Biomechanical Pullout Strength and Histology of Plasmapore®XP Coated Implants: Ovine Multi Time Point Survival Study

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**Background:** The joint complex that allows spinal motion is referred to as a functional spinal unit or “FSU.” An FSU is defined as two adjacent vertebrae and the corresponding joints and ligaments between them, as shown in Figure 1. Spinal implant technologies and the associated surgical techniques often involve two or more vertebrae, and for clarity, are often described in terms of the effects on an FSU.

Although different commercialized cages have various designs and properties, they perform the same function, which is to provide immediate stabilization to the anterior column and appropriate spacing of the vertebrae. The interbody device promotes natural bone growth between the vertebrae and forms a strong vertebral union with the implant.

The majority of interbody fusion cages are manufactured from an inert polyetheretherketone (PEEK) material. The characteristics of PEEK and the implants made from this polymer are well known and have been widely documented. PEEK is a high performance biocompatible polymer that possesses a desirable combination of high mechanical strength, toughness, fatigue resistance, and radiolucent imaging properties. Additionally, PEEK has become ubiquitous as an interbody implant due in part to the polymer’s elastic modulus of 3.6 GPa, which is similar to that of cortical bone. PEEK is also inert in nature which limits the potential for direct bone contact, often resulting in pseudoarthrosis.

Devices made from titanium or titanium alloys offer additional design advantages, such as strength and toughness to spinal implants. Recent advancements in the processing of titanium have allowed for new techniques to develop materials that combine the advantages of PEEK with the well known utility of titanium. The plasma application of titanium onto a PEEK substrate material results in a composite with optimized friction, biocompatibility, and a modulus of elasticity more favorable than non-composite design materials.

When titanium is used as a coating on a PEEK interbody device, two major advantages are evident. The first advantage is the immediate mechanical fixation that is created by the roughness of the coated implant. The roughness provided by the titanium coating helps to prevent implant migration within the interbody space. The second advantage is provided by the natural release of BMP’s and the bony apposition that is known to occur with titanium. When a porous titanium coating is applied to a PEEK interbody implant, an optimal environment for osseointegration at the surface of the implant is created that provides stabilization during arthrodesis.
Plasmapore® and PlasmaporeXP Coatings

Plasmapore porous titanium coatings have been applied to titanium orthopedic and spinal implants for over two decades. The coating provides an attractive surface for bone ingrowth due to the combination of pore size, porosity, and surface roughness. The increased bony apposition and subsequent arthrodesis is referred to as long term or "advanced" implant stability. The Plasmapore coating increases both initial and advanced implant stability. When combined with primary implant fixation, the increased surface roughness of the Plasmapore coated implant helps ensure initial implant stability. The increased bony apposition and porosity provided by the coating help to ensure the advanced stability of the treated motion segment.

The Aesculap process of applying a Plasmapore coating onto a PEEK substrate is referred to as PlasmaporeXP. PlasmaporeXP is a porous pure titanium and osteoconductive surface coating, designed to complement the PEEK interbody implant. Benefits provided by the PlasmaporeXP coating include enhanced initial and advanced implant stability, improved visibility during imaging, and high adhesion strength to PEEK for continuous attachment in vivo.

PlasmaporeXP is a microporous surface coating with a thickness ranging from 60-150 µm. The coating improves the visibility of PEEK implants during imaging, allowing for a clear delineation of implant contours as shown in Figure 3. The thin and microporous nature of the titanium coating allows for excellent visibility during imaging, eliminating artifact or scatter in CT and MRI.

The surface adhesion properties of the coating on PEEK substrates have been well documented, exceeding the industry recommended requirements for metallic spray coatings. PlasmaporeXP was found to have a high adhesion strength to the PEEK implant surface, exceeding the shear and tensile strength of PEEK2. The adhesion strength of the PlasmaporeXP coating to PEEK implants is strong enough to ensure continuous attachment.

The surface of the PlasmaporeXP coating, as shown in Figure 2, is extremely rough (Sa=25.1 ± 1.65 µm) compared to the smooth surface of machined PEEK (Sa=0.43 ± 0.07 µm)1. The roughened surface provides several benefits to the PEEK interbody cage. The roughened PlasmaporeXP coating maximizes the contact area between the PEEK implant and the vertebral endplate, enhancing initial implant stability and increasing implant migration resistance. In addition, the PlasmaporeXP surface coating offers an ideal scaffold for bony ingrowth, reducing the inflammatory tissue response associated with PEEK and improving advanced implant stability.

Figure 2. Photomicrograph of PlasmaporeXP coating showing the microstructure of the pure titanium coating.

Figure 3. X-Ray examples of Aesculap’s Plasmapore® coated interbody devices: a) ArcadiusXP™ L stand alone ALIF device and b) CeSpaceXP cervical interbody device.
Hypothesis

In order to substantiate the use of Plasmapore® on interbody devices, a PEEK dowel study in an ovine model was conducted. The hypothesis stated that a difference should exist in both pullout strength and histological results at the initial implantation 0 week, 12 week, or 24 week survival time points between the PEEK dowels and Plasmapore® coated dowels. Scientifically, the null hypothesis states that no difference in biomechanical and histological characteristics would be detected between PEEK and Plasmapore® coated PEEK at the different time points. If the results support the hypothesis, the design intent for the use of Plasmapore® on PEEK to provide immediate and advanced implant stability will be supported.

Materials and Methods

Implants

This study investigates the comparative osseointegration and concomitant pullout strength from ovine bone samples of two types of cylindrical dowels. One treatment (uncoated) involves PEEK dowels, 8 mm in diameter and 30 mm in length. The other treatment (coated) involves PEEK dowels of the same dimensions coated with a novel titanium surface intended to promote osseointegration (Plasmapore®r, Aesculap).

Surgical Procedure and Specimen Preparation

All surgeries were conducted at a research animal facility after Institutional Animal Care and Use Committee approval was received. Ten sheep were selected for the study, evaluated for general health and randomly assigned to either the 12 week or 24 week survival groups. Three dowels were placed in the lateral epicondyle region of each hind leg of the animals. A sample dowel and implantation are shown in Figure 4. The most distal dowel implant site was identified near the level of the lateral collateral ligament. The remaining dowels were placed approximately 12 mm away from the first dowel, arranged in a triangular pattern. The dowel implant sites were drilled into the femur using sequentially larger drill bits (2 and 5 mm diameter), oriented perpendicular to the condyle surface. The final implant holes were reamed to either 8.0 + 0.1 mm diameter for the uncoated dowels or 8.2 + 0.1 mm diameter for the coated dowels, and a final depth of 31 mm such that each dowel was placed within cancellous bone. The dowel implant sites were then irrigated with saline to remove any tissue fragments. Following preparation of the sites, the dowels were then driven into each hole. The right leg was implanted with Plasmapore® coated dowels, whereas the left leg was implanted with uncoated dowels.

At the completion of the study, animals were humanely euthanized, the distal portion of the femora was cut, and the implant sites were separated such that surrounding bone was maintained for mechanical testing. Samples for mechanical testing were wrapped in saline-soaked gauze, bagged and stored at -20° C until testing.

Figure 4. a) Uncoated PEEK dowel and b) Implantation of Plasmapore® coated dowel.

In addition, six coated and six uncoated dowels were inserted by the same procedure into femora obtained from similarly sized and aged sheep. These specimens were intended to establish a baseline (0 week) for differences in pullout strength due to varying surface roughness between the two types of implants.
Pullout Testing

Two of the three specimens from each leg were identified for pullout testing. Pullout strength testing was conducted with an MTS MiniBionix II system (MTS, Eden Prairie, MN). The bone sections were placed into custom fixtures, and an alignment tool was used to provide an interface between the test system and the dowel, as shown in Figure 5. The dowel was pulled out at a rate of 1 mm/min until a maximum force was observed. Following acquisition of peak load, the rate of testing was adjusted to 10 mm/min. Load and displacement data was collected at a rate of 20 Hz during testing. Ten coated and ten uncoated dowels of specimens harvested at 12 and 24 weeks were tested. Additionally, six coated and six uncoated dowels harvested immediately following implantation were tested (0 week).

A two-way analysis of variance (ANOVA) was conducted with Bonferroni corrected post hoc tests for pairwise comparisons to assess the influence of time and surface coating on mechanical pullout strength. All statistical analysis was conducted using SPSS (IBM, Armonk, NY).

Histology

Non-decalcified histological specimens were taken for both the Plasmapore® and PEEK dowel implants at the 12 week and 24 week time points, as shown in Figure 6. From each group, five were stained and evaluated. New bone formation, bone marrow adipose tissue, inflammation and fibrosis were measured as a percentage of the defect area for each sample. Additionally, bony apposition as a percentage of implant circumference, defined as less than 0.1 mm from the implant surface, was measured for each sample. A two-way analysis of variance (ANOVA) with Bonferroni-corrected post hoc analysis was conducted for each of the outcome measures with time point and treatment group as factors.

Figure 5. Model of test fixture setup with alignment feature to maintain uniaxial loading on harvested dowels.

Figure 6. A representative histological specimen capturing the uncoated dowel (brown), defect (white) and host bone (pink) a) With no analysis in the void and b) The defect space is shown highlighted in yellow.
Results

Biomechanical Pullout Strength

A significant effect was detected for both factors, Plasmapore\textsuperscript{XP} coating on PEEK and time. No significant difference in pullout strength was detected for the 0 week specimens between the Plasmapore\textsuperscript{XP} coated and uncoated groups (p=0.661). The pullout strength for Plasmapore\textsuperscript{XP} coated dowels was significantly greater than the uncoated dowels at both 12 and 24 weeks (p<0.001). A significant increase in pullout strength was detected at 12 and 24 weeks for the Plasmapore\textsuperscript{XP} coated group compared to 0 week (p<0.001), and for 24 weeks compared to 12 weeks (p=0.007), as shown in Figures 7 and 8. No significant increase in pullout strength over time was detected for the uncoated group.

Figure 7. Average peak removal force of Plasmapore\textsuperscript{XP} coated and uncoated specimens over time.
* indicates a significant difference from uncoated samples
† indicates a significant difference from 0 week samples

Figure 8. Scatter of all maximum strength pullout tests at each time point.
**Histology**

A significant increase in new bone formation and bony apposition was detected over time irrespective of treatment group (p<0.001 and p=0.003 respectively). Similarly, new bone formation and bony apposition were significantly greater for the Plasmapore**XP** coated group than for the uncoated group irrespective of time (p=0.004 and p=0.002 respectively). Significantly greater new bone formation was detected at the 24 week time point for the Plasmapore**XP** coated group compared to the uncoated group (p=0.015), while the difference at 12 weeks was not statistically significant (p=0.055). Conversely, significantly greater bony apposition was detected at 12 weeks for the Plasmapore**XP** coated group compared to uncoated group (p=0.002), while the difference at 24 weeks was not significant (p=0.141). The mean and standard deviation of new bone formation and bony apposition for each set of specimens is shown in Figures 9 and 10 respectively.

No significant differences were detected in bone marrow adipose tissue with respect to time or treatment group. Significantly less inflammation and fibrosis was detected for the Plasmapore**XP** coated group compared to the uncoated group irrespective of time point (p=0.022), but significant differences were not detected between the treatment groups when comparing within the 12 and 24 week time points (p=0.123 and p=0.066 respectively).

![Figure 9. New Bone formation (%) by treatment group and time point](image)

![Figure 10. Bony apposition (%) by treatment group and time point](image)
In the histological examination at the 12 week time point, close bony apposition next to the Plasmapore\textsuperscript{XP} is evident as shown in Figures 11 and 12. In contrast, the PEEK surface does not exhibit the same bony apposition.

\textbf{Note:} There is increased bone formation and apposition in the Plasmapore\textsuperscript{XP} coated PEEK dowel compared to the uncoated PEEK dowel. Increased fibrous connective tissue around the uncoated PEEK dowel is evident due to the reduced circumference of the dowel apposed with bone.

Figure 11. Histology results at 12 weeks for
a) Representative Plasmapore\textsuperscript{XP} coated dowel compared to
b) Uncoated PEEK dowel.
Note: There is increased bone formation and apposition in the Plasmapore® coated PEEK dowel compared to the uncoated PEEK dowel. Increased fibrous connective tissue around the uncoated PEEK dowel is evident due to the reduced circumference of the dowel apposed with bone.

Overall, the histology outcomes exhibit bone ingrowth to the Plasmapore® surface at 12 weeks, with little evidence of fibrous connective tissue. Fibrous connective tissue was only evident in the uncoated PEEK implant histological specimen. However, by 24 weeks no significant difference in bone apposition was detected between the Plasmapore® coated and uncoated treatments, as shown in Figure 12.
Discussion

Since its inception over a century ago, spinal fusion methods have become a standard of care for surgical procedures involving the cervical and lumbar spine. Arthrodesis may be achieved by multiple approaches, including posterior, posterolateral, and anterior interbody fusion, alone or in combination with one another. Interbody fusion techniques in the lumbar spine can be broken down based on access and technique into posterior lumbar interbody fusion (PLIF), anterior lumbar interbody fusion (ALIF), transforaminal lumbar interbody fusion (TLIF), and transpsoas lumbar interbody fusion (XLIF). Combinations are also possible, as with posterolateral and anterior interbody fusion, often referred to as a 360-degree fusion. Whether treating spondylolisthesis, degenerative disc disease, disc herniation, or a variety of other medical conditions, the primary goal of these procedures remains the same: to reestablish joint stability in an otherwise unstable joint in order to eliminate pain, which is related to abnormal motion of the vertebrae.

Immediate stabilization would be best supported by implants with increased initial implant stability followed by long term, advanced implant stability. Plasmapore\textsuperscript{XP} supports initial stability through high surface roughness, while long term, advanced stability has been validated through the osseointegration and increased pullout strength demonstrated at both the 12 and 24 week survival time points. With the demonstrated statistical difference of the PEEK dowel with and without Plasmapore\textsuperscript{XP} coating, it is clear that osseointegration occurs over a 24 week period in an ovine survival model. Moreover, pullout strength significantly increases only in Plasmapore\textsuperscript{XP} coated dowels compared to the initial implant pullout strength. Considering the totality of the results, it is clear that osseointegration occurs over time and strongly supports the potential for improved anti-migration strength of the Plasmapore\textsuperscript{XP} coated PEEK anterior interbody devices, such as Arcadius\textsuperscript{XP} L and CeSpace\textsuperscript{XP}, which are shown in Figure 13.

From the results of the histological study, Plasmapore\textsuperscript{XP} facilitates the healing process in two distinct ways. At 12 weeks, the bony apposition is statistically significantly greater around the Plasmapore\textsuperscript{XP} coated implant dowels. At 24 weeks, the defect exhibits statistically greater new bone formation in the defect site, which potentially signifies an important mechanism in the healing response for patients. In the early phases, Plasmapore\textsuperscript{XP} coated implants provide immediate stability quickly followed by improved stability via bony apposition. Over time, the defect site fills in with new bone formation, thereby increasing the advanced implant stability and enhancing long term stability. Therefore, the null hypothesis, that the Plasmapore\textsuperscript{XP} coating has no effect on pullout strength and histological characteristics at the 12 and 24 week time points, must be rejected.

It should be noted, that in both the PEEK and Plasmapore\textsuperscript{XP} coated specimens, that minimal inflammatory response was prominent. Consistent with this finding, the presence of foreign body giant cells was minimized even with the presence of fibrous tissue in the defect site. Recently, studies involving both PEEK and titanium have been reported due to the prevalence of both materials in interbody cages. This is one of the first studies to report on titanium coated PEEK composite implants. The properties of both materials are highly regarded, including the modulus of elasticity which governs the stiffness of the interbody implant, and the inert in situ properties of the PEEK polymer. The histological results confirm the characteristics of PEEK and titanium implants, which have been widely studied as homogenous monolithic materials.
Previously, studies have been conducted to assess the osseointegration characteristics of various surface treatments and materials. Most of these studies involve the placement of cylindrical implants into the bony tissue of an animal model, followed by a combination of mechanical pullout testing and histology for specimens randomized to multiple necropsy time intervals. Aebli et al. evaluated the osseointegration effects in an ovine model, of a rough and highly crystalline hydroxyapatite (HA) coating applied to titanium implants compared to a titanium coating of similar roughness\(^3\). A significant increase in pullout strength was detected at both time intervals (2 and 4 weeks) for both surface coatings, but no differences were detected in pullout strength between coating types at any interval. Histomorphometric analysis revealed significantly greater bone-implant contact for the HA coating at 2 weeks compared to the titanium coating at both 2 and 4 weeks. In a similar study conducted in a minipig model, Schwarz et al. evaluated the effect of four surface finishes (glasspearl-blasting, sandblasting, titanium plasma spray, titanium plasma spray with calcium phosphate coating) applied to cylindrical titanium implants\(^4\). Pullout testing and histomorphometry were conducted after 12 week survival of the animals. A significant increase in pullout strength with increasing surface roughness of the four surface treatments was found with no significant increase detected for calcium phosphate coating. Similarly, significantly greater bone-implant contact was found with increasing surface roughness and with the calcium phosphate coating. To the best of the authors’ knowledge, this study is the first to investigate both the biomechanical and histological effects of a plasma sprayed coating on a PEEK substrate.

Thus, it can be concluded that the Plasmapore\(^{XP}\) coating provides a biomechanical advantage by providing initial stabilization as well as long term, advanced stability. The mechanical and histological results show that a material’s properties determine both the pullout strength and bone growth potential. Moreover, the type of coating, i.e., Plasmapore\(^{XP}\), should be strongly considered for both the biomechanical characteristics and the resulting bone formation including bony apposition.

References

\(^2\) Mechanical Testing Summary: Adhesion Strength of the Plasmapore\(^{XP}\) coating to PEEK. Aesculap Implant Systems, White Paper, 2013 (ART123).


Disclosure
Boyle C. Cheng, PhD is the Director of Neurosurgery Spine & Biomechanics Research Laboratory at Allegheny General Hospital in Pittsburgh, PA. He also serves as a Adjunct Assistant Professor at Carnegie Mellon University, Department of Bioengineering and an Associate Professor in the Department of Neurosurgery at Drexel University School of Medicine, Allegheny campus. Dr. Cheng is a paid consultant for Aesculap Implant Systems, LLC.