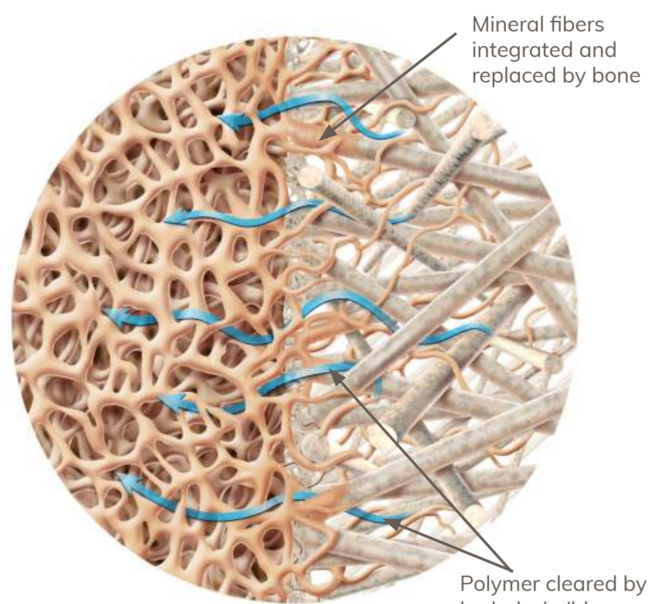
The combination and internal design of the polymer and continuous mineral fibers promote a favorable environment for bone in-growth and replacement. Within the OSSIO*fiber* implants, two biointegrative mechanisms are occurring concurrently: polymer resorption and mineral fiber replacement by bone. This hybrid material degradation mechanism ensures that the resorption of OSSIO*fiber* implants is pH balanced. The alphahydroxy acidic degradation products of the biopolymer are balanced by the alkaline degradation products of the mineral fibers.

The hybrid integration profile has great benefit in that it is balanced, progressive, and gradual. As the implant degrades, interconnected pores are formed through the implant that allow for fluid flow through the implant and facilitate physiological regeneration of bone tissue in place of the implant (**Figure 6**).

> "The hybrid integration profile has great benefit in that it is balanced, progressive, and gradual."

For OSSIO*fiber* implants, the first elements to dissolve out of the continuous mineral fibers in an aqueous solution are sodium, calcium, phosphate and magnesium ions. These alkalis will form basic hydroxides in the interphase resulting in a high local pH. The reaction is water diffusion controlled, which results in surface erosion of the natural mineral fibers once water has penetrated the sizing. The base formed will contact the surrounding matrix and may also diffuse through micro-fissures deeper into the matrix. It is known that the poly(a-hydroxyester) backbone is vulnerable to attack by strong bases, and that chain scission will occur faster in a high pH environment than via acidic autocatalytic reaction caused by polymer degradation products. This catalyzed polymer degradation erodes the interphase, which further increases the degradation rate and thus produces interconnected pores.

Figure 6 illustrates both mechanisms occuring concurrently.



Hybrid Integration Mechanism Continued

In previous bioabsorbable and biocomposite implants, the degradation profile was dominated solely by biopolymer bioresorption. Thus, there was no pH balance to mitigate the acidic degradation products of the polymer. There were no interconnected pores formed through the implant to allow for gradual and progressive clearance of degradation products. The large biopolymer chains would simply become weaker and weaker in place until, eventually, in some cases, a burst release of acidic degradation products would occur. Due to the large size of the polymer chains, this burst release could occur even after several years and result in a severe local inflammatory reaction at the implant site years after the implant was introduced.[12 13]

The controlled degradation profile of OSSIO*fiber* is timed with healing rate of the operated bone fracture or osteotomy. As the bone heals, there is progressive load sharing, which further supports the natural healing process.[1 14] As seen in pre-clinical studies, complete integration of OSSIO*fiber* takes place within approximately 18-24 months thus eliminating the need for implant removal surgery.

Conclusion

OSSIO*fiber* Intelligent Bone Regeneration Technology is a material platform that can be engineered to a variety of fixation devices, with clinical applications throughout orthopedics such as extremities, trauma, and spine. Combining two previously regulatory-approved, clinically proven materials, OSSIO*fiber* is uniquely engineered to achieve high strength and gradual, progressive integration with the surrounding anatomy. In doing so, OSSIO*fiber* creates a new category in fixation materials named "bio-integratives."

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