Spine
SPINE Volume 41, Number 19, pp E1146–E1150

BIOMECHANICS

Evaluating Osseointegration Into a Deeply Porous Titanium Scaffold

A Biomechanical Comparison With PEEK and Allograft

Richard D. Guyer, MD,* Jean-Jacques Abitbol, MD,† Donna D. Ohnmeiss, Dr.Med,‡ and Chang Yao, PhD§

Study Design. This was a biomechanical push-out testing study using a porcine model.
Objective. The purpose was to evaluate the strength of implant-bone interface of a porous titanium scaffold by comparing it to polyetheretherketone (PEEK) and allograft.
Summary of Background Data. Osseointegration is important for achieving maximal stability of spinal fusion implants and it is desirable to achieve as quickly as possible. Common PEEK interbody fusion implants appear to have limited osseointegration potential because of the formation of fibrous tissue along the implant-bone interface. Porous, three-dimensional titanium materials may be an option to enhance osseointegration.
Methods. Using the skulls of two swine, in the region of the os frontale, 16 identical holes (4 mm diameter) were drilled to 10 mm depth in each skull. Porous titanium, PEEK, and allograft pins were press fit into the holes. After 5 weeks, animals were euthanized and the skull sections with the implants were cut into sections with each pin centered within a section. Push-out testing was performed using an MTS machine with a push rate of 6 mm/min. Load-deformation curves were used to compute the extrinsic material properties of the bone samples. Maximum force (N) and shear strength (MPa) were extracted from the output to record the bonding strength between the implant and surrounding bone. When calculating shear strength, maximum force was normalized by the actual implant surface area in contact with surrounding bone.
Results. Mean push-out shear strength was significantly greater in the porous titanium scaffold group than in the PEEK or allograft groups (10.2 *vs.* 1.5 *vs.* 3.1 MPa, respectively; $P < 0.05$).
Conclusion. The push-out strength was significantly greater for the implants with porous titanium coating compared with the PEEK or allograft. These results suggest that the material has promise for facilitating osseointegration for implants, including interbody devices for spinal fusion.
Key words: biomechanical testing, osseointegration, PEEK implant, porcine model, porous titanium scaffold.
Level of Evidence: N/A
Spine 2016;41:E1146–E1150

From the *Texas Back Institute, Plano, TX; †California Spine Group, San Diego, CA; ‡Texas Back Institute Research Foundation, Plano, TX; and §Nanovis, LLC, Columbia City, IN.

Acknowledgment date: February 25, 2016. Acceptance date: April 15, 2016.

The device(s)/drug(s) is/are FDA-approved or approved by corresponding national agency for this indication.

Nanovis funds were received in support of this work.

Relevant financial activities outside the submitted work: board membership, consultancy, royalties, employment, stocks.

Address correspondence and reprint requests to Richard D. Guyer, MD, Texas Back Institute, 6020 W. Parker Rd. No. 200, Plano, TX 75093; E-mail: rguyer@texasback.com

DOI: 10.1097/BRS.0000000000001672

Since the introduction of lumbar and cervical interbody fusion surgery, many graft materials and concepts for fusion cage designs have been introduced. The most common materials used have been allograft, various metals, and more recently polyetheretherketone (PEEK). The appeal for PEEK was primarily that it is known to be a biocompatible material that could be manufactured to have mechanical properties similar to bone, suggesting that it would be a favorable material for interbody spinal fusion. Also, being radiolucent, it offered better assessment of bony ingrowth into the implant and produced less artifact than metallic implants when using imaging modalities such as magnetic resonance imaging and computed tomography. Biomechanical investigation indicated that PEEK implants are associated with less stress at the implant-vertebral body endplate interface, which may reduce the risk of subsidence compared with metallic implants.[1] Several studies have been published reporting good outcomes with PEEK implants for cervical and lumbar interbody fusion[2–4]; however, there is concern that the surface of PEEK is generally smooth and the material is biologically inert, inhibiting osseointegration.[5] Histology studies have found more fibrous tissue, rather than bone, formed in direct contact with PEEK implants.[6] Thus achieving stability and fusion is reliant upon bony bridging through holes in the devices rather than the additive effect of also having bony ongrowth/ingrowth to the device. The lack of bony ongrowth/ingrowth to the device providing osseointegration may slow bridging of bone across segments.

As early as the 1940s and 1950s results of animal studies indicated that titanium was a safe metal for implants and it appeared that bone readily fused to it.[7,8] In trying to improve osseointegration of PEEK implants, combinations of PEEK and titanium have been developed. In animal studies, plasma-sprayed titanium coating on PEEK was found to have significantly greater shear strength at the bone-implant interface than uncoated PEEK.[6] Histological analysis identified direct bone ongrowth onto the coated PEEK samples, whereas on the uncoated samples, there was a fibrous tissue interface with limited direct bone contact. Significant wear debris was, however, created during implantation of a PEEK device coated with thin layer of porous, vacuum plasma-sprayed titanium on the surfaces interfacing with the vertebral bodies.[9] Another strategy for combining the potential advantages of PEEK and titanium is to add a porous titanium scaffold to a PEEK implant, allowing a more robust titanium layer than achieved with a coating. The purpose of the present study was to compare the strength of implant-bone interface of a porous titanium scaffold, PEEK, and allograft.

MATERIALS AND METHODS

The investigational material was a deeply porous (750 μm) three-dimensional titanium scaffold with interconnecting pores. The scaffold has an average pore size of 523 μm with 70% porosity, and 0.75 mm thickness (Figure 1; Forticore, Nanovis, LLC, Columbia City, IN). The implant was made from diffusion bonding of layers of the porous titanium. Cylindrical pins of three types were prepared for use in the study: the titanium scaffold ($n = 12$), uncoated PEEK ($n = 12$), and allograft ($n = 2$). All the titanium and PEEK pins were made to be 4 mm in diameter and 10 mm in length. The allograft dowel was purchased from Community Tissue Services with 12 mm diameter.

After being reviewed and approved by an animal use committee, the study was performed using two adult domestic pigs, at least 1 year old. The animals were sedated, medicated, and anesthetized. The surgical site on each animal's head was shaved and the animal placed on the operating table in ventral recumbency. The surgical site was aseptically prepped for surgery and an incision made through the skin and the periosteum of the skull to expose the implant area. In the region of the os frontale, corresponding identical holes (4 mm in diameter) were drilled to a 10 mm depth. The holes were arranged in a 4×4 array with approximately 10 mm between holes. The cylindrical implants of the three types were randomly placed and each was press fit into a hole (Figure 2). After all pins were placed, the periosteum and skin over the implant site was sutured in two layers. The animals recovered and were returned to their cage.

Five weeks after surgery, the animals were euthanized and the section of the skull containing the implants was harvested. Each skull was cut out into approximately 15 mm sections with each pin centered within a section. The bottom of each pin was carefully exposed by careful grinding of the bone tissues beneath it using a dental drill with fine tip bits. Specimens were wrapped in saline-soaked gauze and frozen at $-20°C$ before overnight shipping to the testing facility.

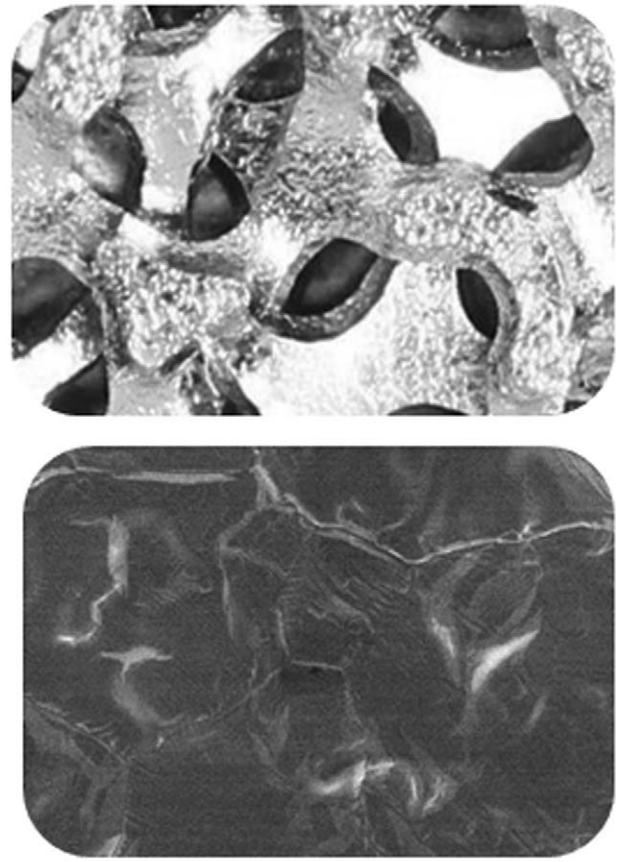

Figure 1. The deeply porous titanium scaffold (upper figure ×30 magnification; lower figure ×1000 magnification; figures courtesy of Nanovis, with permission).

MECHANICAL TESTING

Test specimens were kept frozen until 2 hours before testing to allow them to thaw to room temperature. Biomechanical testing was performed using an MTS machine. A cylindrical load applicator was affixed to the end of a pushrod, which was rigidly attached to the axial load cell. Three and 11.5-mm diameter load applicators were used. The baseplate was rigidly affixed to the load frame actuator. Because of the variability of the shape of the bone specimens, a fixture block, plate, or small vise was used to hold the specimen in position as appropriate to the specimen being tested. A small hole in the support fixture permitted clearance for the pin when extruded. The load applicator was aligned with the implanted pin in the bone specimen (Figure 3). Testing was performed with a push rate of 6 mm/min. A displacement controlled ramp was used to push the implanted pin from the specimen. Data were recorded at a rate of 32 Hz. Load-deformation curves were transported to a personal computer and acquired by Team 490 software (version 4.10, Nicolet Instrument Technologies, Madison, WI). Sigma Plot 7.0 software (SPSS, Chicago, IL) was used to smooth the

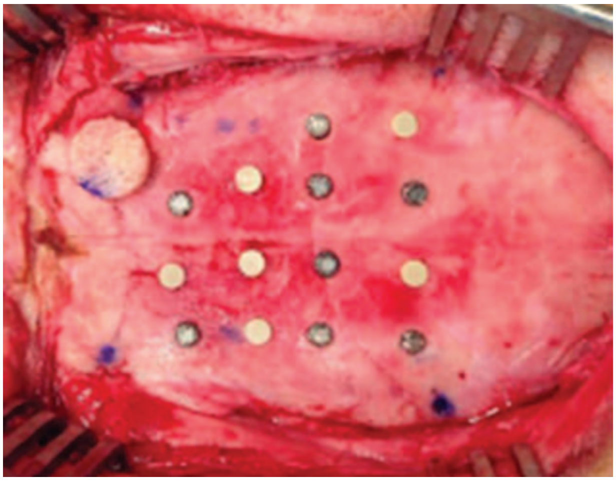

Figure 2. Pins of the three material types placed into the pig skull.

load-deformation curve and compute the extrinsic material properties of the bone samples, including the maximal load (unit: N), ultimate load to failure (unit: N), energy to maximal load (unit: mJ), energy to ultimate load (unit: mJ), and linear stiffness (unit: N/mm). Energies to maximal load and ultimate load were computed as the areas under the load-deforming curves. Stiffness was computed as the slope of the linear portion of the load-deformation curve.

Only maximum force (N) and shear strength (MPa) were extracted from the output to reveal the bonding strength between the implant and the surrounding bone tissues (n = 11). When calculating shear strength, maximum force was normalized by the actual implant surface area that has been in contact with surrounding bone.

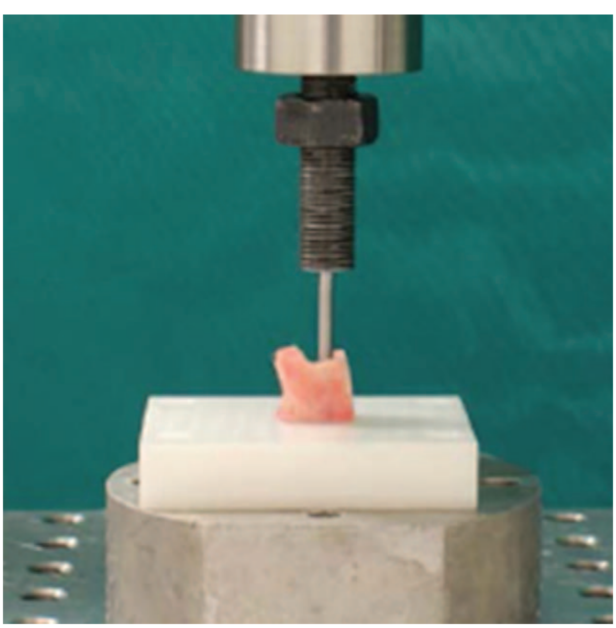

Figure 3. Mechanical push-out testing was performed on all samples to determine the shear strength of the implant-bone interface.

Vertebral Trabecular Bone

In order to gain insight to the comparison of the shear strength of the bone-implant interface being studied and bone, the shear strength of three trabecular bone dowels from porcine vertebral bodies was evaluated. This testing involved determining the static peak stress of the trabecular bone dowels. Bone dowels 10 mm in diameter and 25 mm long were harvested from thawed porcine vertebral body (courtesy of Purdue Veterinary School) using a drill and then sent to Knight Mechanical Testing Lab for shear measurement outlined by ASTM F1044. Bone dowels were potted with bone cement to a calibrated MTS machine (661.19F-03, 15 kN capacity) equipped with an MTS Linear Variable Differential Transducer (100 mm stroke). The test was done at a rate of 0.25 cm/min and data were recorded at 128 Hz.

RESULTS

Not all samples could be tested biomechanically. In the PEEK group, two pins popped out after necropsy/trimming and two other were excluded due to values considered to be outliers. Both of these were noted to be difficult to fit into the holes during implantation. In the titanium scaffold group, one value was excluded as an extreme outlier. Five pins in this group were not successfully pushed out due to the bone splitting during testing. The average maximum force applied before the section split was 1191 N (average was 1449 N for pins which were pushed out). The bone splitting may have been attributable to misorientation between the load applicator and the pin. Thus a total of six porous titanium pins, eight PEEK pins, and two allograft pins were available for data analysis. Among the tested samples, the mean shear strength was statistically significantly greater in the group with the porous titanium scaffold group compared with either PEEK or allograft ($P < 0.05$; Figure 4). The mean value of the porous titanium scaffolds was also the only group with values greater than the mean peak stress of porcine trabecular bone.

DISCUSSION

The results of the present study found that shear strength of a deeply porous titanium scaffold was significantly greater

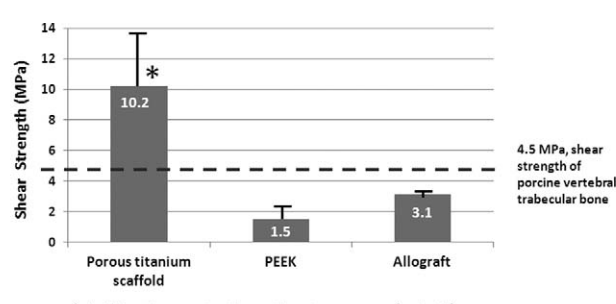

Figure 4. Mean pin push-out strength was significantly greater in the porous titanium group ($P < 0.05$) than in either of the other two groups. The shear strength of porous titanium group is also significantly higher than that of mature porcine trabecular bone ($P < 0.05$). Values are means and the bars represent the standard deviations. PEEK indicates polyetheretherketone.

than that of PEEK or allograft. The increased shear strength was likely due to greater osseointegration into the titanium than is not available with uncoated PEEK or allograft. This type of scaffold molded to PEEK may be beneficial for spinal fusion cages. Such implants may have the potential to take advantage of the benefits of PEEK while addressing the disadvantage of the formation of a fibrous tissue layer around PEEK with little or no direct bony contact.

Several strategies for improving bony ongrowth onto PEEK have been described including altering the surface of the implant itself, spraying a coating onto the implant, or attaching another material to the PEEK surfaces that interface with the adjacent vertebral bodies. Various methods of altering the PEEK surface to increase roughness and/or add an element of porosity have been described[10,11] There may, however, be limitations to the design of the surface of PEEK implants due to manufacturing limitations with this material. In a cadaveric study, it was found that PEEK interbody cages were more easily pulled out compared with titanium cages of a similar design.[12] The authors attributed this at least in part to the anchoring teeth on the PEEK cages not being as sharp as on the titanium cage, due to manufacturing limitations. They suggested that PEEK may provide less stability in the early postoperative period than titanium cages. Currently, many of the stand-alone PEEK cages are fitted for use with an affixed anterior plate and screws that may address this issue.

Plasma-treated PEEK has been associated with increased osteogenic activity.[13] Another strategy to add an osseointegration component to PEEK has been to add a coating or bonding the PEEK to another surface. A logical step in this progression was to turn to materials known to be biocompatible and having favorable osseointegration properties. The primary two investigated being hydroxyapatite and titanium. Several laboratory and animal studies have found various strategies for adding hydroxyapatite surface coatings on PEEK-improved osseointegration.[14–17] The addition of tantalum to the PEEK surface has been found to improve osteointegration of implants in basic science studies.[18] PEEK with a plasma-sprayed titanium coating has been associated with significantly greater bone-implant interface strength than uncoated PEEK.[6,19] One potential disadvantage of a thin porous vacuum plasma–sprayed titanium applied to PEEK noted in a recent publication was that significant wear debris was created during device implantation.[9] No such debris was seen with etched surface titanium implants. The potential generation of wear debris during device implantation may be related to the technique of applying the coating or the placement of the coating on an edge of the device receiving a high-impact force during implantation.

In addition to the implant materials, much is being learned about the importance of implant surface topology at the micro- and nanolevels. It has been found that rough titanium alloy stimulated cells to create an osteogenic-angiogenic microenvironment.[20] The response was greater on rough titanium than smooth titanium, which stimulated a greater response than PEEK. As described by Gittens *et al*, implant surface characteristics such as microroughness and nanostructures may affect osseointegration.[21] Although many strategies have been described to improve the design, materials, and the surface of interbody fusion cages, there is very little literature available upon which to draw conclusions concerning the impact of these factors on clinical outcome.

The results of the present study found that deeply porous titanium scaffold had a significantly greater push-out strength than did PEEK or allograft at 5 weeks after implantation. It is hypothesized that the greater shear strength was due to greater osseointegration, bonding the bone and pin together. There appears to be promise for materials such as the deeply porous titanium scaffold used in the present study as an osseointegrative layer between PEEK and bone. This combination may reduce potential problems with fibrous tissue formation along the PEEK by replacing it with bony ongrowth and ingrowth into deeply porous scaffold while still taking advantage of the imaging and load-bearing/transfer properties of PEEK.

➢ Key Points

- ❑ Osseointegration is an important factor for interbody fusion devices to provide early stability and prevent formation of fibrous tissue along the implant-bone interface.
- ❑ At 5 weeks after implantation, the mean shear strength of the porous titanium scaffolds was significantly greater than that for the PEEK or allograft, as assessed by biomechanical push-out testing.
- ❑ Porous titanium may be a viable material for increasing mechanical stability of spinal implants and further investigation is warranted.

References

1. Vadapalli S, Sairyo K, Goel VK, et al. Biomechanical rationale for using polyetheretherketone (PEEK) spacers for lumbar interbody fusion-a finite element study. *Spine* 2006;31:E992–8.
2. Kersten RF, Van Gaalen SM, De Gast A, et al. Polyetheretherketone (PEEK) cages in cervical applications: a systematic review. *Spine J* 2015;15:1446–60.
3. Lied B, Roenning PA, Sundseth J, et al. Anterior cervical discectomy with fusion in patients with cervical disc degeneration: a prospective outcome study of 258 patients (181 fused with autologous bone graft and 77 fused with a peek cage). *BMC Surg* 2010;10:10.
4. Rousseau MA, Lazennec JY, Saillant G. Circumferential arthrodesis using PEEK cages at the lumbar spine. *J Spinal Disord Tech* 2007;20:278–81.
5. Kurtz SM, Devine JN. PEEK biomaterials in trauma, orthopedic, and spinal implants. *Biomaterials* 2007;28:4845–69.
6. Walsh WR, Bertollo N, Christou C, et al. Plasma sprayed titanium coating to PEEK improves the bone-implant interface. *Spine J* 2015;15:1041–9.
7. Bothe RT, Beaton KE, Davenport HA. Reaction of bone to multiple metallic implants. *Surg Gynecol Obstet* 1940;71:598–602.
8. Leventhal GS. Titanium, a metal for surgery. *J Bone Joint Surg Am* 1951;33-A:473–4.

9. Kienle A, Graf N, Wilke HJ. Does impaction of titanium-coated interbody fusion cages into the disc space cause wear debris or delamination? *Spine J* 2016;16:235–42.
10. Khoury J, Kirkpatrick SR, Maxwell M, et al. Neutral atom beam technique enhances bioactivity of PEEK. *Nuclear Instru Methods Physics Res* 2013;307:630–4.
11. Evans NT, Torstrick FB, Lee CS, et al. High-strength, surface-porous polyether-ether-ketone for load-bearing orthopedic implants. *Acta Biomater* 2015;13:159–67.
12. Spruit M, Falk RG, Beckmann L, et al. The in vitro stabilising effect of polyetheretherketone cages versus a titanium cage of similar design for anterior lumbar interbody fusion. *Eur Spine J* 2005;14:752–8.
13. Waser-Althaus J, Salamon A, Waser M, et al. Differentiation of human mesenchymal stem cells on plasma-treated polyetheretherketone. *J Mater Sci Mater Med* 2014;25:515–25.
14. Ma R, Tang S, Tan H, et al. Preparation, characterization, and in vitro osteoblast functions of a nano-hydroxyapatite/polyetheretherketone biocomposite as orthopedic implant material. *Int J Nanomedicine* 2014;9:3949–61.
15. Deng Y, Liu X, Xu A, et al. Effect of surface roughness on osteogenesis in vitro and osseointegration in vivo of carbon fiber-reinforced polyetheretherketone-nanohydroxyapatite composite. *Int J Nanomedicine* 2015;10:1425–47.
16. Lee JH, Jang HL, Lee KM, et al. In vitro and in vivo evaluation of the bioactivity of hydroxyapatite-coated polyetheretherketone biocomposites created by cold spray technology. *Acta Biomater* 2013;9:6177–87.
17. Abu Bakar MS, Cheng MH, Tang SM, et al. Tensile properties, tension-tension fatigue and biological response of polyetheretherketone-hydroxyapatite composites for load-bearing orthopedic implants. *Biomaterials* 2003;24:2245–50.
18. Lu T, Wen J, Qian S, et al. Enhanced osteointegration on tantalum-implanted polyetheretherketone surface with bone-like elastic modulus. *Biomaterials* 2015;51:173–83.
19. Stubinger S, Drechsler A, Burki A, et al. Titanium and hydroxyapatite coating of polyetheretherketone and carbon fiber-reinforced polyetheretherketone: a pilot study in sheep. *J Biomed Mater Res B Appl Biomater*; in press.
20. Olivares-Navarrete R, Hyzy SL, Gittens RAs, et al. Rough titanium alloys regulate osteoblast production of angiogenic factors. *Spine J* 2013;13:1563–70.
21. Gittens RA, Olivares-Navarrete R, Schwartz Z, et al. Implant osseointegration and the role of microroughness and nanostructures: lessons for spine implants. *Acta Biomater* 2014;10:3363–71.