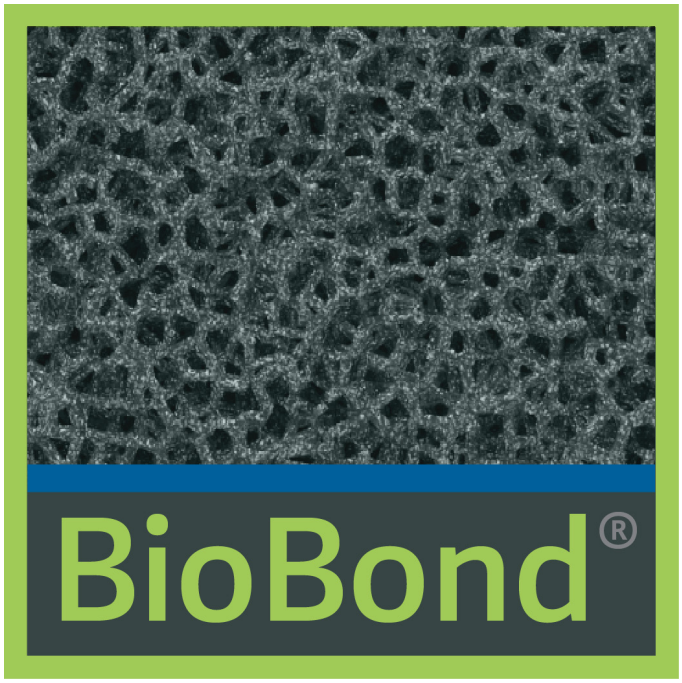
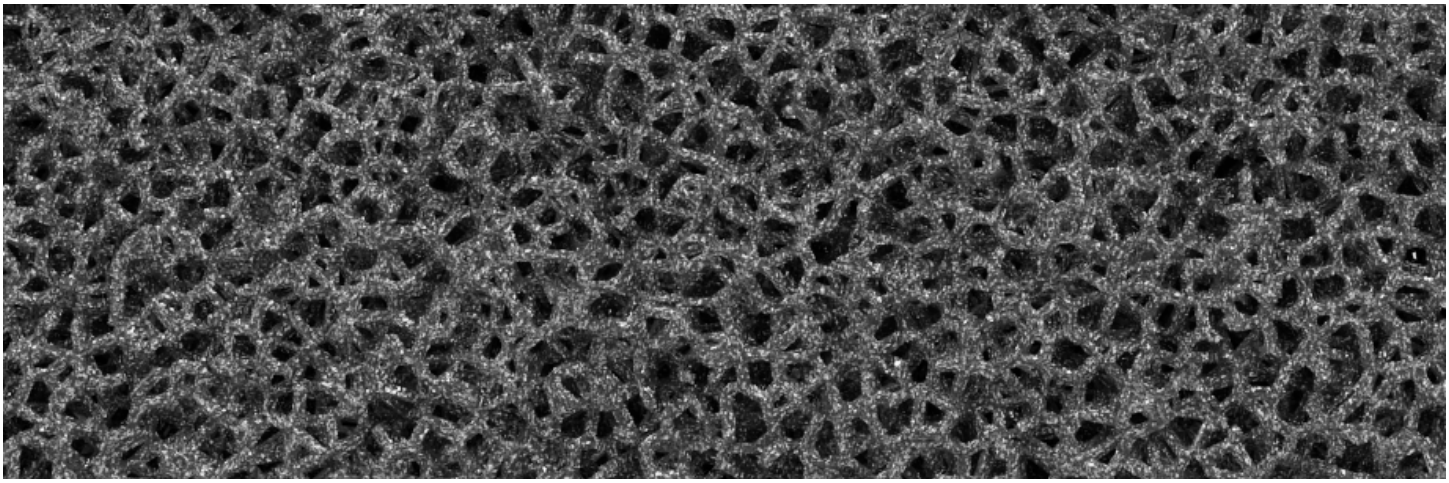
BIOBOND®

Proprietary Porous Trabecular Structure



ChoiceSpine™

Whitepaper



BioBond®: Advancing 3D-Printed Titanium Spinal Fusion Implants with Osteopromotive Porous Structures

Abstract

The growth in the incidence of degenerative spinal disorders, which often require spinal fusion as the preferred surgical intervention, brings a demand for advanced implant technologies. The evolution of implant design reflects a growing understanding of the spine's mechanical, biological, and physiological needs. Historical challenges in spinal fusion, such as implant migration, stress shielding, and modulus mismatch, have been addressed through innovative material and design solutions. Additively manufactured (AM) titanium alloy (Ti6Al4V) implants represent a significant advancement, which feature hierarchal porous structures and rough surface topography at the micro and nanoscale that more closely mimic the native bone structure and improve osseointegration. Our recent cell study evaluated the osteoblastic differentiation of mesenchymal stem cells on BioBond® porous trabecular structure, demonstrating its ability to promote bone growth while minimizing inflammatory and fibrogenic responses. The analysis confirmed active cell proliferation and differentiation, with favorable protein expression profiles supporting the technology's osteoconductive and osteopromotive properties. The 3D printed surface, with its intentional roughness and anatomical porosity, echoes cancellous bone, promoting effective bone-implant integration and healing. These findings affirm the effectiveness of BioBond® technology in spinal fusion devices, offering significant benefits over previous materials and structural designs. This next-generation surface technology is employed across the product portfolio to provide surgeons and patients with advanced, reliable, and effective spinal implants to best suit the anatomic location and surgical approach.

Introduction

As the population ages, the number of individuals in the United States over 65 is projected to rise from 54.8 million in 2020 to 88.5 million by 2050(1). With this increase, the prevalence of degenerative spinal disorders is expected to grow significantly. This trend will drive higher demand for spinal fusion surgeries, a critical intervention for conditions such as degenerative disc disease, spinal trauma, and instability due to infection or malignancy. Correspondingly, the U.S. market for spinal interbody fusion devices is forecasted to grow by 5.8% annually to a 2030 level of $6.1B(2)(3), underscoring the need for advanced and effective surgical solutions.

Spinal fusion procedures typically involve the removal of diseased intervertebral discs, decompression of affected nerves, and stabilization using implants like interbody cages and screw/rod systems. The goal is to achieve a solid fusion of the adjacent vertebral bodies, thereby reducing pain and improving patient outcomes. Historically, the evolution of spinal fusion technology has focused on materials and design innovations to enhance the success rates and durability of these procedures.

The development of interbody fusion devices began in the late 20th century with the shift from autografts and allografts(4) to the introduction of metallic implants(5)(6). However, limitations of early designs were prevalent, such as radiopacity and image artifact, along with subsidence and stress shielding due to the mismatch between the modulus of elasticity or stiffness of stainless steel or titanium and bone. These limitations prompted the innovation shift towards polyetheretherketone (PEEK) cages in the early 2000s, dominating the market for the next 10-15 years. Despite their initial success, PEEK devices exhibit drawbacks related to their hydrophobic nature and poor bone integration. The surface-level interaction with the bony endplate had frequent issues with biofilm, fibrous encapsulation, and overall lack of integration. This could cause micromotion and was often a potential pain generator and impetus for pseudoarthrosis. Hydroxyapatite (HA) infused PEEK material and plasma-sprayed titanium coatings(7) were the primary attempts to address this critical limitation, though delamination became a recurring issue.

Recent advancements in additive manufacturing, commonly called 3D printing, have revitalized the development of titanium-based implants(8). These technologies allow for the creation of implant designs with features and geometries to address historical limitations that were previously impossible to fabricate. Radiolucent metal meshes facilitate improved radiographic imaging. Intricate, natural geometries enhance anatomical contouring, and low-density structures precisely match the construct elastic modulus to native bone. Unfortunately, many competitive devices still utilize outdated design strategies, fail to leverage the innovative potential of additive manufacturing, and lack an understanding of micro and submicron-level interactions regarding bone healing. Enhancing the bony ongrowth and ingrowth with intentional surface characteristics at the micro and submicron levels is crucial for promoting osseointegration and reducing micromotion(9)(10)(11).

A better understanding of the cellular-level interactions with these surfaces has shifted the development focus toward optimizing surface topography and porosity to enhance the osteogenic environment(12). The success of spinal fusion implants hinges on their ability to support the bone healing cascade and elicit a favorable osteoimmunogenic response(13). This involves a complex interplay of cellular activities, including mesenchymal stem cell (MSC) adhesion, proliferation, and differentiation into osteoblasts, essential for bone formation. The BioBond® cell study explores this innovation in surface technology, emphasizing the role of surface architecture and porosity in achieving better clinical outcomes in spinal fusion surgeries.

BioBond® Cell Study

The BioBond® surface technology cell study evaluated the osteoblastic differentiation of human mesenchymal stem cells (hMSC) on the ChoiceSpine 3D printed titanium alloy (Ti6Al4V) porous trabecular structure(14). The study aimed to characterize the ability of these surfaces to promote bone growth while minimizing inflammatory and fibrogenic responses across a controlled range of pore dimensions and porosity. Critical indicators of implant success, including cell adhesion, proliferation, and differentiation, were monitored via protein expression.

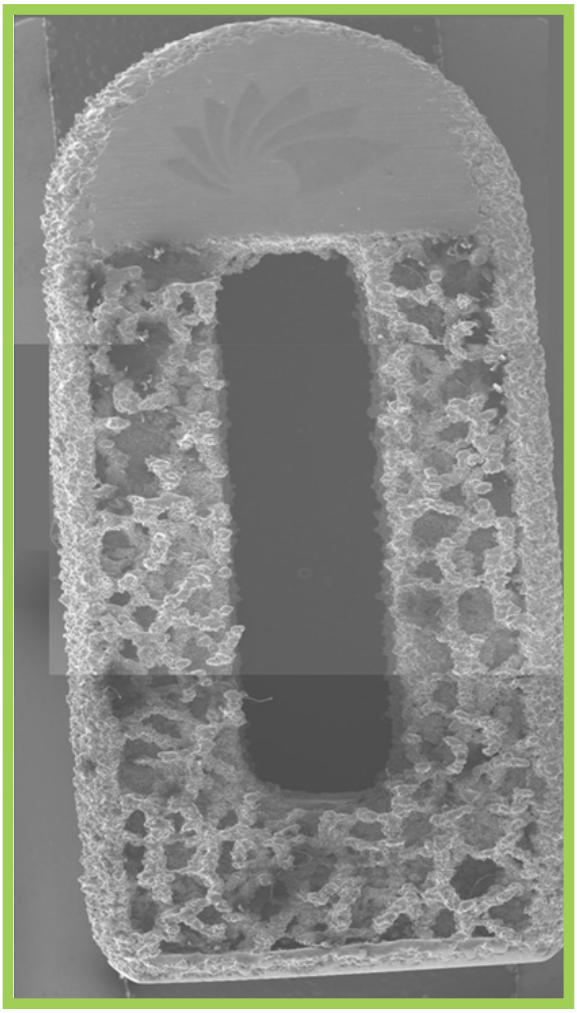


Figure 1: SEM composite image of ChoiceSpine device demonstrating BioBond® porous osseointegration surface technology integrally connected in a macro, micro, and submicron level hierarchal structure.

The study utilized representative sample discs of the BioBond surface technology from ChoiceSpine implants. The additive manufacturing method allows for integrally connected, yet distinct and intentional, regions at a macro scale that serve either a structural loading, radiolucent mesh, or porous osseointegration function. Due to the powder bed fusion fabrication method of these macro geometries, each region features structures and geometry with surface roughness and topography at the micro and sub-micron levels. The resultant surface comprises peaks, valleys, and pits at the appropriate dimensional scale for direct cellular interaction.

The BioBond® samples were cleaned, sterilized, and seeded with Passage 5 hMSC. Cellular growth was allowed until the targeted 7-, 14-, and 28-day time points. The samples were fixed and evaluated using Scanning Electron Microscopy (SEM), Live/Dead Immunofluorescence Imaging, and DNA & Protein Quantification via enzyme-linked immunosorbent assay (ELISA) analysis.

SEM imaging provided detailed insights into the cell attachment and interaction with the semi-ordered porous surface topography over various time points. The surfaces displayed varying characteristic profiles of depths, peaks, and valleys, all contributing to excellent cell adhesion and proliferation throughout the study. At the early stages (1-2 weeks), SEM images revealed hMSCs actively engaging with the surface through the formation of lamellipodia and filopodia, key indicators of robust cell adhesion. These dynamic cytoplasmic extensions, or cellular body protrusions, suggest the early stages of hMSC commitment to the osteoblastic lineage, marked by cellular migration and engagement with the surface architecture. By Week 4, SEM images showed substantial cell proliferation and interconnected networks of cells. The maturing actin filaments indicated healthy osteoblastic activity, demonstrating strong potential for bony ongrowth and apposition in vivo. Cells displayed prominent protrusions as they migrated deeper into the porous structures, utilizing the surface topography in three dimensions as seen in Figure 2. This proliferation pattern suggests that the porous structures supported surface-level cell adhesion and

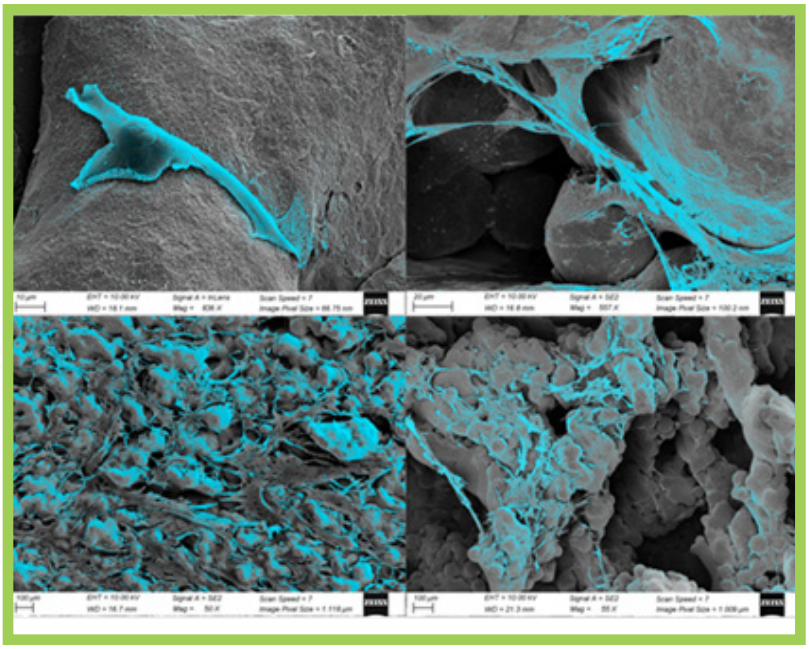


Figure 2: hMSC proliferation and migration through porous hierarchal structure A) 1-week time point and B-D) 4-week timepoints

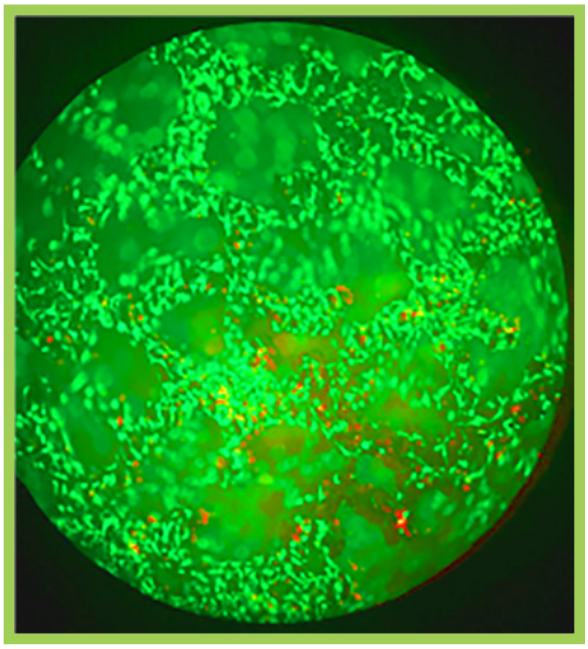


Figure 3: Live (Green)/dead (Red) immunofluorescent stain showing hMSC growth and proliferation on osteoconductive porous trabecular structure.

thorough cell penetration and interaction, mimicking the natural bone architecture and providing evidence of the osteointegration that would likely occur in vivo.

The porous samples, which range around healthy trabecular bone porosity of 70%, promoted cell proliferation and osteoblastic activity. The cells migrated into the open architecture of the surface, forming interconnections that likely result in strong interaction with bone graft materials or host bone in vivo. The pore size and depth facilitated the dynamic extension of cellular projections, confirming that the topography supported three-dimensional cell growth and osteogenic differentiation.

The hMSCs remained viable across all samples tested, with consistent cell viability rates between 70-90% at each time point. Steady proliferation rates were observed throughout the study, indicating that the surface topographies effectively promoted osteoconductivity as seen in Figure 3. The uniformity in viability and consistent distribution of cells across the various porous samples demonstrate that the rough AM titanium alloy material surface characteristics provide a conducive environment for hMSC attachment, activity, and healthy proliferation.

The expression of osteocalcin (OCN) is an early marker of osteogenic differentiation(15). OCN levels had a peak occurring at the 2-week time point across all samples. This peak in OCN expression confirms the initiation of osteoblastic differentiation within the hMSCs and aligns with the SEM findings of active cell adhesion and cytoplasmic extension during this period.

Proinflammatory cytokines IL1β, IL6, and IL8, alongside the anti-inflammatory IL10, were measured across the time points and found no conclusive dependence on the substrate porosity. The expression profiles across the various porous surfaces were consistent with prior studies, supporting a balanced inflammatory response conducive to bone formation and demonstrating a positive association with the Ti6Al4V base material(16)(17)(18).

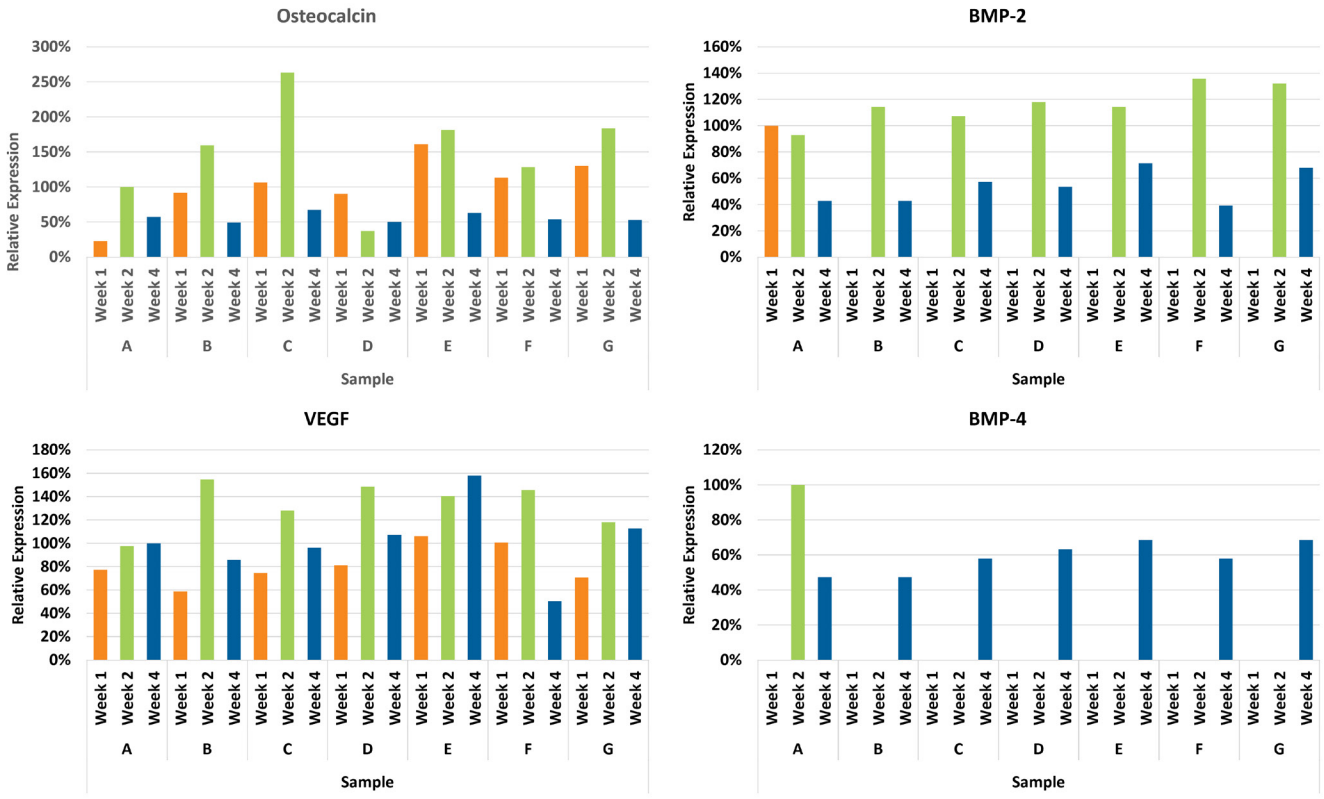


Figure 4: Osteocalcin (OCN), Vascular Endothelial Growth Factor (VEGF), Bone Morphogenic Protein (BMP) response as a function of porosity and timepoint.

Bone morphogenetic protein (BMP) signaling was closely monitored, as it plays a critical role in MSC differentiation towards osteoblastic cells(19). A significant spike in BMP-2 expression was observed at the 2-week interval, confirming the osteopromotive characteristics of the surfaces. BMP-2 expression was consistently and notably higher across the different porosity samples compared to the non-porous surfaces. This spike in BMP-2 was followed by increased BMP-4 expression at Week 4, further supporting the differentiation of hMSCs towards an osteoblastic lineage and promoting bone formation. The porosity did not significantly influence BMP-4 expression, but its steady presence supports the osteogenic potential of the surfaces.

Vascular endothelial growth factor (VEGF) is essential for vascular development and bone formation and was observed at all time points. Its expression indicated ongoing osteogenesis rather than chondrogenesis, with levels of VEGF correlating with the degree of porosity. The presence of VEGF supports the hypothesis that the porous surfaces encourage osteogenesis and vascularization, both critical factors in successful bone regeneration(20).

In summary, the SEM imaging, cell viability, and protein expression data collectively indicate that the BioBond® semi-ordered porous trabecular surface effectively promotes hMSC adhesion, proliferation, and osteoblastic differentiation. The increased BMP-2 and BMP-4 expression, alongside the early OCN peak and sustained VEGF levels, highlight the osteoconductive and osteopromotive nature of these surfaces and guide the pore size and porosity design to enhance a favorable environment for bone fusion applications.

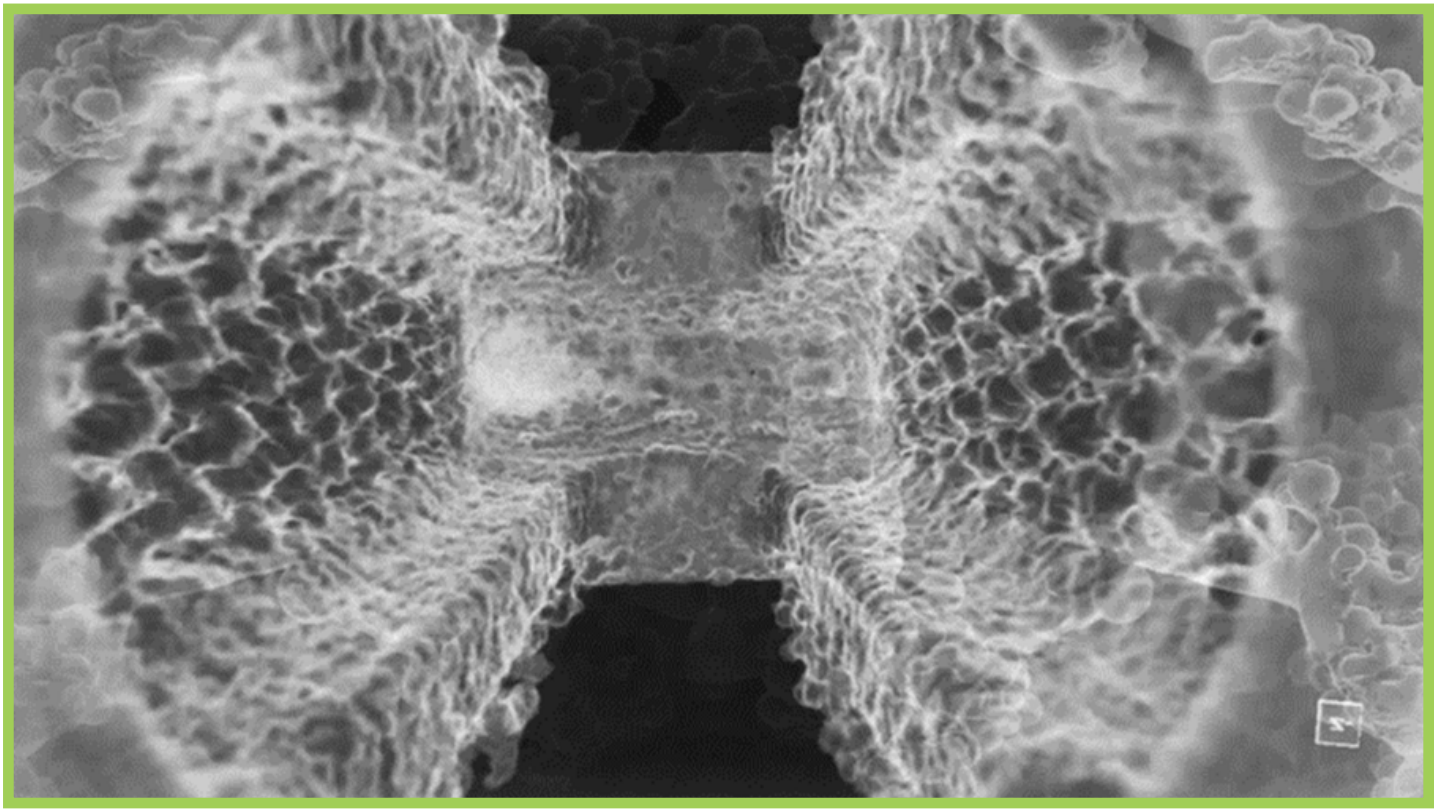


Figure 5: SEM image of the interior volume of the ChoiceSpine TigerShark® Straight PLIF showing the integrally connected yet distinct regions of structural loading, radiolucent mesh, and porous osseointegration function. The structures and geometry of each macro-region feature surface roughness and topography (peaks, valleys, and pits) at the micro and sub-micron levels that prompt direct cellular response and interaction.

Discussion and Application

The integration of additive manufacturing (AM) techniques and advanced BioBond® surface technology represents a significant leap in the development of spinal fusion implants. This innovation addresses longstanding challenges in spinal implant design, enhancing both the mechanical and biological performance of the devices. The combination of AM and surface technology allows for anatomically optimized spinal fusion devices that improve osseointegration and patient outcomes across a diverse product portfolio.

AM enables the production of implants with complex geometries that were previously impossible to manufacture using traditional methods. These biomimetic implant shapes with better anatomical fit should reduce the risk of migration or loosening post-surgery, thereby improving surgical success rates. The flexibility and control in deliberate constructs with optimized stiffness or modulus to closely match natural bone minimize the risks of stress shielding and subsidence, common causes of implant failure in metallic devices. By reducing stress shielding, AM-fabricated implants are designed to encourage more natural bone remodeling and may lead to better long-term outcomes.

BioBond® surface technology demonstrates the ability of AM to enable the advanced design of implants with controlled porosity. The specific porous structures, which mimic the architecture of cancellous bone, significantly enhance the implant's osteoconductivity and osteopromotive characteristics. This architecture fosters robust bone-implant integration by promoting mesenchymal stem cell (MSC)

adhesion, proliferation, and differentiation into osteoblasts, as demonstrated in the BioBond® cell study. The study demonstrated that the surface topography, with its macro, micro, and submicron features, plays a critical role in cellular interactions, driving early and sustained osteogenic responses essential for successful fusion.

The innovative engineering design of these implants also allows for the volumetric maximization of the large internal graft chamber. This provides ample space for bone graft material, which is crucial in supporting the bone fusion process. The interconnection of the BioBond® porous trabecular structure with this maximized graft chamber further enhances vascularization and nutrient flow, as evidenced by the sustained expression of vascular endothelial growth factor (VEGF) in the BioBond® study. VEGF is vital for new blood vessel formation, which is necessary for healthy bone growth and fusion.

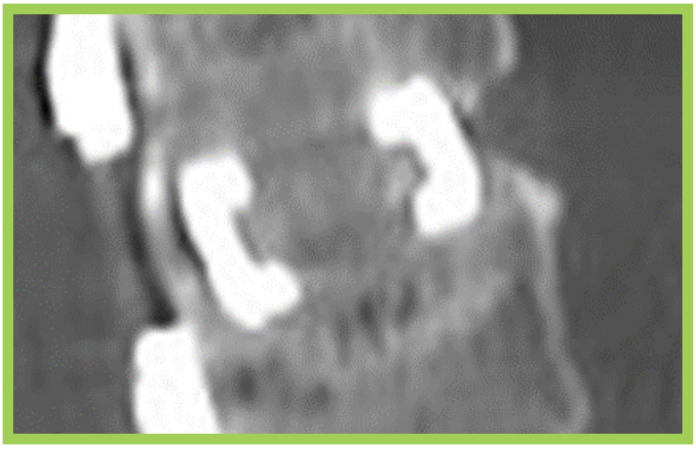
Another key advantage of AM is its ability to ensure homogeneous manufacturing of implants. This eliminates concerns of delamination, a common issue with earlier-generation titanium-coated and hydroxyapatite-infused polyetheretherketone (PEEK) implants. The seamless integration of different regions—whether load-bearing, radiolucent metal mesh, or osseointegration zones—improves the overall structural integrity and long-term stability of the implant.

Furthermore, the radiolucent metal meshes in these AM-produced devices provide superior imaging quality without sacrificing mechanical performance when compared to traditionally machined metal devices. This allows for better post-operative monitoring of the fusion process to ensure the success of the surgery and optimize patient care.

The BioBond® surface technology plays a paramount role in the osteopromotive properties of these implants. By optimizing surface roughness, porosity, and hierarchical structure, BioBond® not only enhances bone cell adhesion but stimulates early osteoblastic differentiation and bone formation. As evidenced by the peak expression of bone morphogenetic proteins (BMP-2 and BMP-4) and osteocalcin in the BioBond® study, these surfaces promote a favorable environment for bone growth while minimizing inflammatory and fibrogenic responses. These bioactive characteristics are critical for reducing the risk of pseudoarthrosis.

The combination of additive manufacturing and BioBond® surface technology positions the ChoiceSpine spinal implant product lines as advanced tools for spinal fusion surgeries. The ability to create anatomically accurate and biologically active implants offers impactful device solutions across a range of surgical approaches and patient needs without imposing additional demand on the surgeon. These innovations may improve short- and long-term surgical outcomes, supporting bone fusion, minimizing complications, and ultimately enhancing patient quality of life.

Figure 6: TigerShark® C Anterior Cervical Spacer System featuring a continuous, open porosity with radiographic mesh windows. 6° lordotic footprints are available in 14 x 12mm, 16 x 14mm, and 18 x 15mm with a height range of 5-10mm in 1mm increments.



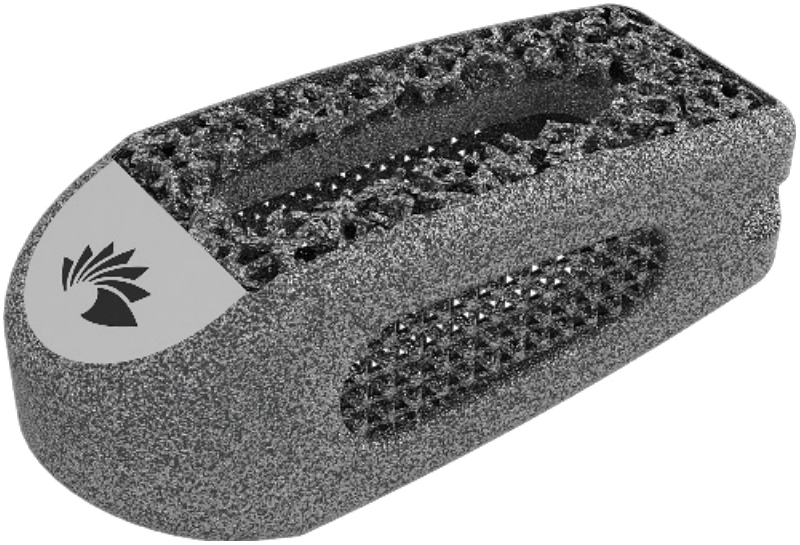
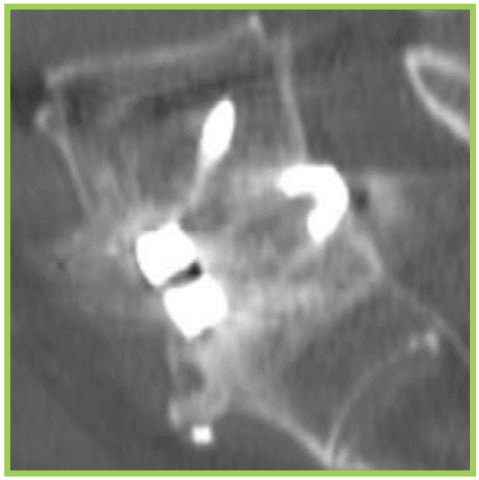


Figure 7: TigerShark® 3D Printed Titanium Lumbar Interbody with a large center graft window for biologics, smooth bullet nose for fast insertion, and built-in 6˚ lordosis. Available in 9mm and 11mm widths, with 24, 28, 32mm lengths. Various heights: 9-18mm in 1mm increments.

Figure 8: TigerShark® M is a 3D Printed Titanium Lumbar Interbody with a modular in-situ design to minimize the insertion profile while achieving impressive height restoration. Available at a 10mm width with either 6˚ or 12˚ lordotic endplates, 2-8mm spacer options in 1mm increments.

Figure 9: TigerShark® Threaded TL 3D Printed Curved Interbody Spacer has a large open graft window to pack biologics. Available in various sizes to accommodate different patient anatomies with 6 degrees of lordosis and 11mm width, lengths of 25, 28, 32, 36mm, and heights: 7-14mm (1mm increments).

Figure 10: Harrier® SA Standalone ALIF System has an integrated cam-locking mechanism and a large graft window for use with biologics. The interbody cage has three lordotic options of 10, 15, and 20 degrees in three footprints: 26 x 32mm, 28 x 36mm, 30 x 40mm. The implant heights are 12, 13.5, 15, 17, 19mm.



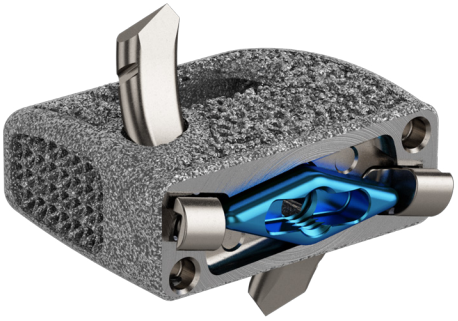
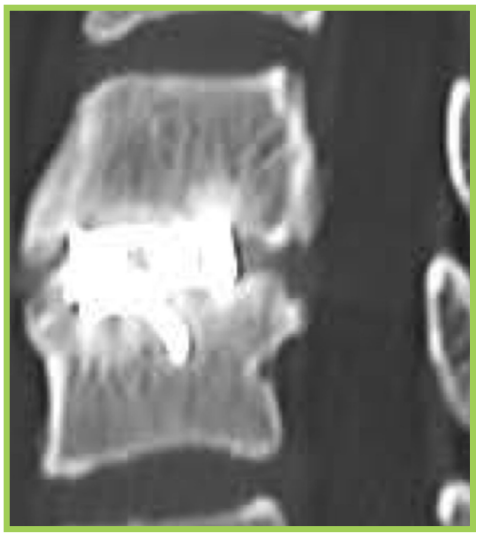
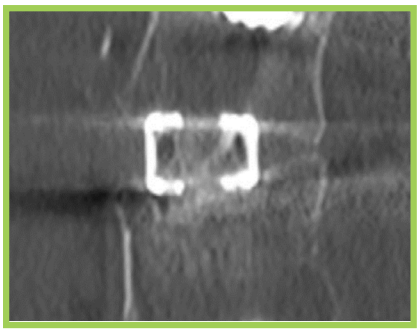


Figure 11: Blackhawk® TI 3D Printed Anterior Cervical Standalone Spacer System has a large open graft window for bone graft containment and lateral mesh windows for maximum visualization. The pre-assembled anchors, sterile packaged delivery, and simultaneous, single-step anchor deployment reduce steps in the operating room. Blackhawk® Ti incorpo-rates an integrated cam-lock mechanism. It provides both visual and tactile feedback during the locking process.





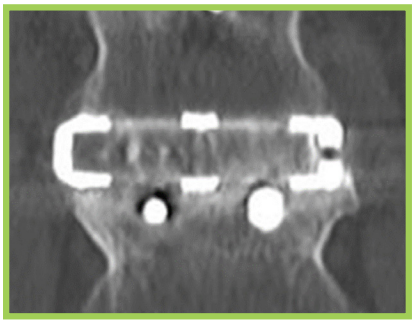
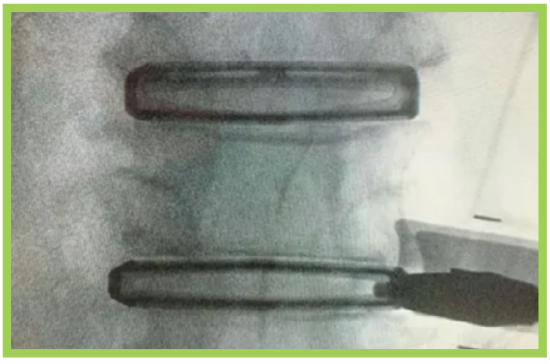


Figure 12: TigerShark® L 3D Printed Lateral Interbody Spacer has 17 and 22mm width choices with built-in 0°, 6°, and 12° lordotic options in multiple lengths and heights. The device features a large center opening for packing bone graft material and is compatible with the Veo® Lateral Access System for minimizing psoas disruption.



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Conclusion

The BioBond® porous trabecular structure is fabricated using additively manufactured titanium alloy. This advanced surface technology demonstrates significant innovation in spinal fusion development by promoting enhanced osseointegration and osteogenic differentiation. Our findings confirm that the hierarchically porous structure effectively mimics native bone architecture with peak and valley topography at a microscale level, which fosters mesenchymal stem cell adhesion, proliferation, and osteoblastic differentiation. The BioBond® osteoconductive and osteopromotive surface properties have been combined with additive manufacturing expertise to develop a complete product portfolio of state-of-the-art spinal implants. This innovation addresses historical and current limitations in spinal fusion, offering a promising solution package that may improve patient outcomes and reduce complications. BioBond® technology represents a critical leap forward in spinal implant design, providing reliable, next-generation options for surgeons.

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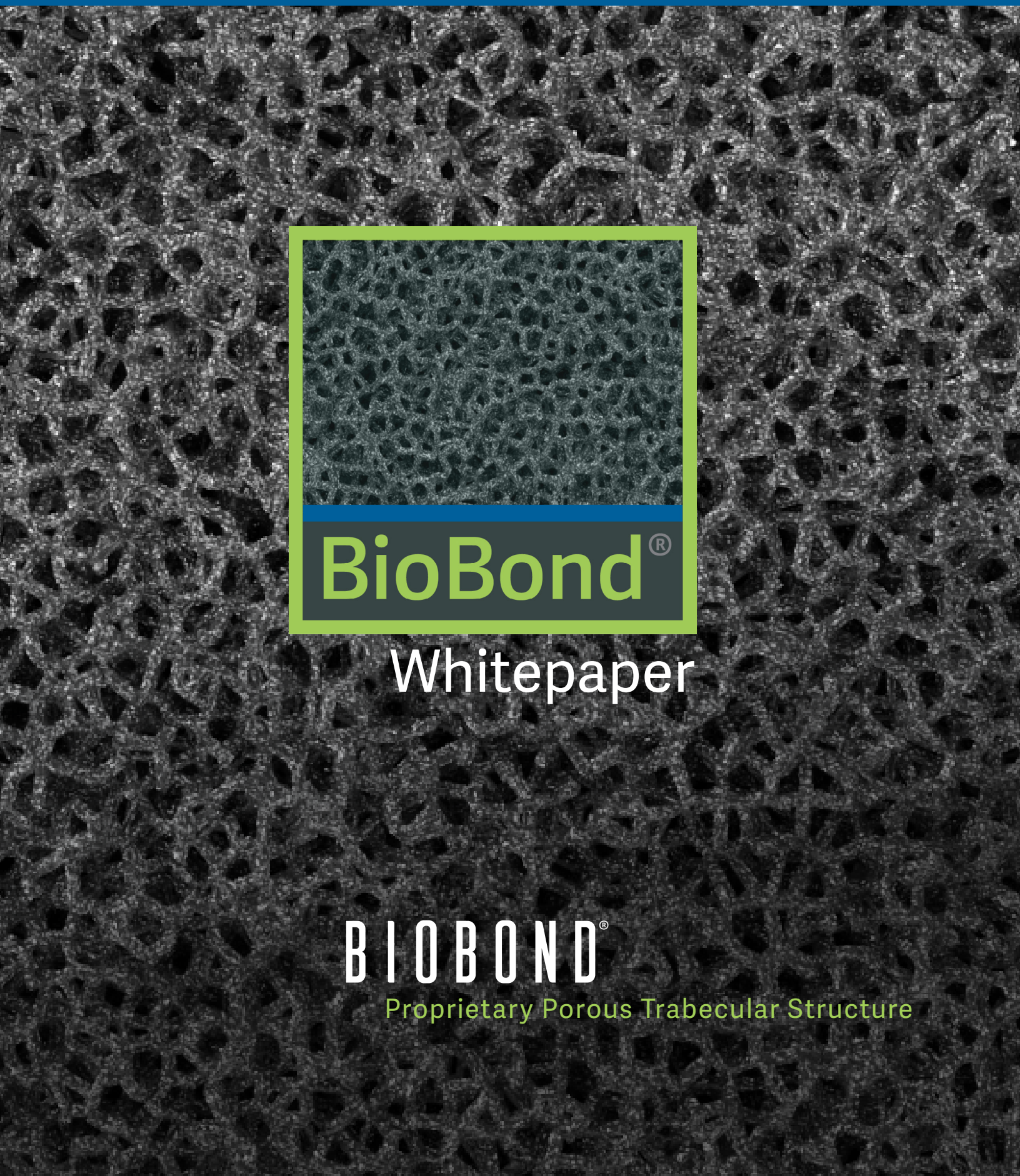

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