Invibio® SPINE

White Paper

Spinal Biomaterials Update: PEEK-OPTIMA® polymers deliver high performance and potential clinical advantages over traditional biomaterials in spinal applications

Established biocompatibility and clinical performance in spine surgery

For more than a decade, PEEK-OPTIMA polymers have been utilized in spinal fusion applications, predominantly in the form of load-bearing interbody cages in spinal interbody fusion surgeries (Fig 1). The properties that make PEEK-OPTIMA polymers one of the leading interbody fusion biomaterials also make it promising for use in other spinal devices such as

1) Spinal rods in pedicle screw systems
2) Spinal arthroplasty discs
3) Anterior column plates

This paper looks to explore the ways in which PEEK-OPTIMA polymers are now being used in these applications and their unique material properties that make them a promising alternative to more traditional spinal biomaterials.

PEEK-OPTIMA Natural: Material Characteristics Ideal for Use in Spinal Implants

PEEK-OPTIMA Natural is the foundation of the PEEK-OPTIMA polymer family and has been utilized in the spine for interbody fusion applications for nearly 15 years due to its inherent material characteristics:

Modulus similar to cortical bone:

The flexural modulus of PEEK-OPTIMA Natural is similar to cortical bone and far less stiff than comparable metal alloys, making it a good fit for applications where load sharing is desired to promote bone remodeling.

Image compatibility:

PEEK-OPTIMA Natural is radiolucent and causes no artifact or scatter under MRI and CT imaging, making it a good option when unobstructed imaging studies are required to assess healing, disease progression or future traumatic injuries.

Biocompatibility:

The biocompatibility of PEEK-OPTIMA Natural is well established[a]. It is inert, highly stable and is able to be repeatedly sterilized without degradation.

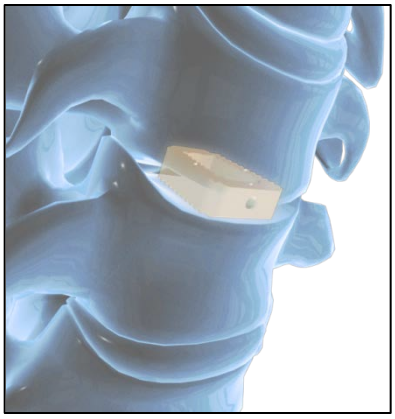


Fig. 1
Cervical interbody fusion cage composed of PEEK-OPTIMA.

[a] Biocompatibility testing to ISO 10993 standards demonstrates no evidence of cytotoxicity, irritation or macroscopic reaction response (REFS).

PEEK-OPTIMA® Product Range: Manufacturing and Device Versatility

PEEK-OPTIMA Natural can be processed with other biomaterials to impart different material properties that are optimized for specific design requirements.

Invibio Biomaterial Solutions offers a range of commercially-available PEEK-OPTIMA polymers, compounds and composites that can be used in spinal applications, providing nearly unlimited design flexibility (Fig 1).

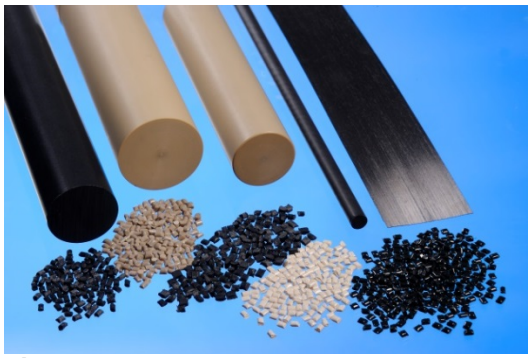


Fig. 1
Commercially available PEEK-OPTIMA polymers and compounds from Invibio Biomaterial Solutions.

TABLE 1: Material properties and composite formulations of PEEK-OPTIMA polymers

Desired Material Property	PEEK-OPTIMA® Product	Composite Formulation	Medical Applications
Typical properties: ▶ Radiolucency ▶ Biocompatibility ▶ Modulus close to bone ▶ Long term stability	PEEK OPTIMA Natural	Unfilled / Neat	• Spine interbody cages • Spinal rods • Interspinous process spacers • Vertebral augmentation devices
▶ **Customized radiolucency**	PEEK-OPTIMA Image Contrast	Compounded with barium sulfate	• Spine interbody fusion • Spinal rods • Vertebral augmentation devices
▶ **Enhanced bone apposition**	PEEK-OPTIMA HA Enhanced	Compounded with hydroxyapatite	• Spine interbody fusion
▶ **Higher strength with low wear**	PEEK-OPTIMA Reinforced	Compounded with carbon fibers	• Spine interbody fusion • Spinal screws & dowels • Spinal discs
▶ **Very high strength with fatigue resistance**	PEEK-OPTIMA Ultra-Reinforced	Composite with continuous carbon fibers	• Anterior column plates

1. Posterior Rods for Pedicle Screw Systems

The global market for posterior pedicle screw systems in 2011 was estimated to be over $2.5 Billion (USD), making it the largest segment of the spine surgery market.[1] The vast majority of rods used in these systems are composed of titanium, stainless steel or cobalt chrome metals, but several manufacturers, including Medtronic and DePuy/Synthes, have introduced PEEK-OPTIMA®-based rods in recent years. These rods allow for less stiff, or semi-rigid constructs, that can bridge the gap between traditional rigid metal screw/rod constructs and constrained dynamic stabilization constructs (Fig 2).[2]

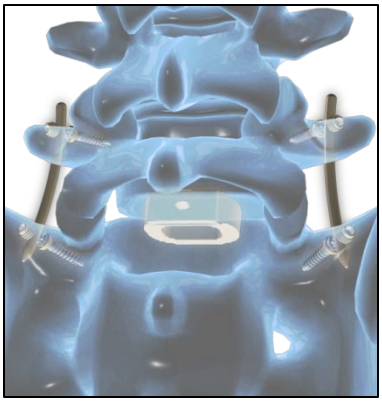
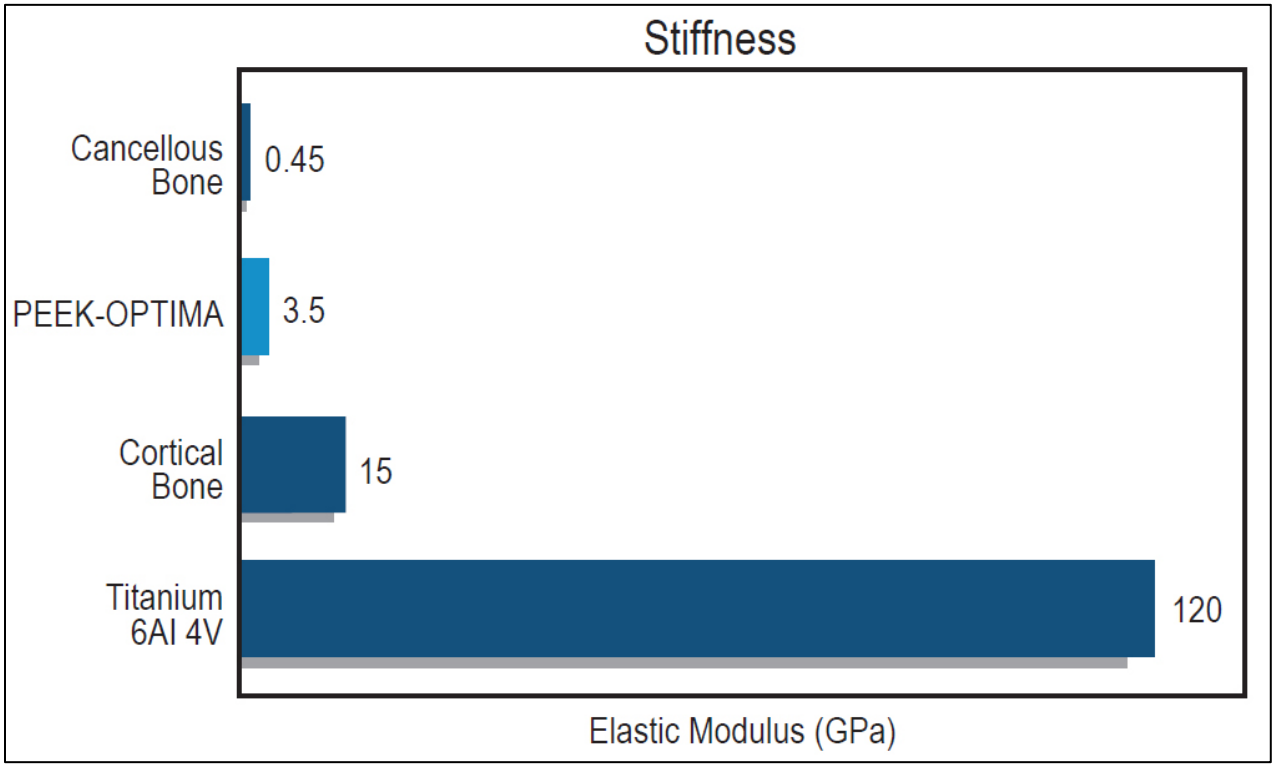


Fig. 2
PEEK-OPTIMA Rods enable semi-rigid fusion constructs.

Load Sharing

One of the drawbacks to the use of metal posterior rods is their relative high stiffness compared to bone (Fig 3).[2] Constructs made of metal materials are likely far more rigid than needed for spinal fusions for instability indications.[2]

Fig. 3: Flexural modulus of bone and posterior spinal rod materials.[3]



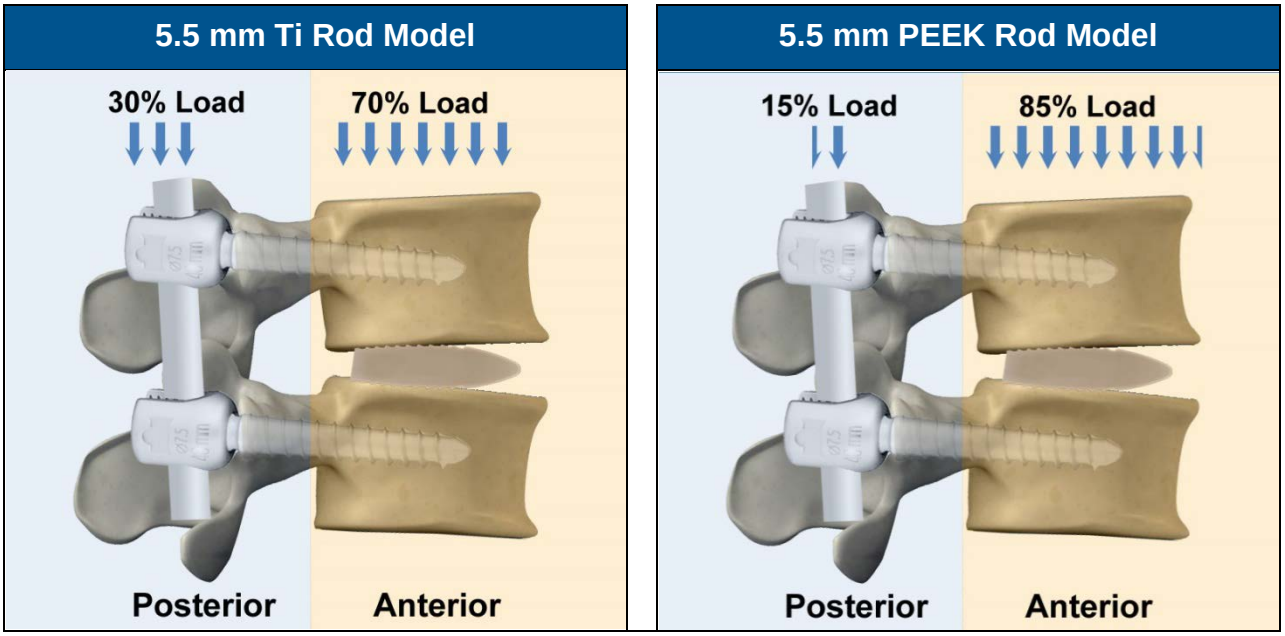
In a cadaveric spine tests designed to measure the stiffness of posterior constructs, PEEK rod constructs demonstrated a lower stiffness than all the metallic rod systems studied, regardless of diameter or metallic composition (Table 2).[6]

Table 2: Stiffness of PEEK-OPTIMA® rods compared to Ti rods in ASTM 1717 Testing[6]

	Ti 5.5 mm rod	Ti 4.5 mm rod	Ti 3.6 mm rod
Stiffness reduction with PEEK 6.35 mm rod	**78%↓**	**66%↓**	**38%↓**

Stiff posterior constructs shift the load away from the anterior column, significantly altering the natural biomechanics of spine. This can cause stress shielding of grafts placed in the anterior column, which is a significant factor contributing to pseudoarthrosis, particularly in the lumbar spine.[4] Since PEEK-OPTIMA has a modulus between that of cancellous and cortical bone, spinal rods made from it can allow for more load sharing with the anterior column (Fig. 4).[5, 6] This can allow more force to be applied to the anterior graft, providing additional stimulus for bone to form and fusion to occur. Small case series studies are beginning to report short term clinical results that indicate that PEEK rods perform as well as Ti rods for achieving fusion,[7, 8] may reduce the incidence of post-operative screw loosening, and maintain perceived reduction in pain longer than Ti rods.[9, b]

Fig 4: PEEK Rods offer 21% Increased Anterior Loading over Ti Rods[51, c]



[b] Based on uncontrolled case studies, clinical relevance not studied.
[c] FEA using validated L1-S1 model with 400N follower load, single level pedicle screw construct with IBF cage at L4-L5.

Adjacent Segment Degeneration

Stiff fusion constructs have been shown to increase motion and pressure in adjacent vertebral segments, which can lead to hypermobility and facet hypertrophy following surgery.[10, 11, 12] Segmental lumbar hypermobility is reported to be associated with non-specific low-back pain.[14] A recent meta-analysis reports radiographic evidence of adjacent segment degeneration after lumbar spine surgery occurred in about one-third of patients two to five years after surgery at the index level.[13] Biomechanical testing of PEEK rods demonstrates a trend toward reduced motion and more natural kinematic loading at adjacent levels compared with Ti rods.[6] This could help to decelerate the rate of adjacent segment degeneration, though long-term clinical studies that study this are required.

Bone Screw Interface

When spinal loads are shifted posteriorly as they are with pedicle screw constructs, there is higher stress at the bone screw interface.[15] The additional stresses applied to the bone screw during dynamic loading can cause screw loosening,[16,17] a clinically significant problem that can lead to pseudoarthrosis and screw pull out. It is sometimes referred to as the “windshield wiper effect” due to the fact that the screws toggle within the soft cancellous bone of the vertebral body, reducing screw purchase (Fig. 5).

Windshield Wiper Effect

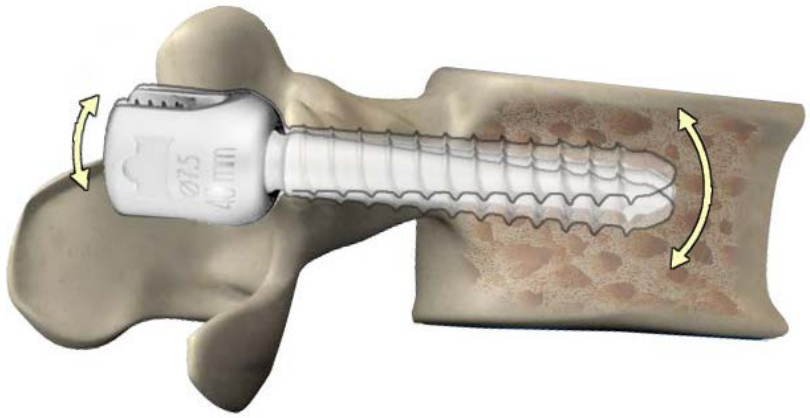


Fig. 5

Small motions at the bone-screw interface during dynamic loading of a stiff construct can toggle screws within the vertebral body, reducing screw purchase, thus allowing the screws to loosen. This effect can be particularly pronounced in osteopenic and osteoporatic bone.

Biomechanical studies suggest that decreasing the stiffness of the rod construct can help reduce the stress at the bone-screw interface,[16] which may prevent screw loosening. In preliminary dynamic testing, constructs made with PEEK rods allowed for a less stiff construct and improved screw purchase after cyclical loading compared to constructs made with Titanium rods.[17, d]

[d] Based on small scale experiment evaluating four screws, clinical relevance not studies.

Imaging compatibility

Due to the fact that PEEK-OPTIMA® is inherently radiolucent, radiologic assessment of fusion is easier than with traditional all-metal constructs.[8] It allows for a better view of the posterolateral fusion bed and provides no artifact under CT or MRI imaging (Fig. 6).[8]

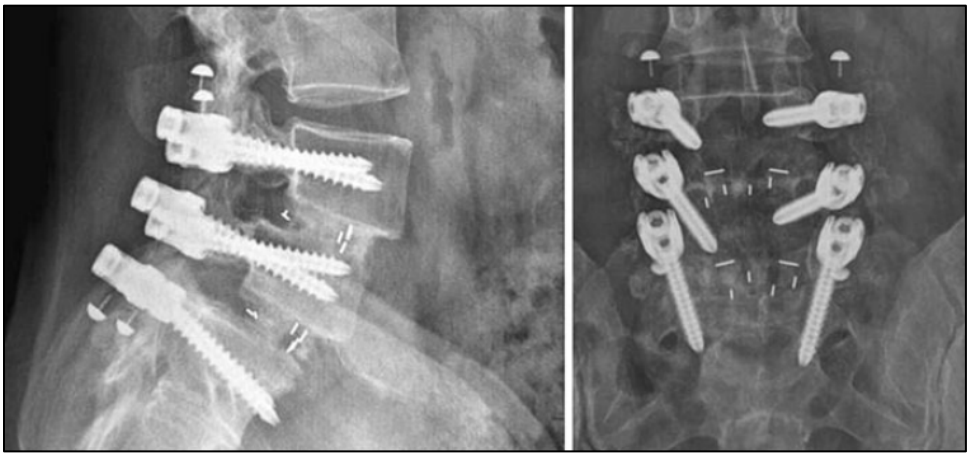


Fig. 6
Radiolucent PEEK Rods allow for easier radiographic assessment of fusion in both the sagittal and coronal planes.

Implant Adaptability

Spinal rods can be manufactured from PEEK-OPTIMA Natural when radiolucency is desired or from PEEK-OPTIMA Image Contrast when some level of radiopacity is preferred. Rods can be pre-lordosed and cut to varying lengths during the manufacturing process, providing the implant flexibility to fit many different patient anatomies and simplifying the surgical technique by eliminating the need for *in situ* rod bending.

Summary: Posterior Rods for Pedicle Screw Systems

- Current posterior spinal constructs made of metals are likely much more stiff than necessary for spinal fusion.
- PEEK-OPTIMA rod constructs provide more anterior loading of the interbody graft.
- Adjacent segment degeneration may potentially be reduced due to the more natural kinematics seen at adjacent segments instruments with PEEK-OPTIMA rods compared to Ti rods.
- PEEK-OPTIMA rods may limit the micromotions at the bone-screw interface, which may prevent screw loosening stemming from the windshield wiper effect.
- PEEK-OPTIMA spinal rods can be efficiently manufactured to varying specifications that match a wide range of patient anatomies and eliminate the need for *in situ* rod bending.

2. Spinal Arthroplasty Devices

Spinal arthroplasty devices that are intended to preserve spinal segmental motion have been in clinical use since the early 1990's. The current market for these devices is relatively small compared to mature fusion technologies. However, the Food and Drug Adminishtration (FDA) approved several new cervical spinal arthroplasty devices in the fall of 2012 (Table 3), and several large insurance companies in the United States have issued coverage decisions in favor of covering spinal arthroplasty procedures[18,19,20,21,22] so this segment could grow over the next several years.

Preserving motion in diseased spinal segments allows surgeons to restore more natural kinematics[23] and reduce the stresses placed on adjacent spinal segments compared to fusion surgeries.[24] Studies comparing spinal arthroplasty to fusion outcomes five years after surgery indicate that surgery with spinal arthroplasty devices may decrease the incidence of adjacent level degeneration and re-operation compared to fusion surgery. [25, 26, 27,28]

Table 3: Spinal Arthroplasty Devices Regulatory Status in the U.S.

Device	Indication	FDA Approval Status	Bearing Materials
Depuy Charité	L4-S1	Withdrawn Jan. 2012	CoCr / UHMWPE
Synthes ProDisc-L	L3-S1	Approved Aug. 2007	CoCr / UHMWPE
Medtronic Prestige ST	C3-C7	Approved July. 2007	Stainless / Stainless
Synthes ProDisc-C	C3-C7	Approved Dec. 2007	CoCr / UHMWPE
Medtronic Bryan	C3-C7	Approved May 2009	Ti / Polyurethane
Globus Secure-C	C3-C7	Approved Oct. 2012	CoCr / UHMWPE
Nuvasive PCM	C3-C7	Approved Oct. 2012	CoCr / UHMWPE
LDR Mobi-C	TBD	Approvable letter Nov. 2012	CoCr / UHMWPE
Kineflex-C (Cervical)	NA	FDA Orthopedic Panel scheduled July 2013	Co/Cr / Co/Cr
Kineflex-L (Lumbar)	NA	FDA Orthopedic Panel scheduled July 2013	Co/Cr / Co/Cr

Wear Debris

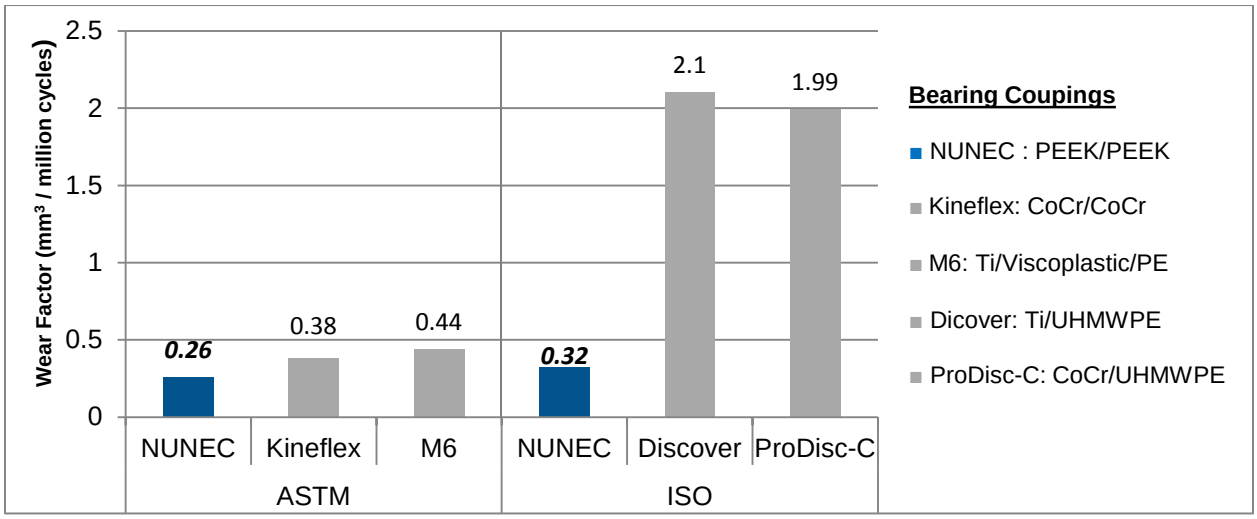
Wear debris is a concern with any motion preservation device. Histological analysis of current generation spinal arthroplasty devices has shown evidence of both metallic and polymeric wear debris, frequently with inflammatory cells in the surrounding tissues.[29] CoCr / UHMWPE is the most common bearing coupling in total joint and spinal arthroplasty devices. These devices are generally well-tolerated, but have been known to cause periprosthetic bone resorbtion, or osteolysis, resulting in implant failure and need for secondary surgery.[30] Similar wear-related complications from CoCr / UHMWPE spinal arthroplasty implants have been reported.[30, 31, 32]

Metal on Metal Concerns

Metal-on-metal bearing implants release metal ion wear debris that can accumulate and lead to tissue necrosis and implant loosing and failure in hips.[33] In the summer of 2012, the FDA issued a report citing unique risks associated with hip arthroplasty surgery using metal-on-metal implants that urges close monitoring of patients with these implants due to the potential for long-term complications.[34] High concentrations of metal ions have also been noted with metal-on-metal spinal arthroplasty devices,[35] and cases of necrotic debris and chronic inflammatory activity attributed to metal-on-metal spinal devices have been reported,[36] raising concern over metal-on-metal spinal arthroplasty designs. Implant designers are seeking alternative bearing materials that minimize wear debris and macrophage response to wear particles.

While clinical studies of spinal arthroplasty devices with PEEK-OPTIMA®-on-PEEK-OPTIMA couplings have not been reported, preliminary dynamic testing indicates that these implants may generate less wear debris than devices with more traditional couplings (Fig. 8),[50] particularly when the PEEK-OPTIMA is reinforced with carbon fiber, as is the case with PEEK-OPTIMA Reinforced.[37, 38] In addition, *in vitro* studies comparing macrophage activity to PEEK and UHMWPE particles of different sizes have shown that PEEK particles induced less inflammatory response than UHMWPE.[39] These studies show promise for the future of PEEK-on-PEEK bearing surfaces for spinal arthroplasty devices

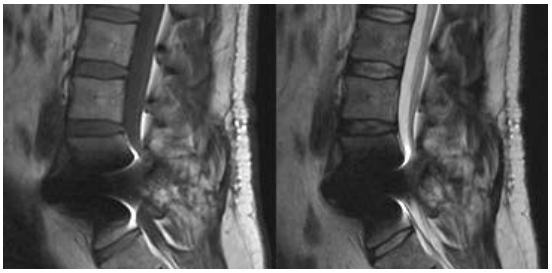
Fig. 8: Wear Factors for Cervical Arthroplasty Devices. Adapted from Brown *et al* (2012)[50]



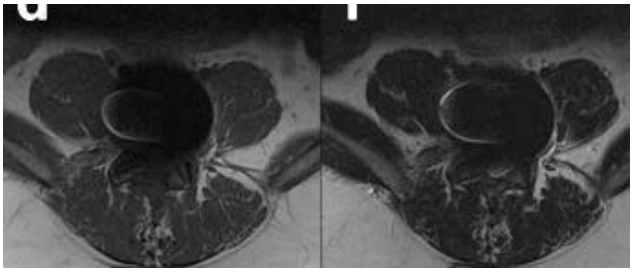
Imaging compatibility

CoCr and Stainless Steel cause artifact under CT and MRI imaging studies that degrade the diagnostic quality of the images.[4, 36] This can have significant impact in the spine, where implants made of stainless materials can disrupt the view of sensitive neural structures such as the spinal cord, making it difficult to assess cord signal changes. The majority of spinal arthroplasty devices that have been approved for use in the United States by the FDA contain metals that degrade CT and MRI images (Fig 9), making follow up imaging problematic. PEEK-OPTIMA is inherently radiolucent and has excellent CT and MRI imaging quality compared to metals.[6, 40, 49]

Fig. 9: Artifact on MRI associated with Cr/Co / Cr/Co artificial disc*



MR imaging in T1 of the Maverick Co/Cr / Co/Cr lumbar disc showing significant image degradation that obscures the spinal canal.



MR imaging in T2 of the Maverick Co/Cr / Co/Cr lumbar disc showing significant image degradation that obscures the spinal canal.

*Originally published in BioMed Central: Yohan R, Bengt S. Spine imaging after lumbar disc replacement: pitfalls and current recommendations. Patient Safety in Surgery. 20 July 2009, 3:15. Reprinted with permission.

Regulatory Status

The Aramis cervical spinal arthroplasty device by OSIMPLANT, which features a bearing coupling of PEEK-OPTIMA® Wear Performance against CoCrMo, has received a CE Mark. In addition, the NUBAC cervical Arthroplasty system by Pioneer Surgical Technology, Inc, which features a PEEK-OPTIMA Natural on PEEK-OPTIMA Natural coupling, has also received a CE mark and is available in Europe.

Summary: Spinal Arthroplasty

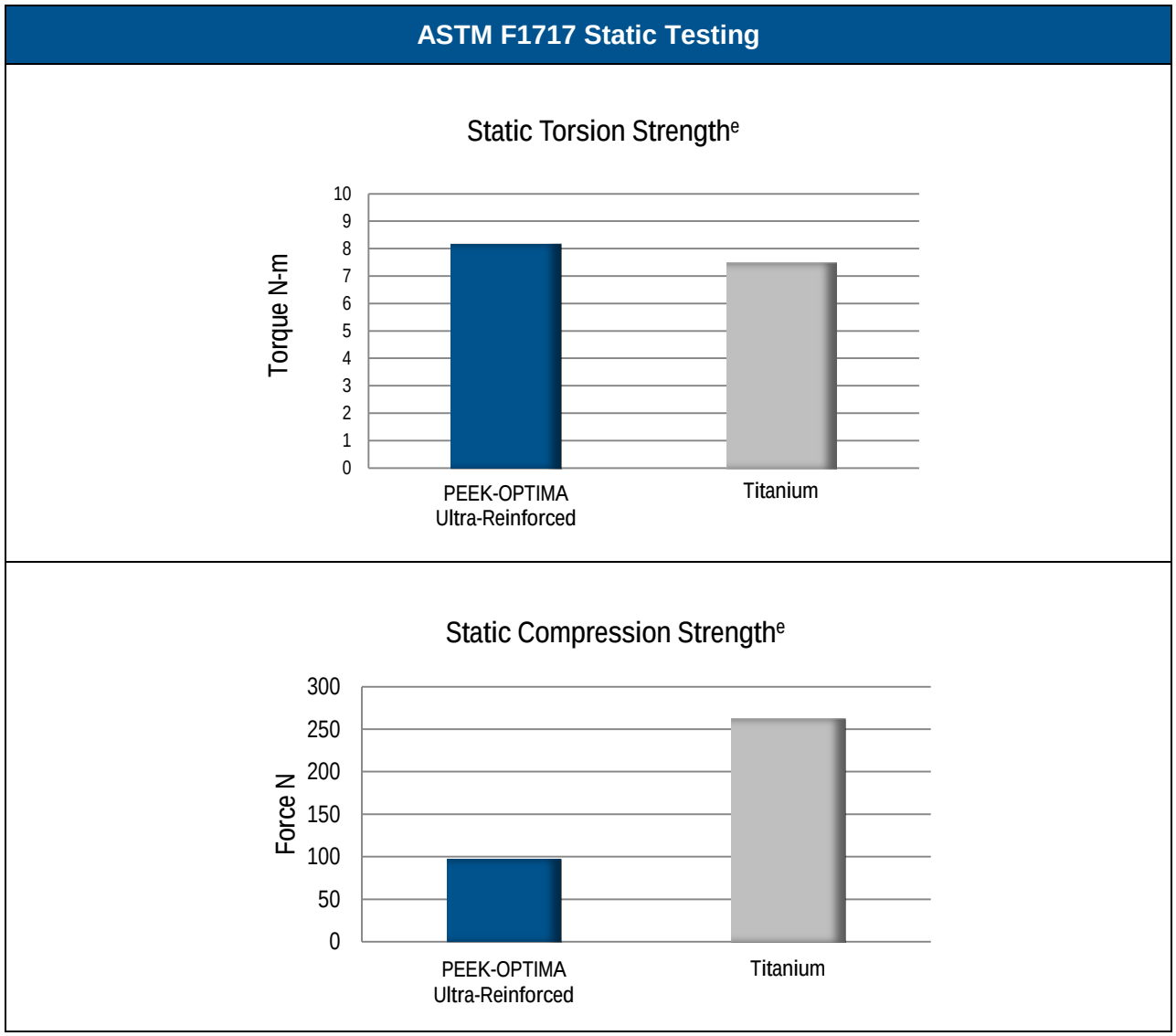
- A growing body of evidence suggests that spinal arthroplasty surgery may decrease the incidence of adjacent level degeneration and re-operation compared to fusion surgery over the medium term.
- Wear related complications such as osteolysis and implant failure due to wear have been associated with Co/Cr / UHMWPE spinal athroplasty devices, which account for the majority of devices marketed today.
- High levels of metal ions have been reported in patients who have received metal-on-metal artificial discs, as have cases of necrotic debris and chronic inflammatory response. This raises concerns over metal-on-metal artificial discs.
- Wear studies of various PEEK-OPTIMA Polymers in bearing surface applications demonstrate relatively low volumetric wear and a decreased inflammatory response compared to UHMWPE.
- PEEK-OPTIMA provides substantially improved MRI and CT imaging compared to the typical metals found in today's spinals discs, such as Co/Cr and stainless steel.

3. Anterior Column Plating

The market for cervical and lumbar anterior column plating devices was worth more than an estimated $1.5 Billion in 2011.[1] Currently, almost all commercially available anterior column plates are composed of metals. These devices are well established in the market, but alternative materials such as PEEK-OPTIMA® Ultra-Reinforced have the potential to provide advantages over current materials.

Cervical plates made from PEEK-OPTIMA Ultra-Reinforced demonstrate comparable mechanical performance in ASTM F-1717 static testing as commercially available metal cervical plates, but with a reduced compressive strength,[e] which may promote more load sharing across the anterior column (Fig.10).

Fig 10: Material Properties of PEEK-OPTIMA Ultra-Reinforced Polymer



[e] Internal data on identical generic plate designs (n=3). Data on file at Invibio.

Dysphagia

Dysphagia, or trouble swallowing, is one of the most common post-operative complications reported by approximately 9.5% after Anterior Cervical Discectomy and Fusion (ACDF) surgery[41], with some reports indicating that as many of 50% of ACDF patients will experience this complication to some degree.[42] The risk of experiencing dysphagia after ACDF surgery tends to increase with the number of surgical levels.[43, 44] Factors contributing to the high incidence of dysphagia include higher plate profile, as well as tissue adhesion to the plate.[45] Titanium, the most common implant material for anterior column plates, is known to promote tissue adhesion. In a case series of patients who had surgery for dysphagia following anterior cervical interbody fusion, a primary finding was adhesions that attached the esophagus to the prevertebral fascia and anterior cervical spine around the periphery of the plate. Dysphagia symptoms improved upon removal of plates.[46] Because PEEK-OPTIMA® is biologically inert, it does not promote tissue adhesion to the extent that Titanium does, which may help to reduce the prevalence and/or severity of dysphagia following ACDF surgery, though comparative clinical studies are required to test this theory.

Fig. 11
Two-level cervical plate composed of PEEK-OPTIMA Ultra-Reinforced.

Imaging

Anterior column plates composed of PEEK-OPTIMA would allow clinicians to easily to assess fusion healing in the coronal plane because it is radiolucent and minimizes artifact. This would be an advantage over metal plates, which obscure the interbody space, making healing assessment difficult.

Regulatory Pathway

While there are currently no FDA-cleared spinal plates made of PEEK-based materials, the recent 510(k) clearance of the Piccolo trauma plate systems[47] sets a precedent for the use of PEEK-OPTIMA in orthopaedic plates, paving the way for clearance of similar devices for other orthopaedic applications, such as anterior column plating.

Summary: Anterior Column Plating

- Cervical plates made from PEEK-OPTIMA Ultra-Reinforced demonstrate comparable mechanical performance in ASTM F-1717, but a lower modulus of elasticity than titanium plates, which may promote more load sharing.
- PEEK-OPTIMA® is biologically inert and does not promote tissue adhesion to the extent that Titanium does. This may help to reduce the prevalence and/or severity of dysphagia following ACDF surgery, though comparative clinical studies are required to test this theory.
- Anterior column plates composed of PEEK-OPTIMA enable clear assessment of the operative interbody space in the coronal plate. Similar imaging is not possible with metallic plates.

Conclusions

PEEK-OPTIMA® is a well-established biomaterial in spinal interbody fusion applications. More recently, PEEK-OPTIMA has shown promise as an alternative to metal alloys in applications such as rods in pedicle screw systems, bearing surfaces in spinal arthroplasty devices, and anterior column plates.

For a more detailed review of the literature and biomechanical testing of PEEK-OPTIMA presented in this paper or to discuss your next development project, contact your Invibio Business Development Manager or email us at *marketing@Invibio.com*.

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