Invibio
BIOMATERIAL SOLUTIONS

INSIDER

Bringing You the Insight and Thought Leadership of Invibio

ANNUALLY • 2017

Welcome to the first issue of the *Invibio Insider* – and to Invibio, where innovation is embedded in our culture. Inside you will be able to gain an insight into our business with focused topics for clinical evidence including case studies, literature reviews, perspectives from healthcare professionals and patients along with resulting outcomes.

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Perspectives from Invibio

In recent months I have travelled to the US, Europe and Asia and spent time speaking with regulators, medical device companies and surgeons. Although the conversations and topics varied, it was clear that every region focused on the same goal: delivering the best clinical outcomes at the lowest costs. Progress towards this goal is gaining momentum, with different approaches around the world. After speaking with different stakeholders, I have concluded that to achieve our common goal will require significant changes in the behaviors and practices of everyone involved, including Invibio.

Clinical Outcomes

So how do we define "best clinical outcomes"? Outcomes are defined as: interventional patient benefits or harms which can be assessed from different measured perspectives including, patient-reported outcome (PRO), clinician-reported outcome (ClinRO), observer-reported outcome (ObsRO), and performance outcome (PerfO) (Ref. Figure 1). All of these measures contribute to determining the progress and treatment efficacy of the chosen intervention.

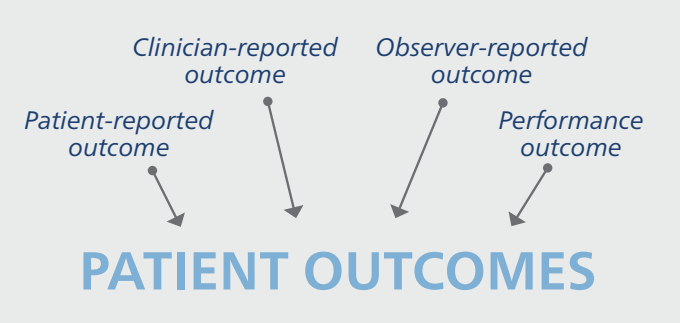


Figure 1

These measures or clinical outcomes are typically obtained through clinical studies, which are expensive and time consuming, and include many operational challenges during execution, to acquire robust clinical evidence. Though approaches vary, each geographic region has taken steps to improve patient outcomes and lower costs.

In the US, the introduction of The Bundled Payments for Care Improvement (BPCI) initiative links payments for multiple services received from providers during an episode of care. Under this initiative, organizations enter into payment arrangements that include financial and performance accountability. It's thought that these models may lead to higher quality and more coordinated care at a lower cost. In knee and hip surgery, for example, hospitals where the surgery took place will be accountable for the quality and costs of care from the start of the surgery through 90 days after discharge. This model focuses resources on the immediate episode of care rather than fee-for-service. However, it does not take into consideration the medium- to long-term issues that may arise. Moreover, it poses the question of how to differentiate between low- and high-risk patient clinical outcomes. Within Europe, the approach to improving patient outcomes and lowering costs even varies by country. For example, in Germany, rising costs are managed with maximum reimbursement levels assigned to each diagnosis-related group (DRG) allowing healthcare professionals (HCPs) to determine which intervention has the potential to provide the best clinical outcome, as long as it fits within the reimbursement framework. Clinical efficacy is aided by disease management programs for common chronic conditions. The programs use evidence-based guidelines to ensure program protocols include the most effective treatments. Despite these measures, Germany struggles to contain healthcare costs.

Although implemented measures throughout Europe have helped, they may also have implications for new product innovation. With reimbursement caps and new Medical Device Regulations (MDR) requiring extensive pre- and post-market surveillance clinical studies, innovation that may improve clinical outcomes may be slow-to-market.

Earlier this year, the Chinese central government took its own measures to lower costs. It issued a notice to deploy a disease-based charge system, similar to DRGs. The government provided a disease reference list from which the regions could then select which diseases to implement. Additionally, the Chinese Tender System (product price proposal) was designed to drive the cost-effectiveness of quality products sold in the market. Consequently, most regional Chinese governments focus on price only and do not emphasize clinical outcome.

In summary, the goal of achieving the best possible clinical outcomes appears consistent worldwide. However, with so much regional variation and an array of different stakeholders requiring different levels of clinical evidence, the medical device industry will have a difficult task of demonstrating that new product innovations are addressing this challenge and, ultimately improving patient care.

Cost Containment

Not only is defining "best clinical outcomes" difficult, but so is delivering healthcare at the lowest cost. The majority of current cost metrics focus on up-front purchasing costs rather than the total cost of care. For example, no standards exist for accurately assessing complication rates, or measuring the cost of revision surgeries, and reflecting these in purchasing decisions. When faced with delivering a consistent, quality of healthcare at the lowest cost, the market has yet to create an environment that encourages more ambitious solutions than simply preserving the status quo at a fractionally reduced price.

Invibio's Contribution

These current healthcare challenges force me to reflect on the changes within our business. Specifically, how can Invibio contribute to the goal of achieving the best possible clinical outcomes and lower costs?

Perhaps the biggest changes have to do with how we establish and maintain clinical efficacy for each of our healthcare solutions. Invibio already focuses on areas (Spine, Trauma, Dental and Orthopedics) where we believe we can deliver the greatest clinical and economic benefit (Ref. Figure 2). To help us raise our own bar for patient care and provide even greater clinical efficacy, we recruited a clinical study manager and are working with HCPs, medical device manufacturers and other stakeholders to determine the clinical and economic impact of our solutions. We have also brought in clinical relations expertise to interact with HCPs, hospitals and payers. Doing so ensures the clinical evidence we develop is not only shared in the marketplace, but accurately supports the benefits our products provide to patients and the entire healthcare community.

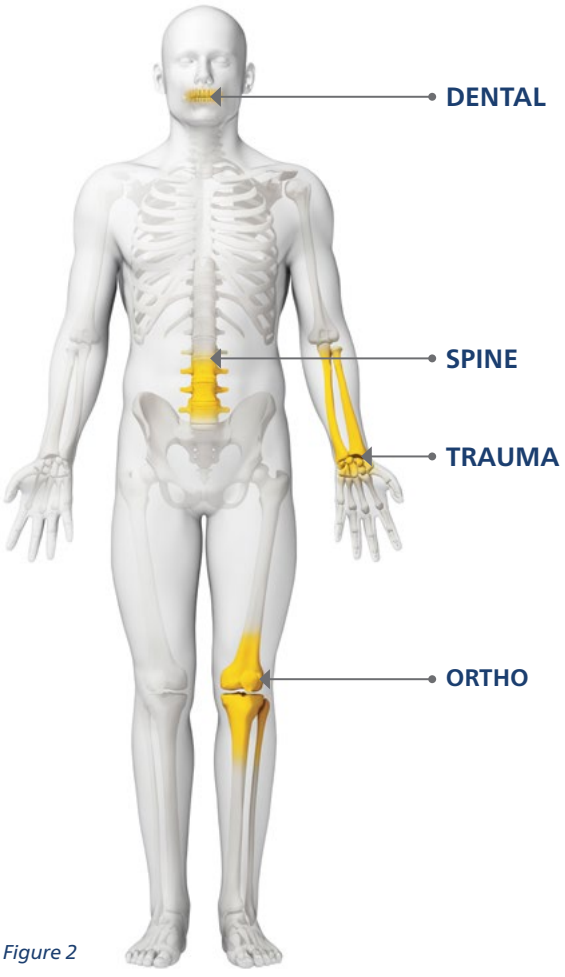


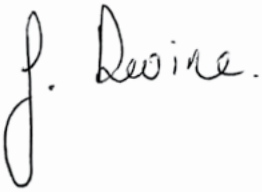
Figure 2

As a result of these enhanced research and clinical data capturing efforts, we have become more certain of the effectiveness of our solutions.

In addition, our investments have made it easier for medical device companies to innovate and change the way they develop new products. Our investment in component manufacturing facilities and component testing, for example, gives us a greater role in the design, development and commercialization of trauma fracture plates. We have also pledged more support to our customers' new product development. We have helped customers worldwide navigate the challenging, regulatory pathway toward product safety and efficacy. It's a win-win for Invibio, our customers, and patients alike.

In This Issue

As you read this issue of Invibio Insider, I hope to provide insight into all of these aspects across our areas of business. Focused topics will provide a greater understanding of the levels of clinical evidence and what that may mean for the patient and clinical outcomes. We will also explore approaches for treating challenging patients, including the HCP's perspective, showcase recent clinical evidence and discuss its potential economic impact. Finally, this issue of the Invibio Insider brings to life some of the investments Invibio has made to help facilitate and accelerate innovation in our key areas of business.



John Devine, PhD
Medical Business Director
Invibio Biomaterial Solutions

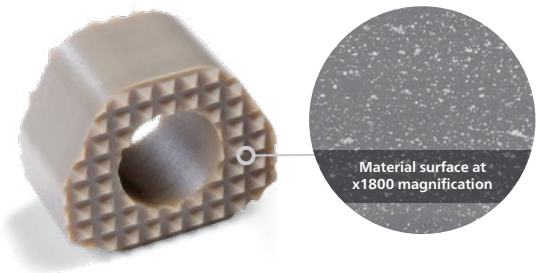
CASE SERIES: PEEK-OPTIMA™ HA Enhanced Polymer Shows Early Clinical Success in Interbody Spinal Fusions

North American Spine Society (NASS) Annual Meeting Presentation of Findings, October 2016

AUTHORS: Timothy Bassett, MD – SouthEastern Spine Specialists, Tuscaloosa, AL
Brad Prybis, MD – Carrollton Orthopaedic Clinic, Carrollton, GA

After years of research, development and pre-clinical studies by Invibio, early clinical results have shown PEEK-OPTIMA HA Enhanced Polymer may optimize bony ongrowth, osteointegration and fusion in interbody spinal fusions. The polymer, which was introduced to the market in 2013, combines PEEK-OPTIMA Natural with hydroxyapatite (HA), a well-known osteoconductive material with a bone-like chemical and crystalline structure that promotes bone remodeling and fusion.

One of the unique aspects of PEEK-OPTIMA HA Enhanced is that it addresses the entire interbody environment. Unlike roughened-metal or coated-metal technologies, HA crystals in PEEK-OPTIMA HA Enhanced are fully integrated, not coated, into the PEEK-OPTIMA matrix, making it available on all surfaces of a finished device. Consequently, both inter-cage and outer-cage graft material are exposed to hydroxyapatite, resulting in enhanced osteoconductivity.



Interbody Fusion Device examples. These products are not cleared for distribution and implantation.

HA crystals in PEEK-OPTIMA HA Enhanced are fully integrated, not coated, making it available on all surfaces of a finished device.

PEEK-OPTIMA HA Enhanced maintains the properties that have made PEEK-OPTIMA Natural, one of the leading interbody fusion biomaterials over the last 15 years; a modulus similar to cortical bone, reduced stress shielding, artifact-free imaging, biocompatibility and processing adaptability. In contrast, titanium can stress shield the bone graft, creating stress concentrations between implants and endplates, resulting in subsidence.

Pre-clinical studies with PEEK-OPTIMA HA Enhanced have indicated greater osteointegrative benefits compared to PEEK-OPTIMA Natural including:

- Enhanced bone apposition, with > 75% direct bone contact after 4 weeks[1]
- Greater new bone formation at 6 weeks[2]
- Higher quality bone bridging at 6 and 12 weeks[2]

Our early clinical experiences using PEEK-OPTIMA HA Enhanced Interbody Fusion Devices for lumbar and cervical fusion demonstrates similar, positive clinical outcomes. Several cases exhibiting these successes, as presented at the 2016 North American Spine Society (NASS) Annual Meeting, are highlighted on the following pages.

Early Clinical Experience - Lumbar Fusions, Timothy Bassett, MD

9-Patient Case Series

Patients in my series included males and females aged 39-76 with varying levels of health, pre-existing diseases or conditions and previous surgeries. Patients also had various combinations of leg pain, cramping and weakness, and back pain necessitating lumbar fusion.

To track and compare clinical results, I took anteroposterior and lateral x-rays at six- and twelve-weeks post-op and CT scans at six-months post-op.

All nine patients underwent a one- or two-level lumbar fusion utilizing the same EVOS-HA Interbody Device from Cutting Edge Spine, cage setup and pure iliac crest bone graft. All devices were made with PEEK-OPTIMA HA Enhanced Polymer by Invibio Biomaterial Solutions. No biologics were used. Post-op anti-inflammatory, caffeine and tobacco* usage was restricted for at least three months. Two patients had Orthofix bone stimulators.

*Patient 2 continued smoking throughout and after treatment

Radiographic Fusion Results

Six-month, post-op CT showed solid fusion for eight** of nine patients; One-year radiographs showed solid fusion in all nine patients.

**Solid fusion at one year in-patient with history of heart problems and smoking

Neurologic Function Results

- No neurologic sequelae

Clinical Results

- More than 50% back pain reduction
- Nearly all leg pain resolved
- No instrumentation failures
- No reoperations

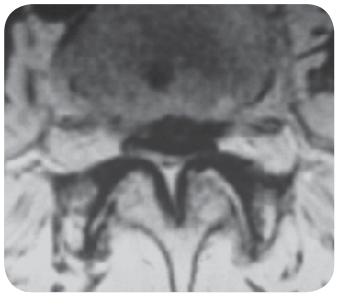
I have selected two cases to illustrate typical clinical and radiographic results from this 9-patient series.

Lumbar Fusion Case Study – Patient 7

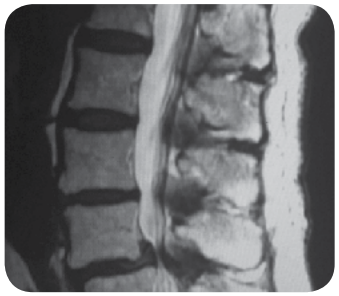
Patient Symptoms and Diagnosis

A 76-year-old female, presented with leg, bilateral hip and posterior thigh pain, and neurogenic claudication with less than 100-yard mobility was diagnosed with severe lumbar stenosis with subluxation.

Pre-operative Images



Axial MRI view showing high grade stenosis at L4-5



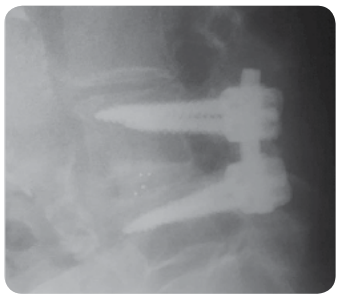
Sagittal MRI view showing L4-5 spondylolisthesis (10mm)

Surgical Procedure Performed

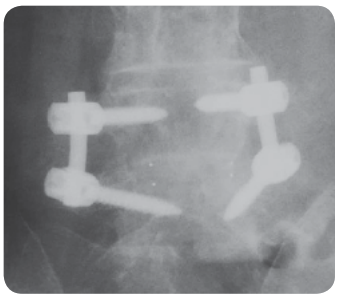
I performed a biologic-free, standard interbody L4-L5 decompression, reduction with fusion utilizing EVOS-HA Interbody Device by Cutting Edge Spine with iliac crest graft and pedicle screw. The device was made with PEEK-OPTIMA HA Enhanced Polymer from Invibio Biomaterial Solutions.

Radiographic Results

Early Follow Up Results

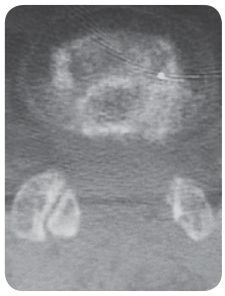


12-week sagittal view radiograph of EVOS-HA cage and pedicle screws

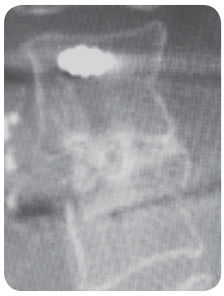


12-week coronal view radiograph of EVOS HA cage and pedicle screws

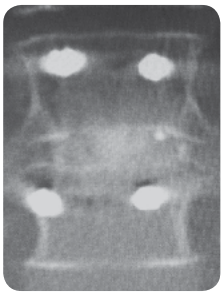
Six-Month Results



6-month axial CT scan showing dense bone apposition around the EVOS HA cage



6-month sagittal CT scan showing dense bone apposition around the cage



6-month coronal CT scan showing solid bone bridging and areas of dense bone

Clinical Results

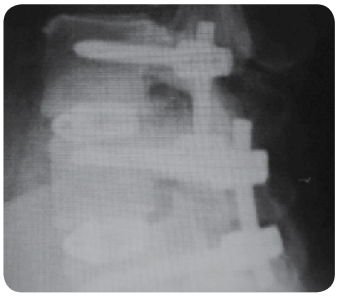
The patient reported no further leg pain and resumed full pre-surgical activity, including daily walks and a 5-day per week workout regimen.

Lumbar Fusion Case Study – Patient 9

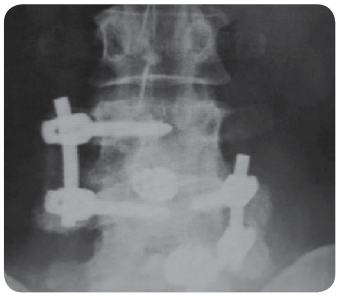
Patient Symptoms and Diagnosis

A female who had two previous, two-level MIS procedures with pedicle screw constructs, titanium cages, infuse bone morphogenetic (BMP) and dbx putty. Both failed. She presented with severe left side back and L3 leg pain, and secondary numbness from BMP foramenal bone overgrowth and non-union.

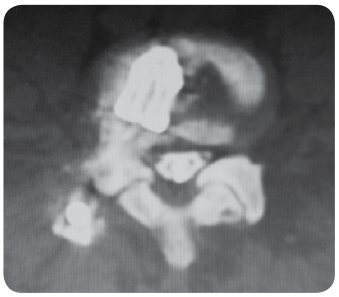
Pre-operative Images



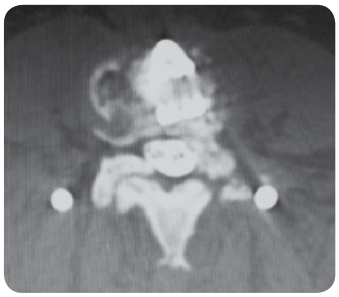
Sagittal radiograph of failed titanium cages



Coronal radiograph of failed titanium cages



Axial CT scan showing foramenal overgrowth from BMP, L3-4



Axial CT scan showing foramenal overgrowth from BMP, L4-5

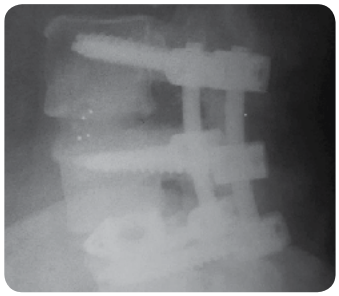
Surgical Procedure Performed

In this case, I performed a wide foramenectomy to remove the extra bone growth and explanted the titanium cage at L3-L4 on the symptomatic side. Fusion was performed at L3-L4 and L4-L5 utilizing EVOS-HA Interbody Device from Cutting Edge Spine with iliac crest graft. The device was made with PEEK-OPTIMA HA Enhanced Polymer from Invibio. Due to explant difficulties and to prevent future nerve pain, I only partially removed the asymptomatic side cage and regrafted using iliac crest craft around the L4-L5 space.

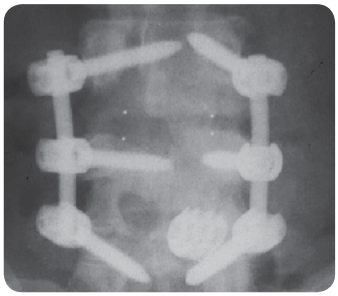
Radiographic Results

Post-op radiographic imagery shows solid L3-L4 fusion and bone growth with good bone abutment and dense bone-cage apposition. Although L4-L5 was progressing, some gaps remained (coronal recon).

Early Follow Up Results

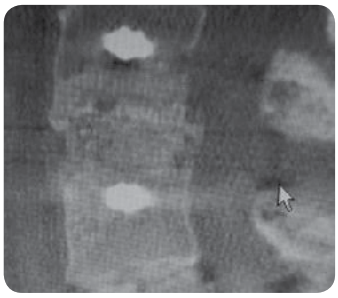


12-week sagittal radiograph with EVOS HA at L3-4 and Titanium cage at L4-5

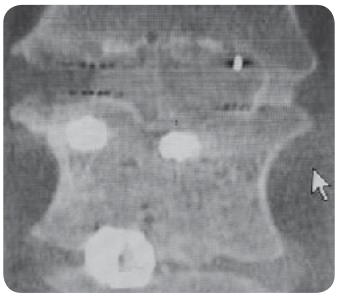


12-week coronal radiograph with EVOS HA at L3-4 and Titanium cage at L4-5

Six-Month Results



6-month sagittal CT scan showing bone bridging and fusion with EVOS HA cage



6-month coronal CT scan showing dense bone apposition around EVOS HA cage and delayed union with titanium cage

Clinical Results

The patient reported no further leg pain and the case was deemed successful.

Conclusion

PEEK-OPTIMA HA Enhanced Polymer shows exciting potential for use in spinal lumbar fusions. In all nine cases, the PEEK-OPTIMA HA Enhanced Interbody Fusion Device exhibited rapid bone fusion in the interbody region and very dense bone growth around the implant as early as six weeks, typically unseen with pure PEEK. With PEEK-OPTIMA HA Enhanced Polymer I can conduct standard format procedures on challenging cases with greater certainty that rapid fusion without instrumentation failure will result. Even at 18-month follow up, no subsidence has occurred. As a result of HA's quick bond, patients are less likely to require anterior posterior reconstructions and can return to everyday function and exercise regimes sooner and with greater confidence.

Early Clinical Experience - Cervical Fusions, Brad Prybis, MD

8-Patient Case Series

In my eight-patient cervical spine case series, I tested whether PEEK-OPTIMA HA Enhanced provides better bony ongrowth and fusion. I observed pain and neurologic function, and took anteroposterior, lateral and flexion extension radiographs at six-months post-op.

Patients included males and females aged 43-66 with chronic neck, arm, hand and finger pain, numbness and weakness. Some patients also reported loss of control, coordination and balance in the affected areas. Diagnoses included various levels and combinations of cervical radiculopathy, cervical myelopathy, myeloradiculopathy, central stenosis with spinal cord impingement, foramenal stenosis and chronic pain.

All eight patients underwent a two-level Anterior Cervical Discectomy and Fusion (ACDF) with devices made with PEEK-OPTIMA HA Enhanced polymer.

I utilized the standard ACDF left-sided discectomy and decompression approach, and removed the posterior longitudinal ligament. Utilizing a high-speed burr to maintain good bone-cage contact and some endplate bleed, I prepared the endplates for a PEEK-OPTIMA HA Enhanced spacer. I then filled the spacer with both local vertebra autograft, including bone marrow aspirate, and Vitoss BA synthetic bone graft. Last, I placed the anterior plate to secure the levels.

Radiographic Fusion Results

Six-month, post-op follow up showed solid fusion at 17 of the 17 levels.

Neurologic Function Results

- Improved neurologic function in all 8 patients
- Residual numbness in 3 of 8 patients
- Residual weakness in 1 of 8 patients

Clinical Results

- Arm pain resolved in all 8 patients
- Neck pain resolved in 5 of 8 patients
- Neck pain improved in 7 of 8 patients
- Neck pain unresolved in 1 patient

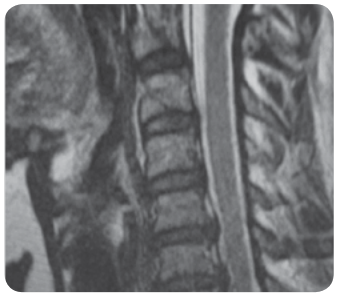
I have selected two cases to illustrate the typical clinical and radiographic results with PEEK-OPTIMA HA Enhanced Devices.

Cervical Fusion Case Study – Patient 1

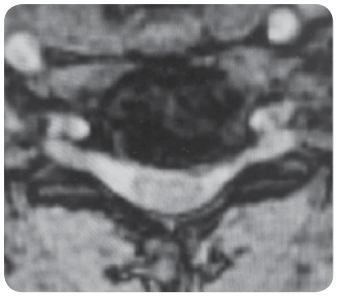
Patient Symptoms and Diagnosis

A 49-year-old female school teacher, presented with mostly left arm pain and numbness, loss of hand sensation and left thumb weakness. She was diagnosed with cervical radiculopathy.

Pre-operative Images



Sagittal MRI showing osteophyte and disc caused stenosis



Axial MRI showing foramenal stenosis and nerve root encroachment

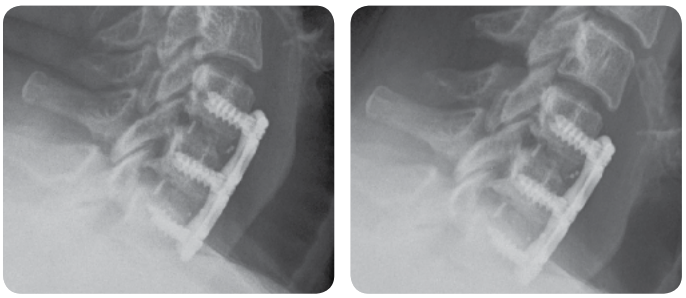
Surgical Procedure Performed

I performed an anterior cervical discectomy and fusion at C5-C7 utilizing a PEEK-OPTIMA HA Enhanced Interbody Fusion Device.

Radiographic Results

Post-op radiographic imagery shows solid, 2-level fusion at 6 months.

Six-Month Results



6-month Flexion Extension radiographs demonstrating solid fusion

Clinical Results

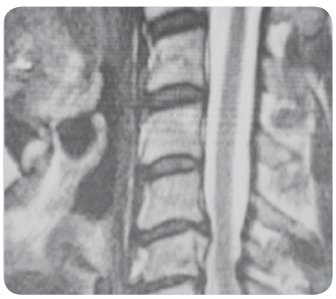
The patient resumed work as a teacher after two weeks, and reported no further neck and arm pain with only mild residual left thumb numbness.

Cervical Fusion Case Study - Patient 2

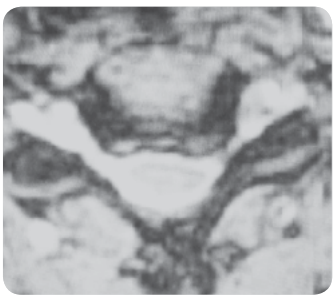
Patient Symptoms and Diagnosis

A 57-year-old male bucket truck worker, presented with neck pain radiating into the left arm and hand, decreased left thumb and index sensation, and thumb weakness. He was diagnosed with cervical radiculopathy.

Pre-operative Images



Sagittal MRI showing osteophyte and disc caused stenosis



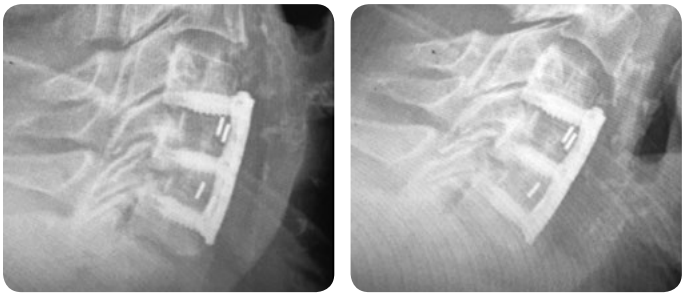
Axial MRI showing foramenal stenosis and nerve root encroachment

Surgical Procedure Performed

I performed an anterior cervical discectomy and fusion at C5-C7 utilizing a PEEK-OPTIMA HA Enhanced Interbody Device.

Radiographic Results

Post-op radiographic imagery shows solid fusion at both disc levels, and bridging between Vertebrae C5-C7 with no lucency, halo or motion between the spinous processes.



6-month Flexion Extension radiographs demonstrating solid fusion

Six-Month Results

Clinical Results

The patient resumed bucket truck work after eight weeks, and reported no further neck and arm pain with only mild residual left index finger numbness.

Conclusion

Overall, I am more confident using PEEK-OPTIMA HA enhanced interbody fusion devices than traditional PEEK devices. All eight cases utilizing the HA enhanced devices provided as good or better clinical and radiographic results than traditional PEEK Interbody Fusion Devices. Patients healed quicker and could return to normal activity after only two weeks. I'm convinced that HA integration does make a big difference in clinical outcomes.

Summary

Fifteen years of surgical implant use shows Invibio's PEEK-OPTIMA Natural is structurally sound and delivers excellent clinical results, including bone remodeling and fusion in interbody spinal fusion. The advanced polymer, PEEK-OPTIMA HA Enhanced, has shown the potential for the same material efficacy with additional osteoconductive benefits and growing case evidence of rapid bone apposition and dense bony ongrowth in interbody spinal fusions. Although, more studies are warranted, the early successes are promising. ▲

ABOUT THE AUTHORS

Timothy Bassett, MD

Dr Timothy Bassett is a board-certified orthopedic surgeon at The SouthEastern Spine Specialist Clinic in Tuscaloosa, Alabama. He earned a medical doctorate from the University of Florida, completed his residency in orthopedic surgery at the University of South Carolina, and did his one-year fellowship in adult and pediatric spinal disorders and reconstruction at the University of Wisconsin-Madison. Dr Bassett specializes in cervical and lumbar spine problems with primary focus on adult degenerative lumbar spine problems and failed lumbar fusions. He also has over 23 years-experience using interbody implants and grafts.[3]

Brad Prybis, MD

Dr Brad Prybis is a board-certified orthopedic surgeon at Carrollton Orthopaedic Clinic in Carrollton, Georgia. He earned a medical engineering degree from Georgia Tech and medical doctorate from the Medical College of Georgia. Later Dr Prybis completed his residency in orthopedic surgery at the University of South Carolina and one-year fellowship in spine surgery at the renowned Scoliosis and Spine Center in Baltimore, Maryland. He specializes in spine, neck and back pain, scoliosis, herniated discs, degeneration, injuries and tumors.[4]

REFERENCES

1. Invibio Data on File. Unloaded Long Bone Ovine Model, Bone Implant Interface Study. Data has not been correlated with human clinical data.
2. Invibio Data on File. Loaded Cervical Fusion Ovine Model, Functional Biomechanics Material Impact Study. Data has not been correlated with human clinical data.
3. Since 2016, Timothy Bassett, MD has provided ad hoc consultancy services to Invibio Ltd.
4. During 2016 to 2017, Brad Prybis, MD provided ad hoc consultancy services to Invibio Ltd.

Using Evidence-Based Medicine to Evaluate Interbody Spinal Fusion Device Materials

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Many spinal interbody fusion technologies are being brought to market today. Unsurprisingly, their introduction also brings an array of research data and clinical studies detailing bone ongrowth, fusion rates, and complications such as subsidence and delamination.

With such a rapid introduction of new technologies, how can today's surgeons determine the most effective technologies and products for enhancing their patient's standard of care? The answer is Evidence-Based Medicine (EBM).

What is Evidence-Based Medicine?

The most common definition of evidence-based medicine is 'the conscientious, explicit and judicious use of current best evidence in making decisions about the care of the individual patient'.[1]

This means the integration of clinical expertise, patient values and the best research evidence into the decision making process for patient care. Clinical expertise refers to the clinician's cumulative experience, education and clinical skills. The patient brings to the encounter his or her own personal preferences and unique concerns, expectations and values. The best research evidence is usually found in clinically relevant research that has been conducted using sound methodology.[2]

Ultimately, the goal of evidence-based medicine is to improve patient outcomes, quality of care and provide standardization of treatment.

When reviewing clinical evidence in a particular therapeutic area it is important to understand there are different levels of evidence; that is, not all forms of evidence can be considered equal in value. Evidence-based medicine essentially classifies available clinical evidence and assigns a quality level, based on its freedom from various biases and most importantly determines its correlation with positive clinical outcomes.

Levels of Evidence

The key to evidence-based medicine and effective clinical decision-making is the level of evidence supporting the performance of medical devices and therapeutics. Several organizations have developed level of evidence grading systems for assessing the quality of evidence. For this article, we will utilize the Oxford (UK) CEBM (Centre for Evidence-Based Medicine) Levels of Evidence, which were last updated in March 2009.[3]

In simple terms, the levels of evidence can be summarized below:

Levels of Evidence

Level 1a	Evidence from systematic review of randomized controlled trials
Level 1b	Evidence from an individual randomized controlled trial
Level 2a	Evidence from systematic review of cohort studies (with homogeneity)
Level 2b	Evidence from individual cohort study or low-quality randomized controlled trial
Level 2c	Evidence from outcomes research and ecological studies
Level 3a	Evidence from systematic review of case-control studies (with homogeneity)
Level 3b	Evidence from an individual case-control study
Level 4	Evidence from case-series or low-quality cohort and case-control studies
Level 5	Expert opinion without explicit critical appraisal or based on physiology, bench research or 'first principles'

Level 1 data is the most rigorous and is generally accepted as the most reliable evidence of whether a treatment is effective. In contrast, Level 5 data offers the least amount of evidence in this regard. For example, while basic animal and *in vitro* data are helpful, they do not necessarily correlate to patient clinical outcomes and should be viewed only as a supplement to higher level clinical evidence.

To understand what these levels of clinical evidence offer, further explanation is provided:[3]

Level 1 Clinical Evidence

- **Systematic Reviews** are literature reviews of peer-reviewed publications about a specific health problem. They use rigorous, standardized methods for selecting and assessing articles, and may or may not include a meta-analysis, which is a quantitative summary of the results.
- **Homogeneity** is a systematic review that is free of worrisome variations (heterogeneity) between individual studies. Studies displaying worrisome heterogeneity should be tagged with a "-" at the end of their designated level.
- **Randomized Control Trials** randomly allocate subjects into study and control groups, either receiving or not receiving an experimental preventive, therapeutic

or diagnostic procedure. They are then followed to determine the interventional effects. The results are assessed by rigorous comparison of outcomes in both groups.

Level 2 Clinical Evidence

- **Cohort Studies** involve subsets of a defined population that have been or may be exposed to factors, which may influence the probability of a disease occurrence or other outcome. Large numbers are typically observed over a period of years with incidence rates compared in groups with different exposure levels.
- **"Outcomes" Research; Ecological Studies** seek to understand the end results of particular health care practices and interventions that people experience and care about. Measures can include quality of life and preferences, effectiveness of health-care delivery, cost-effectiveness, health status and disease burden.[4]

Level 3 Clinical Evidence

- **Case Control Studies** include subjects with a specific disease or outcome and a control group without the disease or outcome. A specific disease attribute is studied by comparing it against the non-diseased with regard to frequency of presence or the quantitative levels in each group.

Level 4 Clinical Evidence

- **Case Series** consist of a group of case reports including patients who were provided similar treatment. They typically contain detailed information about the individual patients including: demographic information, diagnosis, treatment, treatment response, and post-treatment follow-up.

Level 5 Clinical Evidence

- **Non-Human Clinical Studies** include animal and biomechanical studies, *in-vitro* studies and expert opinions.

When considering new interbody spinal fusion materials, surgeons must consider not only key clinical data such as fusion and subsidence rates, but also how robust the data is in terms of level of evidence.

The following review and evaluation considers key clinical data, results and the associated level of evidence for some of today's interbody spinal fusion device materials including:

- PEEK-OPTIMA™ Natural
- PEEK-OPTIMA HA Enhanced
- Titanium-Coated PEEK
- Titan Spine Endoskeleton®
- Porous Trabecular Metal™
- 3D Printed Titanium

Existing Standard of Care

PEEK-OPTIMA Natural

PEEK-OPTIMA Natural polymer with over 15 years of clinical history, has been used in approximately nine million implanted medical devices worldwide, including interbody fusion devices. Among the product's benefits are its high mechanical strength and biocompatibility. However, of greatest clinical significance are its radiolucency and bone-like modulus of elasticity, which promotes higher stress distribution and consequently, bone remodeling and fusion. In contrast, titanium can stress shield the bone graft, creating concentrations between implants and endplates resulting in subsidence.

PEEK-OPTIMA Natural spinal cages are backed by years of quality, high-level clinical evidence reporting high fusion rates and correspondingly good clinical outcomes. Systematic reviews and meta-analyses (Level 1a Clinical Evidence) have reported at least equivalent fusion rates and lower subsidence rates with PEEK-OPTIMA Natural compared to titanium interbody spinal cages.[5-7] Dozens of peer-reviewed clinical papers and a majority of the clinical studies have yielded similar results, as indicated in the charts below.

PEEK Clinical Literature Review

Systematic Review: PEEK and PEEK CF-Reinforced vs. Titanium in ACDF[5]

Cage Material	Good-to-excellent Clinical Outcome (%)	Fusion Rate at 12 months (%)	Subsidence (%)
CF-Reinforced PEEK	76.8	62-98	29.2-49
Titanium	46-95	86.5-99	9-45
PEEK	80-96	93-100	0-14.2

Chart 1: "a majority of studies have reported improved fusion rates, lower subsidence rates and radiolucency with PEEK versus Ti cages"

Meta-Analysis: PEEK vs. Titanium[6]

Cage Material	Clinical Functional Status by Odom	Fusion Rate at 12 months	Subsidence
Titanium	70/101	93/124 (75%)	33/211 (15.6%)
PEEK	70/98	86/91 (94.5%)	11/84 (6%)

Chart 2: "Although more subsidence occured in the titanium group, the effects of loss of local segmental angle or the whole cervical Cobb angle on cervical function in the long-term are still not clear"

Although the literature reports overwhelmingly positive clinical outcomes, PEEK-OPTIMA is not a perfect material. The surface of PEEK-OPTIMA is relatively inert and not osteoconductive, therefore bone does not consistently attach to PEEK-OPTIMA. Consequently, surgeons who choose not to use PEEK-OPTIMA frequently cite its lack of bone ongrowth as the primary reason they select other materials.

PEEK-OPTIMA HA Enhanced

To address this market need for earlier bone ongrowth, Invibio developed PEEK-OPTIMA HA Enhanced, a unique compound material that incorporates the well-known oseteoconductive material hydroxyapatite (HA) into the bulk PEEK-OPTIMA matrix.

HA has a chemical and crystalline structure similar to the mineral component of bone. In fact, apatite crystals comprise around 70% of bone's dry mass.[8] HA's proven medical success spans four decades in applications including dental and orthopedic implant coatings, bone void fillers and coated screw systems for improved fixation. Its make up and benefits are also ideal for interbody spinal fusion.

Unlike surface coatings and roughened metal technology for interbody spinal fusion, PEEK-OPTIMA HA Enhanced addresses the entire environment. HA particles are fully integrated into the PEEK-OPTIMA matrix, making it available on all surfaces of a finished device. Consequently, both inner- and outer-cage graft materials are exposed to HA, resulting in enhanced osteoconductivity and eliminating delamination. Like PEEK-OPTIMA Natural, it offers a bone-like modulus of elasticity, reduced stress-shielding of bone graft and artifact-free imaging.

Pre-Clinical Studies

Pre-clinical animal studies (Level 5 Clinical Evidence) with PEEK-OPTIMA HA Enhanced are encouraging. They demonstrate greater osteointegrative benefits when compared to PEEK-OPTIMA Natural (ref. figure 1, 2).

- Enhanced bone apposition with greater than 75% direct bone contact as early as 4 weeks[9]
- Greater new bone formation at 6 weeks in a cervical fusion study[10-11]
- Higher quality new bone bridging at 6 and 12 weeks in a cervical fusion study[10-11]

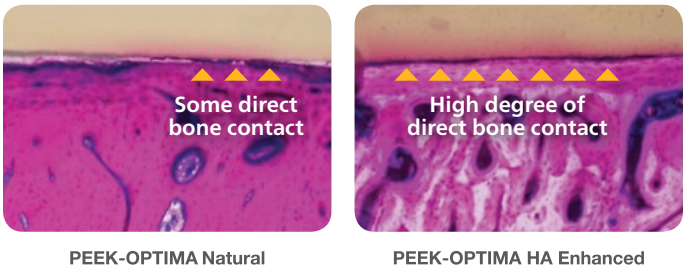


Figure 1: Cortical bone histology: Enhanced bone apposition at 12 weeks, greater direct bone contact with PEEK-OPTIMA HA Enhanced compared with PEEK-OPTIMA Natural.[9]

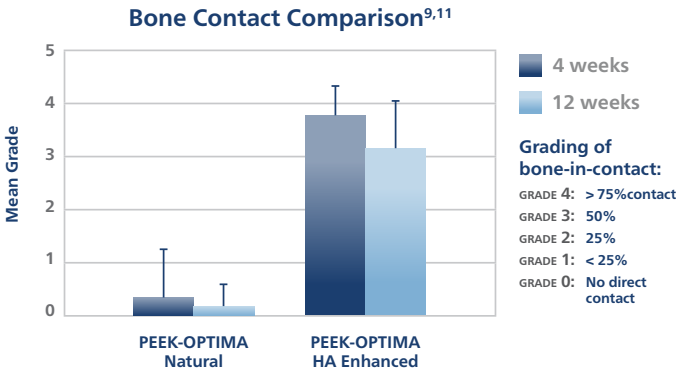


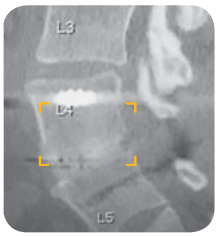
Figure 2: Earlier Bone Ongrowth: PEEK-OPTIMA HA Enhanced promotes greater than 75% direct bone contact after 4 weeks compared with PEEK-OPTIMA Natural.

Early Clinical Results

Early human clinical evidence for PEEK-OPTIMA HA Enhanced, including findings by Dr Timothy Bassett, concur with the pre-clinical studies.

Dr Timothy Bassett (SouthEastern Spine Specialists, Tuscaloosa, AL, USA) has been in private practice for 23 years and specializes in cervical and lumbar spine problems with primary focus on adult degenerative lumbar spine problems and failed lumbar fusions. He also has over 23 years experience using interbody implants and grafts.[12*]

Between October 2015 and October 2016, Dr Bassett conducted Transforaminal Lumbar Interbody Fusion (TLIF) procedures on 59 patients (78 levels). In all cases, he used the Cutting Edge Spine EVOS-HA cage made from PEEK-OPTIMA HA Enhanced. Dr Bassett later presented findings from nine cases at the 2016 North American Spine Society (NASS) Annual Meeting. In this 9-patient case series (Level 4 Clinical Evidence), 9 of 10 levels were definitively fused as shown on the 6-month, post-op CT scan, while the final case was progressing toward complete fusion. Notably, areas of dense bone apposition were observed around the implant in several patients (ref. figure 3). Correspondingly, good clinical results were achieved in this case series despite some challenging patients.



"CASE SERIES: PEEK-OPTIMA™ HA Enhanced Polymer Shows Early Clinical Success in Interbody Spinal Fusions." For further results see page 3-7.

Figure 3: Solid lumbar fusion at 6 months on CT scan.
Image courtesy of Timothy Bassett, MD

Although more quality, high evidentiary level studies are warranted, PEEK-OPTIMA HA Enhanced early successes, as an interbody spinal fusion material are promising.

Titanium (Ti) Coated PEEK

Capitalizing on PEEK-OPTIMA Natural's clinical benefits and titanium's natural propensity for bone ongrowth, Ti-Coated PEEK Cages were developed and first gained FDA 510(k) clearance in 2011. Since then, this technology has been adopted by several medical device manufacturers in their interbody spinal fusion devices. Various Levels of Clinical Evidence have been developed for this technology since its introduction into the marketplace.

A 2016 biomechanical study (Level 5 Clinical Evidence) investigated whether wear debris or delamination occurred following simulated impaction of Ti-coated PEEK cages into the disc space. It also tested whether similar sheer loading resulted in failure in surface-etched titanium cages.[13]

The same study showed mechanical testing negatively impacted Ti-coated PEEK, but not surface-etched titanium.[13] Ti-coated PEEK cages showed partial delamination, wear debris and surface damage, with more than half of the detached particles being in the size range capable of being phagocytosed.[13]

One 2017 clinical study (Level 1b Clinical Evidence) has pointed to the potential of Ti-coated PEEK devices in facilitating rapid and stable fixation with a high fusion rate.[14] However, other studies directly comparing Ti-coated PEEK and PEEK only devices have been less than definitive. A 2015 randomized clinical and radiological trial aimed to compare fusion rates and clinical results of titanium-coated PEEK cages vs. PEEK-OPTIMA Natural cages for Posterior Lumbar Interbody Fusion (PLIF) surgery.[15]

Radiographic results between the two groups were indistinguishable. At 12-month follow up, there was no migration or dislocation observed in either the Ti-coated PEEK or PEEK-OPTIMA Natural cages groups. Clinically, the two cages also performed equally well with 100% fusion rates at 12 months (ref. chart 3).

Randomized Clinical and Radiological Trial: PEEK vs. Ti-Coated PEEK Cages in PLIF[15]

	PEEK-OPTIMA	Ti-Coated PEEK
Oswestry score reduction	45 to 20	43 to 20
VAS low back pain reduction	5.2 to 2.6	6.1 to 2.6
Fusion by CT scan:		
Bone growth through cage pores	100%	100%
Bone growth outside cages	61%	48%
Fusion Rate	**100%**	**100%**

Chart 3: "Pure PEEK and Ti-coated PEEK cages for PLIF produce equally favorable clinical and radiological results 12-months post-surgery."[15]

A final prospective single-arm clinical study (Level 2b Clinical Evidence) recently published in *Patient Safety in Surgery* merits consideration.[16] This study reported outcomes for Ti-coated PEEK cages and PEEK-OPTIMA Natural cages in Anterior Cervical Discectomy and Fusion (ACDF).

As seen in Chart 4, PEEK & Ti patients had somewhat better fusion scores at 6 months. However, these differences did not persist at 12 and 18 months. The authors thereby concluded that partial Ti coating of PEEK cages does not improve the fusion rate sufficiently or confer other lasting clinical benefits.[16]

Despite the popularity of Ti-coated PEEK devices, clinical evidence, fusion and biomechanical studies to date have shown mixed results.

Multi-Center Comparative Analysis: Ti-Coated PEEK vs. PEEK-OPTIMA Natural Cages in ACDF[16]

49 patient pairs	Both PEEK & Ti PEEK Fused	Both PEEK & Ti PEEK **not** Fused	Only PEEK Fused	Only Ti PEEK Fused
6 month	14	17	5	13
12 month	28	6	6	9
18 months	33	4	6	6

Chart 4

Titan Spine Endoskeleton®

Titan Spine received 510(k) clearance for their Endoskeleton interbody fusion implants, made from Titanium, with proprietary nanoLOCK™ surface technology in 2014. The technology is promoted as having a unique combination of roughened topography at the macro, micro and nano levels. Such topography is claimed to create optimal host bone response, up-regulate osteogenic and angiogenic growth factors that promote bone growth, and encourage natural production of bone morphogenetic proteins (BMPs).

These claims are supported only by *in vitro* cell studies (Level 5 Clinical Evidence) and strictly measure material-cell response. While *in vitro* cell data is reasonable basic science for assessment of cell response to materials, these results do not take into account biomechanical factors such as stress, micro-motion, and potential patient co-morbidities including diabetes, smoking and poor bone quality, which contribute to a more complex clinical environment. These studies represent the lowest level of clinical and scientific evidence available in the literature. Therefore, conclusions on clinical benefits cannot be reached based on *in vitro* cell studies alone.

Market adoption of Endoskeleton spinal implants with the nanoLOCK surface technology will require studies with higher quality and Level of Evidence.

Porous Trabecular Metal

Introduced in 2006, porous Trabecular Metal technology is not new to the spinal industry and has demonstrated clinical use in a variety of orthopedic applications.[17-19] It is a highly porous biomaterial made from tantalum with structural, functional and physiological properties similar to that of bone.[20] Early animal studies (Level 5 Clinical Evidence) comparing porous Trabecular Metal to PEEK-OPTIMA Natural appeared promising.

In one study, porous Trabecular Metal supported bone growth into and around the implant margins better than PEEK-OPTIMA Natural.[21] Its open-cell porous nature facilitated the host-bone ingrowth and bone bridging through the device. However, subsequent clinical human data did not correlate with the animal results.

In a higher level, prospective randomized, controlled clinical study (Level 1b Clinical Evidence), porous Trabecular Metal fusion rates were just 69%.[22] Another 2013 study indicated even lower fusion rates of 38% and showed significant device fragmentation (ref. figure 4).[23]

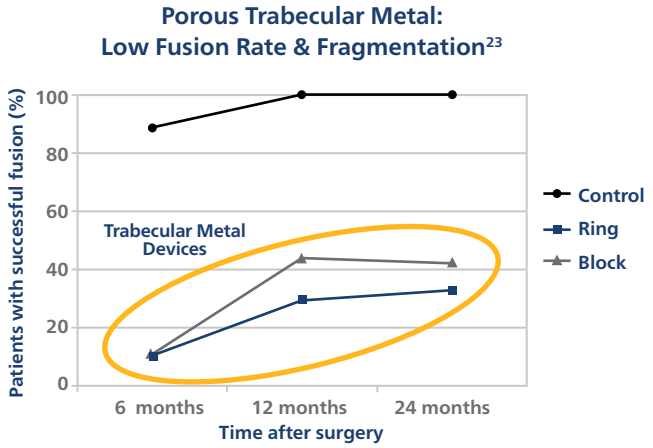


Figure 4: Only 38% of patients fused at 24 months; 27.8% exhibited device fragmentation.[23]

Animal and clinical data ambiguity again shines a spotlight on the importance of Level of Evidence in determining clinical efficacy. Moreover, such ambiguities clearly indicate a need for further non-animal, high Level of Evidence studies for effective evaluation of and confidence in new technologies.

3D Printed Titanium

3D Printed Titanium devices are offered by several companies including Stryker, K2M and 4Web. This technology is new to the interbody spinal fusion market and these devices have been developed to promote bone ongrowth. In addition to promoting bone ongrowth, K2M claims bone in-growth with 70% porosity and rough surfaces for enhanced cellular activity.[24]

Due to the technology's short history, little clinical data is available in the public domain. Proving clinical efficacy for 3D Printed Titanium lies with each device manufacturer.

Summary

As new spinal fusion technologies are introduced and before device selection, surgeons must continue to carefully weigh the Level of Clinical Evidence behind the claims to determine if it correlates to actual human clinical benefit (ref. chart 5 for a summary of the Level of Clinical Evidence for studies reviewed in this article). For their part, device and material manufacturers must continue to conduct high Level of Evidence studies that provide the proof required to demonstrate patient benefit, drive market adoption and continue to advance medical, and particularly, spinal interbody fusion materials and technology. ▲

Technology	Highest Level of Clinical Evidence	Type of Study
PEEK-OPTIMA	Level 1a	Systematic Reviews and Meta-Analyses
PEEK-OPTIMA HA Enhanced	Level 4	Case Series
Titanium (Ti) Coated PEEK	Level 5	Mechanical Testing
	Level 1b	A Randomized Clinical and Radiological Trial
	Level 2b	Prospective Single Arm Clinical Study
Titan Spine Endoskeleton	Level 5	*in vitro* cell studies
Porous Trabecular Metal	Level 5	Animal Studies
	Level 1b	Prospective Randomized Controlled Clinical Study
3D Printed Titanium	Level 5	Animal Studies

Chart 5: Table is based on the studies reviewed in this article.

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Dr Sheryl O'Farrell holds the position of Clinical Study Manager at Invibio Biomaterial Solutions. Previously, Dr O'Farrell worked at Medvance Ltd. for 10 years as the Head of Clinical Operations & Quality Assurance, Johnson & Johnson as Project Manager for Spine, Bio-medical Research, Ltd. as Head of Clinical Research, among other medical technology companies. In 2003, she received her PhD from the University of Liverpool, United Kingdom.

Mark Brady, PhD

Dr Mark Brady is the Senior Spine Technology Manager for Invibio Biomaterial Solutions where he was responsible for leading the development of PEEK-OPTIMA HA Enhanced. Prior to his position at Invibio, Dr Brady was a Principal Scientist at Renovo working on the mechanism of action of lead drug candidates and, prior to that, a Senior Research Associate at the University of Liverpool. In 2001, he received his PhD from the University of Liverpool, United Kingdom.

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* The case studies and testimonial presented have been provided by a practicing orthopedic surgeon. His view and experiences are his own and do not necessarily reflect those of others. "Invibio" disclaims any liabilities or loss in connection with the information herein.

FDA Reclassification Paves Regulatory Pathway for Invibio PEEK-OPTIMA™ Spinal Rods

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Request for Reclassification

Until recently, posterior spinal rods and rigid pedicle screw systems, fell under the FDA Order 522 for Class III devices. Class III devices are considered "highest risk" and must follow the FDA's most stringent regulatory pathway, which requires a vigorous Premarket Application (PMA). Class III devices require a robust and completely independent clinical history not based on predicate devices, and therefore can lengthen the time and cost to market.

Invibio Biomaterial Solutions, along with other medical device manufacturers, were requested to submit to the order to reclassify spinal rods and rigid pedicle screw systems, supporting a modification to allow semi-rigid spinal rods to remain Class II devices.

Clinical and biomechanical evidence from over 51,000 PEEK Rod implantations was submitted in support of reclassifying PEEK-OPTIMA Spinal Rods as a Class II device. Class II devices, like Class III devices, require general and special controls that ensure compliance with the FDA's best quality and manufacturing processes, proper labeling and reporting, and adherence to other FDA-imposed special controls that ensure device safety and effectiveness. However, in lieu of the very involved PMA process, Class II devices typically follow the Premarket Notification 510(k) pathway, which provides a much clearer and timely route to market.

Substantial evidence indicated PEEK-OPTIMA Rods were technologically and physically similar to other Class II rigid pedicle systems, not the Class III dynamic stabilization system devices, in which the device had previously been grouped. As a result of the device design and material properties, PEEK-OPTIMA Rods maintain interpedicular distance, eliminating compression and elasticity often found in Class III dynamic stabilization systems. Furthermore, the predominant indication for use as an adjunct to spinal fusion, not dynamic stabilization, offered a new context for reclassification. Several clinical publications have reported high fusion rates, low re-operation rates due to adjacent segment disease and good to excellent clinical outcome scores with PEEK Rods.[1-5]

FDA Reclassification Ruling

The FDA issued a final ruling on December 29, 2016, crediting all stakeholders who contributed to this effort.

Under the final ruling:

1. Pedicle screw systems, including PEEK-OPTIMA polymer-based rods, when used as an adjunct to spinal fusion procedures are:
   a. Reclassified from Class III to Class II devices.
   b. Renamed "thoracolumbosacral pedicle screw systems."
2. Dynamic stabilization systems, when used as an adjunct to fusion are:
   a. Reclassified from Class III to Class II devices with special controls.
   b. Renamed "semi-rigid systems". PEEK-OPTIMA polymer-based rods are included in this sub-type.
3. Thoracolumbosacral pedicle screw systems will be more precisely defined to delineate between rigid and semi-rigid systems.

The FDA also indicated that device technology, like Invibio PEEK-OPTIMA Rods, could fit the new semi-ridged system product class, but would require clinical performance data supporting clear and adequate technological evaluation. Data would need to be representative of design and footprints, correspond to the product being submitted for FDA 510(k) clearance, and along with other Class II general and special controls, provide a reasonable assurance of semi-rigid system safety and effectiveness.

Under the reclassification, manufacturers of current marketed semi-rigid systems, for all indications for use, must submit a 510(k) amendment and comply with ruling-defined special controls by June 30, 2019. To that end, Invibio will enlist a sponsor to assist with obtaining 510(k) clearances for its newly named Class II device, the PEEK-OPTIMA Spinal Rods for spinal lumbar fusion.

The FDA also suggested a continued industry-wide collaboration in eventually removing the clinical data requirement. Doing so would make the 510(k) clearance for Class II semi-rigid devices even more timely and efficient, and foster further technological innovation. That's good news for manufacturers and patients alike. ▲

Why Metal Rod Alternatives Are Necessary

Spinal rods composed of metal are not without challenges, including, but not limited to, rod breakage, screw loosening, and accelerated degeneration at adjacent spinal segments. The high stiffness inherent in all-metal constructs is believed to contribute to these clinical challenges and negatively impact patient outcomes.[6-7] In addition, metals like titanium lack artifact-free imaging, which impacts a surgeon's ability to assess posterior decompression and fusion post-operatively.

Semi-Rigid Rods May Bridge Treatment Gap

PEEK-OPTIMA Spinal Rods offer a polymer-based stabilization. The material exhibits sufficient strength to reduce the range of motion[7-8] and stabilize the treated segment.[9] And, with a modulus similar to cortical bone, PEEK still permits physiological movement on adjacent upper and lower segments.[8] As a result, clinical results increasingly suggest that PEEK-OPTIMA Spinal Rod components preserve or slow down the degeneration of adjacent discs.[3] Consequently, patients may benefit from improved load sharing that encourages fusion,[7,10-11] and more physiologic loading at adjacent levels, which may decelerate degeneration.[1,12]

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Craig Valentine

Craig Valentine is the Director of Quality and Regulatory Affairs for Invibio Biomaterial Solutions. Having graduated from the University of Wales at Cardiff in Polymer Chemistry and Technology, Craig moved to the United States, where he spent 12 years in various technical and R&D roles. In 2007 he moved back to his native England to join Invibio. In his present role, Craig oversees Quality Assurance, Compliance and accreditation for Invibio. In addition, he leads the global RA support team and all product registration activities.

Further information on the final ruling can be found at "Orthopedic Devices; Reclassification of Pedicle Screw Systems, Henceforth To Be Known as Thoracolumbosacral Pedicle Systems, Including Semi-Rigid Systems."

For more information on Invibio PEEK-OPTIMA Rods, please visit https://invibio.com/

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Imaging Benefits Across Trauma Patient Care

AUTHOR: Sherri Gambill – Invibio Biomaterial Solutions

The imaging characteristics of PEEK-OPTIMA™ Ultra-Reinforced offer numerous benefits intraoperatively and throughout the healing process. Implants composed of a composite of carbon fiber and PEEK-OPTIMA Polymer are radiolucent, providing surgeons 360° fracture visibility during and after surgery. This enhanced visibility enables better, safer, and quicker procedures and increased confidence in returning patients to load-bearing activities.

OR Improvements with Potential Cost Reduction

Better Procedures

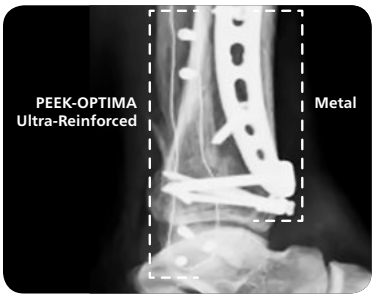

Photo courtesy of Joshua Niemann, M.D.

Unimpeded visibility of the fracture can help surgeons ensure proper alignment. In 11 publications reporting on implantations of carbon fiber based PEEK implants for fracture treatment, all discuss more accurate assessment of fracture reduction due to the implant radiolucency.[1-11] More specifically, in a study of 17 proximal humerus fractures, reduction accuracy was assessed as anatomic or near-anatomic in all cases, with the only exception in cases where the deforming forces precluded an anatomic reduction.[5]

Safer Procedures

With the two cortices visible in all radiographic planes, the risk of adverse events during surgery can be reduced. In three publications of proximal humerus fractures, there were no primary screw perforations.[5,8,9] This non-occurrence may be attributed to the radiolucency of the plate, as the rate of screw perforation in metal plates ranges from 1-12%.[12,13]

As a benefit to healthcare workers, the ease of visualization may reduce radiation exposure. A case series of proximal humerus fractures demonstrated that the PEEK-OPTIMA Ultra-Reinforced plates required less than 1.35 minutes of fluoroscopy on average[5] compared to an average of 1.4 to 6.4 minutes for metallic plates.[13-15]

Quicker Procedures

Enhanced visualization may reduce surgical times, leading to reduced cost of the overall procedure. A distal fibula case series demonstrated an 18% reduction in surgical time for tri-malleolar fractures.[2]

Increase Confidence to Progress Patients Through Recovery

In addition to the benefits provided intraoperatively, the improved visualization offers benefits throughout the healing process. Surgeons can gain better visibility of fracture healing during follow-up visits and increase confidence in returning patients to function quicker.

> "How quickly do you let them walk on it? How quickly do you release them from their sling or brace and start working towards their daily life, and their original function? With better visibility, you get better assurance that what you're seeing is what you're really seeing, and you can progress people a little faster."*
>
> **- Joshua J. Neimann, MD[16]**
> Liberty Orthopedics, Liberty, MO

Benefits in Tumor Treatment

The imaging characteristics over the follow-up period are particularly advantageous in the treatment of pathologic or impending fractures due to bone tumors, especially when local adjuvant radiotherapy is indicated. The adjuvant radiotherapy is often critical in reducing the risk of local disease progression, and its success depends on the accuracy of target identification and dose prescription. Traditional titanium or stainless steel implants can obstruct the postoperative surveillance imaging, particularly in areas adjacent to the implant, making it more challenging to detect recurrent disease, and increase inaccuracies in radiotherapy dosing.

In a comparative analysis of titanium and carbon fiber PEEK nails, the carbon fiber PEEK nails had significantly less MRI and CT artifact, allowing for greater visualization of the anatomic areas adjacent to the implant.[17] In two studies comparing carbon fiber reinforced (CFR) PEEK devices with titanium alloy devices, the difference between measured and calculated doses demonstrated a maximum overdose of 10% and underdose of 20% to 30% for the titanium alloy implants. For CFR-PEEK implants, the differences were within 0-5%.[18,19]

Conclusion

The use of osteosynthesis devices composed of PEEK-OPTIMA Ultra-Reinforced offers benefits across the continuum of patient care. Intraoperatively, the 360° fracture visibility can improve functionality, may be better and safer for the patient, and has the potential to reduce surgical time. The unobstructed imaging makes it easier for surgeons to assess healing with the potential to progress patients a little quicker. For patients needing follow-up MRI or CT diagnostics, the artifact-free imaging improves visualization of surrounding tissues. In cancer patients, monitoring for disease progression or recurrence is easier and radiotherapy dosing has been shown to be more accurate. The benefits of the radiolucency extend beyond just an easier surgery, and have the potential to provide benefits to the surgeon, hospital system, and ultimately, patients from initial surgery through the healing process. ▲

ABOUT THE AUTHOR

Sherri Gambill

Sherri (Wykosky) Gambill is currently Trauma Technology Manager at Invibio Biomaterial Solutions where she is responsible for product development. Previously, as Business Development Associate she maintained relationships across client organizations as they adopted new biomaterials. Prior to Invibio, Sherri was a Product Development Engineer at DePuy Synthes and BD Opthalmic Systems, where she designed and developed implants and instrumentation for orthopaedic trauma and glaucoma treatment. In 2006, Sherri received a Bachelor of Science (BS) degree in Bioengineering at the University of Pennsylvania in Philadelphia, PA, USA.

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*The testimonial presented has been provided by a practicing orthopedic surgeon. His view and experiences are his own and do not necessarily reflect those of others. "Invibio" disclaims any liabilities or loss in connection with the information herein.

COMMENTARY ON:

Is Locking Screw Fixation in Carbon Fiber Composite Plates Mechanically Equivalent to Stainless Steel Plates?

COMMENTARY AUTHOR: David J. Hak, MD, MBA, FACS – Interim Director of the Department of Orthopedics at Denver Health/ University of Colorado

AUTHOR OF ORIGINAL ABSTRACT: David J. Hak, MD, MBA, FACS

PRESENTED AT: 3rd International PEEK Meeting, April 27, 2017; Orthopaedic Research Society (ORS) 2016 Annual Meeting, Poster 2213

LEVEL OF EVIDENCE: Peer Reviewed, Pre-clinical, *In-vitro* Study[1]

Overview

Carbon fiber reinforced PEEK is gaining popularity for fracture fixation due to its high fatigue strength, favorable modulus of elasticity, and radiolucency.

This study sought to compare the mechanical stability of locking screws in locking proximal humerus plates composed of PEEK-OPTIMA™ Ultra-Reinforced polymer versus stainless steel, finding that the screws inserted into PEEK-OPTIMA Ultra-Reinforced plates tolerated an equivalent or superior load to failure.

Figure 1 - Proximal humerus plate made with PEEK-OPTIMA Ultra-Reinforced polymer

Courtesy of CarboFix Orthopedics, Inc.

Summary

This study compared proximal humerus locking plates manufactured from PEEK-OPTIMA Ultra-Reinforced polymer (CarboFix Orthopedics, Inc., ref. figure 1) and stainless steel (DePuy Synthes, Inc.). Screws were inserted in both the proximal and diaphyseal portions of the plate, and the stiffness and load to failure were measured under cantilever bending.

The load to failure of the diaphyseal locking screws was significantly greater in the PEEK-OPTIMA Ultra-Reinforced plate. The load to failure of the proximal screws was comparable for both materials. Stiffness was comparable between materials in both the proximal and diaphyseal sections of the plate (ref. figures 2,3).

The study further assessed the implication of inserting, removing, and reinserting a screw at the same angle, and found no difference after the second insertion. Stiffness and load to failure were greater when inserting a screw on-axis versus a 10° off-axis deviation.

Key Findings

PEEK-OPTIMA Ultra-Reinforced locking plates provide comparable or superior locking screw fixation strength when compared to traditional stainless steel locking plates.

Locking strength is not significantly compromised by reinserting a screw.

Inserting a screw on-axis increased the mechanical stability versus insertion at 10° off-axis. This finding is in line with other systems, as reduction in strength of polyaxial locking screws inserted off-axis is also seen in metallic systems.[2,3]

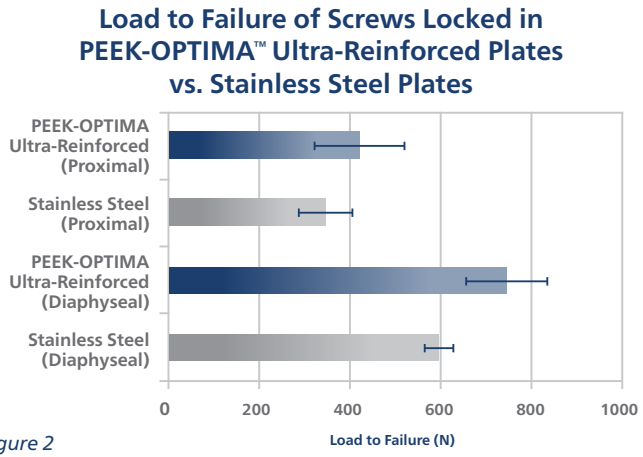

Figure 2

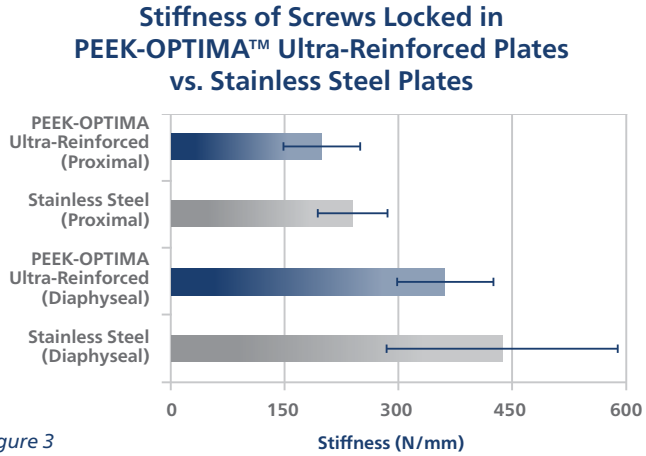

Figure 3

Commentary

This study demonstrates comparable, and in some cases superior performance of currently marketed carbon fiber reinforced PEEK plates compared to stainless steel plates when assessing screw stability. While this study is a laboratory study and cannot completely simulate the *in vivo* environment, there are clinical studies demonstrating favorable outcomes of carbon fiber reinforced PEEK proximal humerus plates including: improved functional scores, fewer complications,

reduced surgical time, and improved lateral imaging compared to metallic plates.[4-7]

Point of View

Carbon fiber based PEEK locking trauma plates afford excellent mechanical stability and improved intraoperative visualization compared to traditional stainless steel locking plates. Their use in the treatment of proximal humerus fractures may decrease the incidence of postoperative complications relative to traditional treatment methods. Additional studies are necessary to inform their optimal use *in vivo.* ▲

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Dr David J. Hak is the Interim Director of the Department of Orthopedics at Denver Health/ University of Colorado. Dr Hak is a member of the American Academy of Orthopaedic Surgeons, American Orthopaedic Association, Orthopaedic Research Society, and the Orthopaedic Trauma Association. He currently serves on the Editorial Board of the Journal of Orthopaedic Trauma, as Chair of the ORS/ISFR Committee, and recently served as Chief Financial Officer of the Orthopaedic Trauma Association.

Dr Hak is a graduate of the Ohio State University. He completed his internship and residency training at the University of California, Los Angeles and a Trauma Fellowship at the University of California, Davis. He has served on the faculty at the University of Michigan and at the University of California, Davis prior to assuming his current position. Dr Hak is actively involved in both clinical and basic science research relating to fracture healing biology, bone morphogenetic proteins, role of mesenchymal stem cells in fracture healing, and the effects of aging on fracture healing.[8]

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Manufacturing Trauma Fracture Fixation Implants: Partnering with Invibio

AUTHOR: Sherri Gambill – Invibio Biomaterial Solutions

Overview

Metal implants have been used for over 50 years with generally good outcomes, but in some fractures, complications related to non-unions, delayed unions, and implant failure continue to be a challenge, with overly stiff constructs as a reported risk factor.[1,2] PEEK-OPTIMA™ Ultra-Reinforced is a composite material growing in popularity as an alternative to stainless steel and titanium for fracture fixation devices, and has seen clinical success in a variety of application areas.[3-6]

PEEK-OPTIMA Ultra-Reinforced combines the high performance material properties of PEEK-OPTIMA Polymer with the strength imparted by continuous carbon fibers. When manufactured into trauma devices, PEEK-OPTIMA Ultra-Reinforced enables semi-rigid fixation with improved fatigue and imaging properties over metal.[7] Unlike metals, the carbon fiber PEEK offers the ability to tailor the mechanical properties of the implant without altering the geometry, offering increased design flexibility to meet the device requirements.

Partnering with Invibio enables medical device companies to expand their trauma product offerings beyond metal technologies at a fraction of the time and investment it would take to translate from a metal to composite solution internally. Medical device manufacturers can leverage Invibio's expertise in composite technology, state-of-the-art tools, and dedicated manufacturing facility to bring new fracture management solutions to market.

Idea to Innovation – do more with fewer resources

Medical device manufacturers are experts in implant design, but converting those designs to composites requires time and money to build the knowledge, processing capabilities and supply chains internally. Invibio has invested heavily to build the capabilities required to deliver these components including: basic research, composite processing knowledge, and application-specific knowledge. A dedicated staff, assembled from the polymer/composite and medical device industries, works with partners from concept through production to overcome design and manufacturing challenges by offering comprehensive assistance, including design for manufacturing, prototyping, testing, and regulatory support. Invibio's state-of-the-art manufacturing facilities are operated under ISO 13485 certified quality management system and feature dedicated medical testing laboratories and a controlled manufacturing environment. These investments enable medical device companies to iterate quickly with low risk and decreased investment compared to developing on their own.

Design for Manufacturing

Prototyping and Testing

Components of any size and length can be produced, from small extremity plates to large distal femur plates. The process of plate creation is controlled by Invibio, from monomer through plate production. The process begins with the production of PEEK-OPTIMA Natural, which is then combined with carbon fibers into a tape. The tape is cut and compression molded into semi-finished components, and then finished to the customer's design specifications and inspected.

Continuous Carbon Fiber & PEEK-OPTIMA Polymer | *PEEK-OPTIMA Ultra-Reinforced Tape* | *Manufactured to Design Specifications* | *Finished Component*

Clinical Relevance – why change materials?

Locked plating is a significant advancement in fracture care resulting in improved patient outcomes for certain fractures.[8] However, early reports of clinical success were followed by reports of clinical failures, which suggested that in some applications, the plate and screw construct may be too rigid, inhibiting the interfragmentary micromotion necessary to permit secondary healing by callus formation.[9,10] Distal femur fractures are an often cited example where overly stiff locking plate constructs may lead to healing difficulties, with recent studies reporting non-union rates up to 20%[2,11-15]

Strategies have been developed for reducing construct stiffness in three areas: (1) modifications in the surgical technique for existing plates and screws, (2) new screw designs, and (3) material advancements. Focusing on material advancements, studies have shown that a material with a lower elastic modulus may improve outcomes. More flexible titanium plates produce more callus and have fewer non-unions than stainless steel plates.[2,9,14-16] PEEK-OPTIMA Ultra-Reinforced provides another alternative to the goal of more flexible fixation.

Testing demonstrates a plate produced from PEEK-OPTIMA Ultra-Reinforced can have reduced stiffness and greater fatigue strength than a titanium plate of the same geometry.[7]

Performance – Design Flexibility through Material

Carbon Fiber PEEK polymer plate stiffness and strength come not only from the plate geometry, but from the orientation of the carbon fibers throughout the plate, offering a huge array of choices to meet device specifications. This design flexibility is why carbon fiber devices have been adopted not only in medical devices, but in many advanced applications including the aerospace and automotive industries.

The plate geometry does not need to change in order to alter mechanical properties. In a 4-point bend test (per ASTM F382) of four identical generic distal femur plates, changes to the order of fiber orientation enabled a reduction in stiffness without a significant impact to the yield strength. In the example of Variant A to B, reducing stiffness by 12% resulted in a loss of yield strength of only 2% (ref. figure 1).[7]

Distal Femur Plate: 4-Point Bend Testing[7]

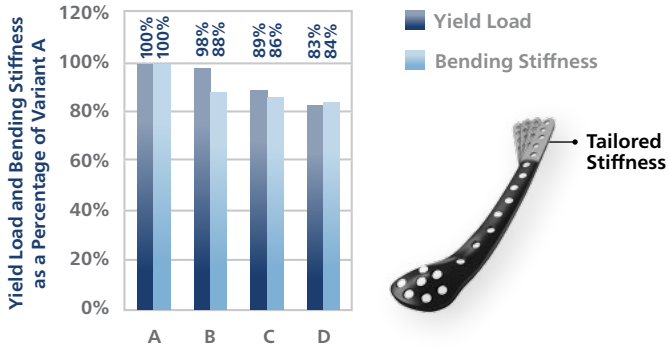

Figure 1

Conclusion

Invibio's investment in research and development, staff, and facilities to produce composite trauma plates enables medical device manufacturers to provide new options for treating traumatic injuries, with the potential for improved OR and point of care efficiencies, increased confidence to progress patients through recovery, and fewer and easier revisions.[7]

ABOUT THE AUTHOR

Sherri Gambill

Sherri (Wykosky) Gambill is currently Trauma Technology Manager at Invibio Biomaterial Solutions where she is responsible for product development. Previously, as Business Development Associate, she maintained relationships across client organizations as they adopted new biomaterials. Prior to Invibio, Sherri was a Product Development Engineer at DePuy Synthes and BD Opthalmic Systems, where she designed and developed implants and instrumentation for orthopaedic trauma and glaucoma treatment. In 2006, Sherri received a Bachelor of Science (BS) degree in Bioengineering at the University of Pennsylvania in Philadelphia, PA, USA.

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Advantages of PEEK Dental Prosthetic Frameworks over Metal

A Clinical Case Review

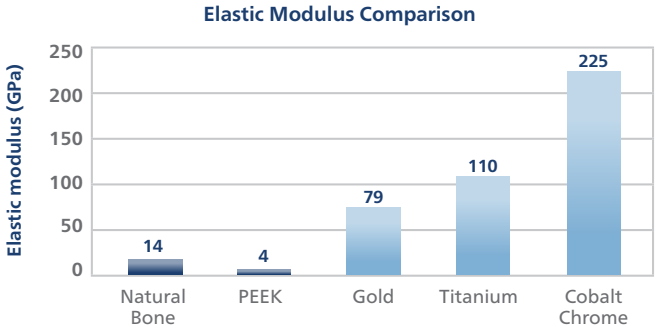
AUTHOR: Marcus Jarman-Smith, PhD – Invibio Biomaterial Solutions

Since 1978, Polyetheretherketone (PEEK) high performance polymer has been a dependable metal alternative across many industries. For medical applications, PEEK is valued for its strength, corrosion resistance, radiolucency and bone-like modulus of elasticity. Invibio Biomaterial Solutions pioneered many of the medical market applications with PEEK-OPTIMA™, a proven medical-grade polymer that has been used in approximately nine million implanted devices worldwide.

The dental industry has taken note. First used in temporary abutments and healing caps, PEEK-OPTIMA polymer usage has been extended to other dental applications including long-term fixed and removable prosthetic frameworks via the JUVORA™ dental disc.

The Benefits of PEEK (PAEK) Prosthetic Frameworks

The high-performance polymer offers several mechanical benefits over metal frameworks – namely, a more favorable strength-to-weight ratio and the potential for shock absorption[1] (Ref. Figure 1). Metal prosthetics are naturally stronger and exhibit higher compressive strengths than PEEK, however resilience and patient comfort are also clinically significant.[2]



Rho, JY (1993). "Young's modulus of trabecular and cortical bone material". Journal of Biomechanics 26 (2): 111-119.

Figure 1: PEEK has a bone-like elastic modulus of 4-5GPa, considerably less stiff than metal. As a result, PEEK prosthetic frameworks provide the potential for added shock absorption.[3]

Just as the physical properties of PEEK are attractive, so is its flexibility in fabrication. CAD/CAM PEEK milling has been used as an alternative to injection-molding since 2012. CAD/CAM milled implant prosthetics are fabricated more quickly, and in a reproducible, highly precise, lower cost fabrication process without compromising material composition, shape or quality.[4]

JUVORA Dental Disc
Made from PEEK-OPTIMA, a high performance polymer solution for long-term[1] fixed and removable prosthetic frameworks, provides 26x more shock absorption[3] than titanium for superior comfort.

PEEK Case Studies

Professor Paul Tipton and Dr Bernd Siewert have practiced, taught and authored papers on dental implants and prosthetics for 60-plus years combined. They have experienced considerable success using non-metal, PEEK high performance polymers in fixed and removable prosthetics.

Tipton and Siewert have conducted case studies to test PEEK fabrication methods, CAD/CAM milling versus traditional injection-molding pressing, and their effects on material structure and long-term clinical reliability. They have also tested PEEK's clinical outcomes in patients with bruxism and as long-term, complex and semi-removable prosthetic frameworks. The following summarizes two published case studies.

Professor Paul Tipton, BDS MSc DGDP RCS is an internationally renowned Prosthodontic Specialist. Now Professor of Restorative and Cosmetic Dentistry at the City of London Dental School, he has over 30 years experience in private practice, founded Tipton Training, Ltd. dental training academy, and has authored over 100 scientific articles.[5]

Dr Bernd Siewert has been in private practice for over 20 years. Since 2007, he's been an instructor at Germany's International Training Center for Dental Implantology (IFZI), and authored and spoken internationally about his specialty, implantology.[6]

Case 1[4]

A 55-year-old female presented with severe bruxism and heavily damaged bar-supported overdenture over four implants (Ref. Figure 2). The initial prosthetic restoration included a fixed, removable and horizontally screw-retained bridge, accompanied by four implant crowns and two molars with PEEK bridge framework (Bio XS, Bredent). After 3 years in situ, the patient's bruxism had first abraded, and then split the posterior occlusal acrylic

veneers. Despite the undamaged PEEK frameworks, a complete prosthetic remake was necessary.

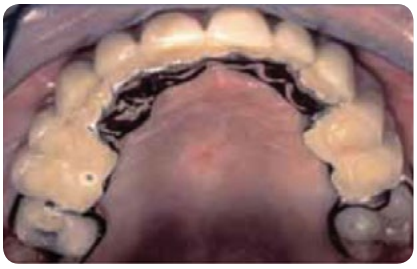


*Figure 2: Severe bruxism and heavily damaged bar-supported overdenture over four implants.[4]

The second prosthetic restoration included four adhesively retained implants fitted with a fully anatomical CAD/CAM fabricated, screw-retained PEEK prosthetic framework, JUVORA Dental Disc by Invibio (Ref. Figure 3).

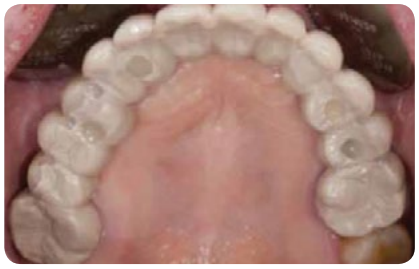


*Figure 3: The bridge in the patient's mouth after ten months in situ.

The secondary telescope UL6 and bridge pontic UL5 have been designed fully anatomically. The shade of the non-veneered PEEK (JUVORA Dental Disc) is acceptable for the occlusal surface in the posterior region. The gingival conditions are excellent.[4]

In conclusion, where bruxism is a problem the focus is on producing a durable, functioning restoration. The shock absorbing properties of JUVORA Dental Disc should protect the implants and the patient's natural teeth against the destructive forces of bruxism.

Case 2[7]

A 67-year-old female presented with jaw pain, asymmetric occlusion and advanced periodontitis. The patient had a combined fixed, removable restoration consisting of cemented, metal-ceramic bridge and clasp-retained partial denture.

The restoration included a fixed denture on four implants utilizing the ALL-ON-4[3] treatment concept. 3D planning software determined ideal implant placement and the most precise, comfortable prosthetic framework. After a four-month healing period, the temporary restoration model was digitally mastered and a PEEK framework CAD/CAM designed using JUVORA Dental Disc. Veneer fit, basal area shape and gingival pressure, screw canal design, connector positioning and milling path calculations were determined.

The resulting precise, full contour design was then milled immediately and successfully placed on the four implants. The patient reported comfortable chewing and high aesthetic satisfaction (Ref. Figure 4).

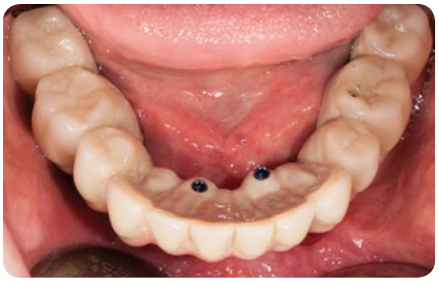


*Figure 4: Occlusal view of the bridge after placement and before closure of the screw holes.

Conclusions

JUVORA Dental Discs by Invibio have been ANVISA, CE and FDA-cleared for long-term implant borne, fixed and removable prosthetic frameworks made with precision through CAD/CAM workflows. PEEK-OPTIMA's physical properties and benefits including shock-absorption, bone-like modulus, resilience, and CAD/CAM fabrication are not only recommended by Professor Tipton and Dr Siewert, but make it and other PEEK-based prosthetic frameworks ideally suited for modern, prosthetic dentistry. ▲

ABOUT THE AUTHOR

Marcus Jarman-Smith, PhD

Dr Marcus Jarman-Smith is a Strategic Marketing Manager with Invibio Biomaterial Solutions. He has worked specifically on medical applications for the high performance polymer PEEK (polyetheretherketone) for dental applications, for over a decade. In 2001, he received a PhD in chemical engineering, tissue engineering and biomaterials from the University of Bath, in the United Kingdom.

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*Images, Figures 2-4, provided courtesy by Dr. Bernd Siewert.

COMMENTARY ON:

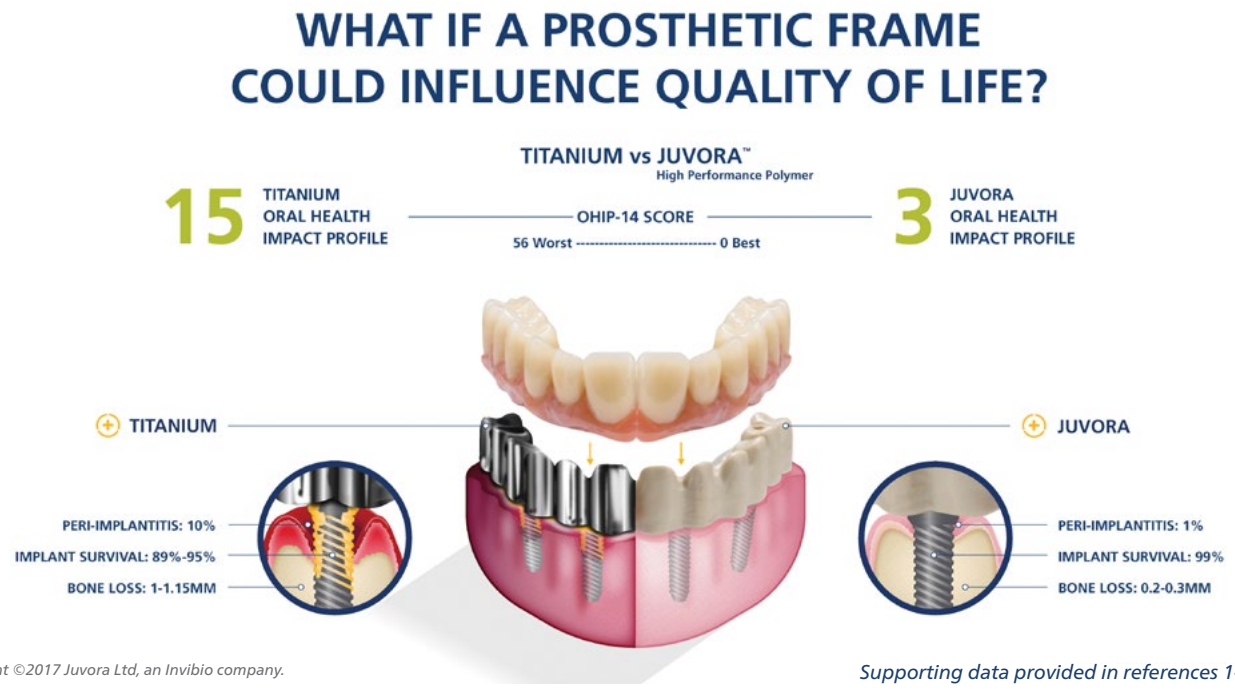
A Retrospective, Single Centre Clinical Evaluation Using Peek Frameworks for Full Arch Implant Supported Prosthetics

COMMENTARY AUTHOR: Marcus Jarman-Smith, PhD – Invibio Biomaterial Solutions

ORIGINAL PRESENTER: Dr Bernd Siewert, Clinica Somosaguas, Madrid, Spain

KEYNOTE SPEECH: B. Siewert (2017), PEEK in Dental Prosthetics (PEEK in der zahnärztlichen Prothetik Warum? Wann? Wie?), SSO Dental Meeting, Lugano, Switzerland, 11 February 2017

LEVEL OF EVIDENCE: Level 3 Retrospective Cohort Study



Supporting data provided in references 1-10

Summary

There is increased interest in the long term clinical outcomes and quality of life of patients treated with a high performance polymer for the framework material for full-arch implant-supported dental prosthetics, rather than the traditionally used metal or ceramic materials.

Dr Bernd Siewert has been in private practice for over 20 years. Since 2007, he's been an instructor at Germany's International Training Center for Dental Implantology (IFZI), and authored and spoken internationally about his specialty, implantology.[11]

Dr Siewert reported on his retrospective, single center clinical study using JUVORA frameworks for full-arch implant-supported prosthetics, made from PEEK-OPTIMA™ high performance polymer. Dr Siewert conducted clinical and radiological assessments to measure the survival rates of the dental implants and prosthetics, rate of bone loss and the incidence of any biological complications. In addition, scores were collated to measure the oral health and patient quality of life and the satisfaction of patients fitted with a PEEK-based prosthetic.

The retrospective data review investigated 21 patients which corresponded to a total of 96 dental implant fixtures. Patients were treated with full-arch implant-supported prosthetics manufactured with an internal substructure made from Invibio's PEEK-based polymer. The average follow-up post-prosthetic placement was 56 months (4 years, 8 months) ranging from the shortest time of 1 year and 2 months to the longest time of 8 years and 9 months.

Key Findings

Dental implant fixture survival rate was reported as high as 99%, and PEEK-based prosthetic survival rate was 100% versus 89-95%[1,2] and 92%[3,4] for titanium[5] respectively. An average bone loss of 0.2 mm (+ 1.0) on the mesial aspect and 0.3 mm (+ 0.8) on the distal aspect was observed versus 1-1.5mm[6,7] for titanium. Patient Peri-Implantitis incidence was low at 1% versus 10%[1,8] for titanium. The

mean total oral health and patient quality of life score was 3.1 points (± 3.3), with patient satisfaction deemed "extremely satisfactory". For titanium the score averaged at 15.[9,10] Overall, when compared with the literature values of Titanium, JUVORA frameworks for full-arch implant-support dental prosthetics showed:

- Up to 10% better implant survival rate
- Up to 5x less bone loss
- Up to 10x less incidence of Peri-Implantitis
- Up to 8% better prosthetic survival rate
- Nearly 3x better mean total score for oral health and patient quality of life

Commentary

These results from a retrospective, single center study are limited, but do provide some initial clinical insight into the long-term outcomes and potential benefits of using a more shock absorbing high performance polymer substructure for full-arch implant borne prosthetics. ▲

ABOUT THE AUTHOR

Marcus Jarman-Smith, PhD

Dr Marcus Jarman-Smith is a Strategic Marketing Manager with Invibio Biomaterial Solutions. He has worked specifically on medical applications for the high performance polymer PEEK (polyetheretherketone) for dental applications, for over a decade. In 2001, he received a PhD in chemical engineering, tissue engineering and biomaterials from the University of Bath, in the United Kingdom.

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Changing the Face of Prosthetic Dentistry

AUTHOR: Marcus Jarman-Smith, PhD – Invibio Biomaterial Solutions

Overview

Patient comfort. Shock absorption. Durability. These are just a few of the reasons prosthodontists are choosing Polyetheretherketone (PEEK) high performance polymer over metal alternatives in fixed and removable prosthetic frameworks.

PEEK's resilience could be an ideal fit for dental restorations and prosthetics. First used in temporary abutments and healing caps, PEEK was proven effective in other dental applications including fixed and removable prosthetic frameworks. Today more than ever, these polymers have the dental world talking.

"High performance polymers are going to disrupt dentistry because it's a game changer," says Professor Paul Tipton, Prosthodontist in the United Kingdom.

One such "game changer" is the JUVORA™ Dental Disc, made of PEEK-OPTIMA™ high-performance polymer for precise and cost-effective CAD/CAM milling. The JUVORA Dental Disc is ANVISA, CE and FDA-cleared for removable restorations and implant prosthetics, including crowns and bridges. Its bone-like modulus of elasticity and shock-absorbing properties result in better fitting, and more comfortable, durable, natural restorations.

"The ability to change these high performance polymers into just about any kind of restoration is significant," says Jonathan Parkinson, Allport & Vincent Dental Laboratory in the United Kingdom.

While material adoption gains momentum, JUVORA is proving its real value in patient satisfaction – the underlying driver of industry change. See what these patients have to say about the life-changing benefits of JUVORA.*

Terence's Story

Before JUVORA

Terence was just "managing" his dentures. With rapidly deteriorating teeth and after multiple, frustrating dental visits, he needed a new solution for the top and bottom teeth. The thought of more loose-fitting dentures was actually depressing.

After JUVORA

"With the removable prosthetic like JUVORA, I felt absolutely fantastic! It was exactly what I wanted." Terence could eat comfortably and enjoy food once again.

Robert's Story

Before JUVORA

Robert is a taxi driver and works with the public on a daily basis. He was very self-conscious about his broken teeth and current loose-fitting dentures. He was tired of regluing his dentures after eating and drinking - up to four times per day. "I spent more time messing around with my teeth than anything else!"

After JUVORA

Gone were the hassles and embarrassment. Robert was confident again. "They're just like my own teeth! I don't even think about them. They're just perfect for me!"

Barbara's Story

Before JUVORA

Barbara had been hit in the mouth at work, and several of her teeth died and turned black. She worked with the public a lot and was extremely self-conscious. "I needed to do something about it before I lost all confidence!"

After JUVORA

A prosthetic framework like JUVORA was completely new to Barbara. "It changed my life completely!" Barbara started going out more with friends and speaking more. Even though it's a prosthetic, JUVORA "Feels so good! Feels so normal. It feels exactly like having my natural teeth. And it's worth every penny!"

Victor's Story

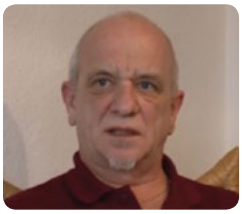
Before JUVORA

Dentures weren't new to Victor. He had worn them for 15 years. However, he was tired of his painful gums and his dentures were heavy and broken on a regular basis. His dentist recommended a JUVORA prosthetic because it was lightweight, long lasting and hypoallergenic.

After JUVORA

For Victor, JUVORA felt better and fit perfectly. "It's easy to handle and does not slip away while chewing." Victor found JUVORA to be a great material that is beautiful, light and comfortable.

Gerhard's Story



Before JUVORA

Gerhard was a long-time amalgam denture wearer, but his teeth had gone from bad to worse. He needed something new. Gerhard talked with his dentist, researched high performance polymer versus traditional amalgam material and ultimately chose JUVORA.

After JUVORA

Now comparing the two, Gerhard has found JUVORA to be lighter, more comfortable, allergy-free and easier to clean. "I can recommend this material without any reservation!"

Summary

For these and many other patients, JUVORA Dental Disc made with PEEK-OPTIMA polymer is a good fit. The use of high performance polymer prosthetics is not only positively changing patients' attitudes and lives, but also the face of prosthetic dentistry. ▲

ABOUT THE AUTHOR

Marcus Jarman-Smith, PhD

Dr Marcus Jarman-Smith is a Strategic Marketing Manager with Invibio Biomaterial Solutions. He has worked specifically on medical applications for the high performance polymer PEEK (polyetheretherketone) for dental applications, for over a decade. In 2001, he received a PhD in chemical engineering, tissue engineering and biomaterials from the University of Bath, in the United Kingdom.

*Testimonials have been provided by dental professionals and their patients. Their views and experiences are their own and do not necessarily reflect the view and experiences of others.

PEEK-OPTIMA™ POLYMER KNEE – A More Natural Solution to Total Knee Replacement

AUTHOR: Ian Revie, PhD – Invibio Biomaterial Solutions

Total Knee Replacement Satisfaction Levels

According to the Organization for Economic and Co-operation Development (OECD) health statistics, in 2015, there were approximately 2.6 million total knee replacement (TKR) surgeries reported for the 35 member countries.[1] Yet, a significant number of people who have undergone TKR are unhappy with the results.[2] An estimated 20% of TKR patients, totaling about 520,000 worldwide, are unsatisfied.[2-3]

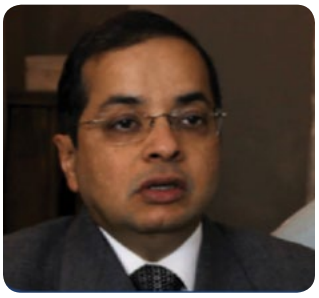
Why are Patients Dissatisfied?

The literature proposes various reasons for TKR dissatisfaction, but little is proven.[4-5] One researcher linked positive patient expectation to improved outcomes.[4] Moreover, fulfilling kneeling, squatting and stair climbing expectations correlated highly with satisfaction.[4] In fact, preparing patients for surgery and setting an expectation of recovery timeframes and outcomes resulted in a 5% improvement in patient satisfaction.[4]

Surgical precision and materials used may also play a part in patient satisfaction levels. Some unsatisfactory TKR results were due to primary malalignment of the femoral component.[5] Different femoral component materials can also affect a patient's ability to perform normal daily activities post-operatively. TKR patient feedback across social media and forums listed TKR post-operative side effects ranging from knees feeling heavy or loose, to being cold in the winter, to knee creaking, popping or rattling, which may all potentially be associated with metal.

Introducing the PEEK-OPTIMA Polymer Knee Implant

The PEEK-OPTIMA Knee Implant has been developed with these problems in mind. It offers surgeons and patients a femoral component that has the potential to improve both operative procedure and post-operative outcome. Most importantly the goal is to improve a patient's quality of life.



"Patients want two things... one is obvious relief from pain, but more importantly they hope that their replacement knee will last."

Dr Hemant Wakankar[6*]
Orthopedic Surgical Consultant
Devchhaya Clinic
Maharashtra, India

Pre-clinical testing has demonstrated the potential for a femoral component made of PEEK-OPTIMA to offer equivalent performance to metal, while maintaining the benefits of a non-metallic solution.[6] PEEK-OPTIMA exhibits properties closer to cortical bone than metal or ceramic materials, including its elastic modulus and density, and may offer a more natural solution to knee replacement.[7-8] Used in approximately nine million implanted devices worldwide, including spinal cages and bone anchors, PEEK-OPTIMA has a strong clinical history with patients benefitting from this less stiff material.[9]

"Invibio is best placed to lead the development of a new innovative knee replacement solution because they have been successful in other areas and other arenas."

Dr Asit Shah[11*]
Orthopedic Surgical Consultant
Englewood Orthopedic Associates
Englewood, NJ

"Technically it's very challenging but it's a very innovative concept and that's going to stimulate the team to rise to that challenge."

Professor John Fisher CBE[*]
Director Institute of Medical & Biological Engineering
University of Leeds

"It will give designers a real opportunity in the future to change the way that we think about knee replacements."

Dr Jon Conroy[12*]
Consultant Orthopedic Surgeon
Harrogate District General Hospital
North Yorkshire, England

Based on this pre-clinical work, a pathway for clinical trials to demonstrate PEEK-OPTIMA Knee's safety and clinical efficacy has been provided. These trials will assess post-operative knee performance and patient satisfaction levels. We are confident clinical trial results will show PEEK-OPTIMA Polymer Knee improves TKR outcomes and patient quality of life, while raising the bar for patient care. ▲

ABOUT THE AUTHOR

Ian Revie, PhD

Dr Ian Revie is Invibio Biomaterial Solutions' EU Developing Markets Marketing Leader responsible for the PEEK-OPTIMA Knee program. Prior to Invibio, Dr Revie was CEO for Activ4Life Healthcare Technologies where he patented a novel patient monitoring application focused on orthopedics. Previously, Dr Revie held progressively responsible roles in Johnson & Johnson's orthopedics business where he was credited for turning technical visions into commercial success. In 1995, Dr Revie received his PhD in biomechanical engineering from Queen's University, Belfast, Northern Ireland.

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*The testimonials presented have been provided by practicing orthopedic surgeon(s) and researcher(s). Their view and experiences are their own and do not necessarily reflect those of others. "Invibio" disclaims any liabilities or loss in connection with the information herein.

COMMENTARY ON:

PEEK-OPTIMA™ as an Alternative to Cobalt Chrome in the Femoral Component of Total Knee Replacement : A Preliminary Study

COMMENTARY AUTHOR: Adam Briscoe, PhD – Invibio Biomaterial Solutions

AUTHORS OF ORIGINAL PAPER: Raelene M Cowie PhD, Dr Adam Briscoe PhD, Prof Dr John Fisher PhD CEng FIMechE CSci FIPEM FREng CBE and Louise M Jennings PhD CEng FIMechE

JOURNAL: Proceedings of the Institution of Mechanical Engineers Part H: Journal of Engineering in Medicine, 2016 Nov; 230(11): 1008–1015. Published online 2016 Sep 16. doi: 10.1177/0954411916667410

LEVEL OF EVIDENCE: Peer Reviewed, Pre-clinical, *In-vitro* Study

Summary

In order to demonstrate the suitability of a bearing solution in total joint replacements, experimental wear simulation testing *in vitro* is considered the norm. ISO 14243 provides a gait profile for standard testing methodologies in the dynamic simulation of a knee prosthesis. It has recently been shown that this standard may not represent a worst case when analyzing these components. Several research groups have begun to examine how this standard can be improved upon. Previous work from the University of Leeds has shown that by increasing the anterior-posterior (AP) displacement during testing, some prostheses may also display a dramatic increase in the amount of observed wear.

This paper compares the wear performance of a total knee replacement (TKR) with a novel PEEK-OPTIMA polymer femoral component to that of an identical bearing design made from cobalt chrome (CoCr) alloy. Initial testing was carried out under standardized conditions (intermediate kinematics) and, after three million cycles, testing was continued under high kinematic conditions to a total of six million cycles.

The gravimetric results from this study showed that both CoCr (metallic) and PEEK-OPTIMA components produced statistically similar quantities of wear under both intermediate and high displacements. There was little change in the wear when changing the level of AP displacement. In all scenarios the amount of wear measured was low when compared to current alternative TKR designs. Figure 1 shows the comparison between the wear rate under intermediate kinematics for both CoCr and PEEK-OPTIMA femoral components and a comparison with a referenced data point of a current TKR femoral component brand, from the literature, under the same conditions.[1]

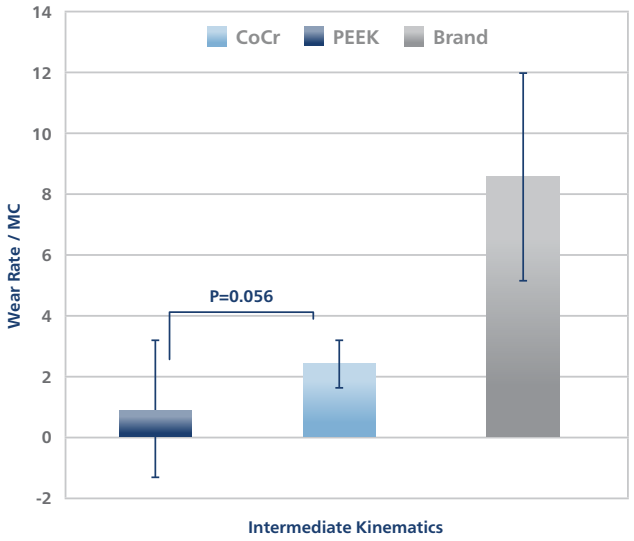

Fig. 1: Comparative volumetric wear rate between a CoCr knee, PEEK-OPTIMA knee and a current TKR femoral component brand.[1]

Key Findings

Based on this intermediate and high kinematic knee gait simulation wear test, there is no statistically significant difference in tibio-femoral wear produced between CoCr or PEEK-OPTIMA femoral components with the same bearing geometry.

Commentary

This paper provides a useful insight into the effects of a revolutionary change of biomaterial for one of the two most commonly replaced joints. A first look at the wear performance of a PEEK-OPTIMA polymer on Ultra-high-molecular-weight polyethylene (UHMWPE) TKR indicates that it can be potentially used as an alternative to CoCr alloy for the development of these types of devices.

Additional mechanical tests have now been performed to establish pre-clinical safety and suitability for the device to be used in a clinical setting. ▲

ABOUT THE AUTHOR

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Dr Adam Briscoe is the Technology Manager for Orthopedics at Invibio Biomaterial Solutions. He has more than 15 years of experience working in research and development for orthopedic medical devices. In 2007, he received a PhD in biomechanical engineering from the University of Southampton, in the United Kingdom. Since April 2017, he has been a visiting research fellow at the University of Leeds, in the United Kingdom, focused on tribology research.

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COMMENTARY ON:

A Preclinical Numerical Assessment of a Polyetheretherketone Femoral Component in Total Knee Arthroplasty During Gait

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AUTHORS OF ORIGINAL PAPER: Lennert de Ruiter MSc, Dennis Janssen PhD, Adam Briscoe PhD and Prof Dr Ir. N.J.J. Nico Verdonschot PhD

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LEVEL OF EVIDENCE: Peer Reviewed, Pre-clinical, *In-vitro* Study

Summary

According to OECD health statistics, in 2015 there were approximately 2.6 million total knee replacement (TKR) surgeries. Studies estimate that 20% of people who have undergone TKR surgery are not happy about the result.[1,2] In order to improve patient satisfaction there is current interest in the effects of replacing the metal (cobalt chrome, CoCr) femoral component in a TKR device with a component manufactured from PEEK-OPTIMA™ high performance polymer. This paper has used established computational techniques to model the gait cycle in a segmented representation of the knee that has been implanted with a TKR device and to compare the physical effects on the stresses and strains seen in the system when changing to a PEEK-OPTIMA high performance polymer femoral component.

Because this testing was computer based, stiffness properties for bone, to represent the distal femur, were calculated using a CT scan. For all other components, properties were assumed to be homogeneous. Loading conditions were as described for gait simulation in ISO 14243. The stresses in the implant, cement and bone were analysed, as well as the expected influence on the bone cement-to-implant interface. Results were expressed as a percentage of material failure stress to give a good indication for the likelihood of one component failing compared to the other.

The results demonstrate that, while cobalt chrome is an inherently stronger material than PEEK-OPTIMA polymer, the change in the stiffness leads to a very different sharing of stresses throughout the system. This, in turn, potentially enables the PEEK-OPTIMA femoral component to bear more than enough load to remain safe under the levels of stresses expected in this study. Additionally, the sharing of this stress with the underlying materials means that the bone experiences a closer load stimulus to that of the intact state, potentially minimizing stress shielding (often seen as a problem with metal femoral components), and maintaining healthy mass (ref. figure 1).

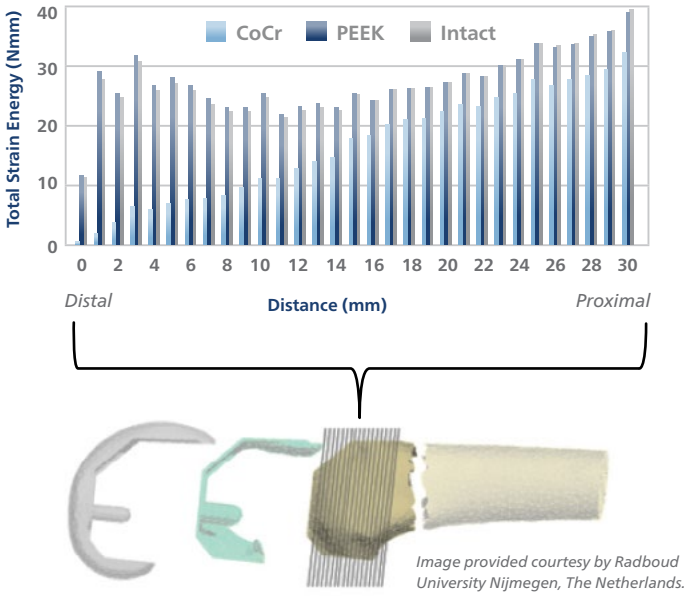

Fig 1: Modeling reflecting the comparison of the natural bone with PEEK-OPTIMA™ and CoCr femoral components. It shows the significant difference all-round the distal femur.

Key Findings

Based on this computational study there is no expected difference in the safety of a PEEK-OPTIMA component, compared with a CoCr alternative with the same geometry. There is strong evidence to suggest that load stimulus seen in the peri-prosthetic bone will be close to the intact case under a PEEK-OPTIMA polymer prosthesis and this may lead to a healthy bone mass retention.

Commentary

This paper gives confidence for the potential of an all-polymeric total knee replacement and assists in the pre-clinical demonstration of expected safety. Caution must be taken as this computational analysis model reflects only one walking pattern and may not account for other patterns experienced *in-vivo*. Further computational and physical experimental evidence has now been collated on the component for use in a clinical setting. ▲

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