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Implant Surface Technologies to Promote Spinal Fusion: A Narrative Review

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ABSTRACT

The technology surrounding spinal fusion surgery has continuously evolved in tandem with advancements made in bioengineering. Over the past several decades, developments in biomechanics, surgical techniques, and materials science have expanded innovation in the spinal implant industry. This narrative review explores the current state of implant surface technologies utilized in spinal fusion surgery. This review covers various types of implant surface materials, focusing on interbody spacers composed of modified titanium, polyetheretherketone, hydroxyapatite, and other materials, as well as pedicle screw surface modifications. Advantages and disadvantages of the different surface materials are discussed, including their biocompatibility, mechanical properties, and radiographic visibility. In addition, this review examines the role of surface modifications in enhancing osseointegration and reducing implant-related complications and, hopefully, improving patient outcomes. The findings suggest that while each material has its potential advantages, further research is needed to determine the optimal surface properties for enhancing spinal fusion outcomes.

Focus Issue Article

Keywords: spinal fusion, spinal implants, surface technology, interbody, pedicle screw

INTRODUCTION

Spine surgery has been greatly transformed by continual improvements in biomechanics and engineering. Optimizing the development of solid arthrodesis with enhanced implant surface properties has become an area of growing interest over the past decade. While it remains the standard to use spinal instrumentation with rods and screws for cervical and thoracolumbar pathology, it is still within recent memory that these implants were unavailable for spine surgeons.¹ In 1891, Dr. Berthold Earnest Hadra attempted to treat a patient with Pott's disease suffering with progressive neurological decline from a fracture dislocation of the cervical spine by wiring together the sixth and seventh cervical vertebrae for stability.² In the early 1910s, Drs. Russell Hibbs and Fred Albee continued to develop the nascent field of spine surgery by laying down the spinous process autograph along the interspinous space to promote fusion in a pediatric patient with a severe kyphotic deformity.³ The next leap forward came in 1958 when Dr. Paul Harrington introduced the first successful implantable spinal instrumentation system, the Harrington Rod, a laminar hook and rod system designed to treat polio-related neuromuscular scoliosis.⁴ Building on this innovation, Drs. Yves Cotrel and Jean Dubousset developed

the Cotrel–Dubousset instrumentation system in 1978, a dual-rod system with multiple fixation points using hook and rod combinations, allowing for 3D correction of the spine.⁴

With the development of modern pedicle screw systems, interbody devices, and osteoinductive and osteoconductive bone grafts, the ability to achieve solid fusion has advanced significantly. Alloying titanium with other metals or creating polyetheretherketone (PEEK) composites and alternative cross linking are methods that can alter the material's intrinsic mechanical properties. Recently, there has been increasing interest in understanding how these implantable materials interact with native spinal bony tissue. In this narrative review, we sought to (1) summarize the current state of implant surface technology and (2) describe the impact of implant surface technology on bone fusion.

INTERBODY IMPLANTS

A critical component of an interbody implant is choosing the implant material, which must have sufficient mechanical strength to bear compressive forces, particularly in the lumbar spine, where it will be subject to repetitive and constant compressive forces across the interbody space. At the same time, implants must resist

shear and axial rotation forces. The material should also ideally have a similar elastic modulus, also known as Young's modulus, to that of native bone. A material's elastic modulus is the ratio of stress to strain and is often used to quantify a material's stiffness.⁵ Native cortical bone possesses a Young's elastic modulus of 18 GPa, whereas cancellous and trabecular bones have elastic moduli of 2 and 3–4 GPa, respectively.⁶ To put these values into perspective, the 2 most common implant materials are titanium and PEEK, which have elastic moduli of 102–110 and 3–4 GPa, respectively.⁷ In native tissues, the presence of surface chemical and protein markers signals cells to adhere and grow. Similarly, the reaction of bony tissue to an implant is dictated by material surfaces.^{8–10} As such, the field of implant technology has given greater focus on modification, functionalization, and bioactivation of surfaces to improve osseointegration.

TITANIUM

Ti-6Al-4 V alloy is a commonly utilized metal alloy for spinal interbody devices in large part due to its ability to form a titanium dioxide (TiO₂) surface layer that shows resistance to corrosion and can facilitate bone growth in and around the implant.¹¹ Other implant surface properties, such as surface roughness and topography, have also been shown to impact activity at the cell–material interface, thereby affecting the formation of new tissue.¹² The surface of titanium (Ti) implants can therefore be modified to influence the way native tissues interact with the implant to improve both on-growth and in-growth of bone. On-growth of bone is the direct apposition of bone onto the surface of the material, while in-growth involves the interlocking or growth of bone into a porous surface of a material.¹¹

On-Growth

A particularly useful surface modification to achieve bone on-growth is surface roughening. At a basic level, surface roughening helps improve initial fixation of implants and helps limit motion through simply increasing the static friction between the implant surface and bone.^{13,14} Surface roughening not only increases initial bony adhesion but is also known to induce differentiation and phenotypic maturation of osteoblasts, resulting in increased osteointegration and bone formation.^{15–17} Even when unmodified, surface-roughened titanium without the addition of bone graft has been shown by Krayenbuhl et al¹⁸ and Kroppenstedt et al¹⁹ to be able to achieve successful cervical and lumbar fusion. When

compared with smooth Ti, roughened Ti has been shown to stimulate higher local levels of bone morphogenic proteins, osteoclast inhibitors like transforming growth factor beta (TGF-β) and osteoprotegerin, as well as promoters of angiogenesis including fibroblast growth factor 2, vascular endothelial growth factor A, and angiopoietin-1.²⁰ These effects can occur with surface roughening at both the micro- and nanoscales. At the microscale, roughened Ti spine implants often have roughness sizes ranging from 3 to 30 μm, depending on the manufacturer.^{21,22} For comparison, cementless total hip stems typically have an on-growth segment with a roughness size ranging from 3 to 8 μm.^{23,24} Alternatively, innovations in spinal fusion sciences has taken Ti roughening down to the nanoscale (10⁻⁹ m), better mimicking the architecture of natural tissues and providing host cells the ability to interact with implants on a molecular level through direct interactions with cell membrane receptors.^{20,25} While studies show positive effects from the nanostructures alone in terms of osteointegration and bone formation, there is also believed to be a synergistic effect when combined with microrough surfaces.¹⁶

In-Growth

Titanium alloy can be machined to achieve a higher degree of porosity and interconnectivity, thereby promoting bone in-growth. One of the challenges of titanium is its relatively higher elastic modulus compared with that of native bone, which can lead to stress shielding and subsequently progress to subsidence, interspace collapse, and bone atrophy.^{5,11} On a macroscale, increasing the porosity reduces the elastic modulus, bringing it closer to that of native bone or PEEK, reducing the subsidence issues seen with early titanium alloy and nonporous titanium cages.^{11,26} Studies have also demonstrated increased osteoblast adhesion, proliferation, and differentiation in porous titanium cages compared with nonporous cages, attributable to the porous structure mimicking trabecular bone and allowing for osteoblast migration.^{26,27} Additionally, Ti cages with bulk porosity have been shown to have significantly superior load sharing properties than their nonporous Ti cage counterparts.²⁸ Fujibayashi et al,²⁹ in their prospective trial, used a porous titanium cage for transforaminal lumbar interbody fusion. The authors found that all 5 cases achieved bony fusion by 6 months. At 12 months, the authors did not find evidence of subsidence, which was thought to be attributed to the lower elastic modulus, with a subsequent lower chance of subsidence and higher rate of osseointegration due

to surface modification as contributors to the success rate.²⁹ Wu et al³⁰ designed an even more porous titanium interbody cage with full interconnectivity using electron beam melting in sheep models. This particular design demonstrated superior bony in-growth with less micromotion relative to a PEEK alternative. One area of potential concern with the porous design is the increased risk of wear debris, which is caused by a decrease in the surface contact area at the implant–bone interface. This leads to pressures and increasing the likelihood of mechanical wear leading to debris formation.^{26,31}

Chemical Modification—Hydroxyapatite

Another benefit of TiO₂ is its ability to generate negatively charged hydroxide ions (OH⁻) when exposed to humid environments.³² These hydroxide ions can bind to calcium (Ca⁺²) and phosphate (PO₄⁻³) ions, forming a bone-like appetite and stimulating osteoblastic activity.³² This property can be advantageous by coating titanium with hydroxyapatite (HA). HA can be sintered at high temperatures³³ or deposited as a plasma spray³⁴ apatite layer that mimics the bone surface, allowing for chemical integration when implanted. While HA-modification has not been extensively studied in titanium interbody spacers, it has been shown to enhance osseointegration of other spinal hardware such as pedicle screws and has also been shown to enhance osseointegration of other orthopedic implants.^{35–37}

PEEK

PEEK spinal cages were originally developed in the late 1980s by a polymer engineer, Carl McMillin, and were first implemented in the early 1990s by Brantigan et al.^{38,39} PEEK cages are widely used today as surgical implants due to their excellent mechanical strength, elastic modulus similar to that of bone, biocompatibility, and ease of manufacturing.⁴⁰ Another major advantage of PEEK over titanium is its radiolucency, which makes PEEK particularly useful in monitoring for implant migration and for accurate assessment of fusion postoperatively.⁵ Although it possesses an elastic modulus profile closer to native bone than that of traditional solid titanium, it lacks osseointegrative properties.¹⁵ This is largely attributable to the hydrophobic nature of untreated PEEK, which renders it bioinert and unable to bond to bone and achieve solid fusion.⁴¹ As a result, research has shown that PEEK implants may be associated with cage migration and pseudarthrosis.⁵ To enhance bony growth with PEEK implants, multiple methods have been explored.

Composites

One of the primary methods developed to improve the effectiveness of PEEK implants was the implementation of PEEK composites, in which PEEK is combined with a more biologically active material. In an in vivo and in vitro study, Wu et al⁴² found that an n-TiO₂/PEEK composite resulted in significantly more bone volume compared with PEEK alone. In an ovine lumbar model, McGilvray et al⁴³ found that PEEK-titanium composite implants resulted in a significant decrease in the range of motion following implantation. In addition to Ti-containing PEEK composites, PEEK has also been impregnated with other materials such as HA in an attempt to more closely mimic bone. In sheep cervical fusion models, Walsh et al found that incorporating HA directly into the PEEK matrix resulted in increased direct bone apposition, concluding that the HA-PEEK composite provided a more favorable environment than PEEK alone for bone on-growth.⁴⁰

Coatings

Another breakthrough was the use of various biologically active coatings for PEEK implants, a method often used to augment composite materials. The 2 major composite and coating pairings were Ti and HA. Since natural bone is a composite of fine HA reinforced on a network of collagen, a biocompatible PEEK scaffold with HA particles would theoretically be capable of supporting bone growth to mimic normal bone. Other metals were introduced in small quantities to modulate the mechanical properties of coating. Wong et al introduced a strontium-containing HA and PEEK composite to create an elastic modulus similar to that of cortical bone (9.6–10.6 GPa).⁴⁴ Other potential composites with PEEK that have been explored include calcium silicate and β-tricalcium phosphate, among others.^{45,46} Most findings, however, were purely related to osseointegrative properties in animal studies with a substantial lack of clinical trial data.⁴⁷ Titanium composites and coatings offer mechanical improvements along with significantly enhanced osseointegration. Han et al applied a coating of Ti to PEEK with electron beam deposition and found improved cell proliferation as well as greater bone contact following implantation.⁴⁸ HA in addition to Ti applied by plasma spray onto a PEEK implant has also demonstrated a promising mechanical adhesive strength.⁴⁹ These findings suggested that PEEK composite implants and biologically active coatings may be promising approaches to enhance the osseointegrative properties of PEEK cages in interbody fusion procedures. Although bioactive treatments have shown

potential advantages and demonstrated a great deal of promise, most are not readily available for clinical application yet because most studies have been conducted in animal models.⁵⁰ Additional barriers to the use of these products are their highly specialized manufacturing demands, increased cost, altered physical properties, or simply because they have not been fully characterized for use in humans.

Porous PEEK

While PEEK composite materials and coatings have shown improvements in osseointegration, an alternative approach has also been developed by implementing the concept of porosity originally utilized in titanium implant modifications.⁵¹ Designed to mimic the structure of human trabecular bone, early generation porous PEEK cages have demonstrated both a greater expulsion resistance compared with smooth PEEK cages and a greater adhesion strength compared with plasma-sprayed Ti-coated PEEK surfaces. In vitro studies have confirmed that porous PEEK is able to facilitate cell attachment, proliferation, and osteogenic differentiation of multiple bone cell lineages as well as enhance mineralization at the cellular level in a manner similar to roughened and porous titanium surfaces. At the implant level, in vivo animal studies have shown comparable bone in-growth into porous PEEK as those previously reported for porous titanium, leading to twice the fixation strength of smooth PEEK implants.⁵¹⁻⁵⁵

OTHER IMPLANT SURFACES

Many other possible implant materials are currently under consideration. Silicon nitride and tantalum are 2 commonly discussed surfaces. Silicon nitride is a non-oxide ceramic with osteoconductive properties similar to porous Ti; it not only demonstrated promising high mechanical properties and a wear-resistant profile but also exhibited partial radiolucency and a high fracture resistance.⁵⁶⁻⁵⁸ While implants have been designed, the interbody cages made of silicon nitride have not been fully explored.

Tantalum is a metal with a high compressive strength. Porous tantalum has demonstrated good osseointegration after treatment with alkali and heating.⁵⁹ Animal studies have shown that tantalum implants were a better bridge between autograft bone and native vertebral bone compared with PEEK implants.^{60,61} In a randomized controlled human trial, trabecular tantalum cervical implants without graft were compared with tricortical iliac crest autograft and plating in one-level

anterior cervical discectomy and fusion.⁶² Although the findings were not statistically significant, the results showed slightly higher rates of radiographic fusion in the tantalum implant group at both 6 and 12 months postoperatively.

PEDICLE SCREWS

Much like the advancements made in implant surface technology, large strides have also been made in the surface technology of instrumentation components, particularly in pedicle screws. While posterior instrumentation with traditional titanium or stainless steel pedicle screws has been shown to increase fusion rates, pedicle screw loosening remains a significant complication, with loosening rates reported to range from 0.6% to 11%.^{63,64} The risk of loosening is even greater in patients with osteoporosis, with an incidence reported as high as 60%.^{65,66} Pedicle screw loosening can lead to further issues such as pain, rod or screw breakage, pseudarthrosis, and loss of spinal alignment.⁶⁷ Given the aging population and the increasing requirements for spine surgery with posterior instrumentation, much attention has been devoted to augmenting the surface material of pedicle screws to optimize fixation.⁶⁸

Roughened Titanium

Because roughened titanium interbody implants have been previously shown to improve interbody fixation, the same methodology has also been applied to pedicle screws in an effort to improve pullout strength. In an in vitro and in vivo study by Schwartz et al,⁶⁹ investigators compared untreated, smooth titanium screws to screws that were grit blasted to generate a rough, nanotextured surface. In the in vivo arm, after implanting the screws into sheep models, they found the roughened screws to have significantly greater pullout strength compared with the smooth screws. In the in vitro arm, they cultured human osteoblast-like cells on smooth and roughened titanium discs and found the roughened discs to have increased levels of growth factors and cytokines such as prostaglandin E₂, transforming growth factor- β 1, and osteoprotegerin, which promote osteoblastic activity and inhibit osteoclastic activity.⁶⁹

Hydroxyapatite

Akin to its use in interbody surface augmentation, HA has also been extensively studied as a surface coating material for pedicle screws. When a titanium or stainless steel pedicle screw is coated with HA, the HA serves as a promotor of bone deposition along the

screw surface.^{63,67,70,71} In perhaps the first clinical study analyzing HA-coated screws in patients, Sanden et al compared implanted titanium screws in the lumbar spine with and without HA-coating in patients undergoing lumbar fusion and found that the HA-coated screws had significantly higher extraction torque postoperatively and a significant decrease in the incidence of loosening compared with noncoated screws.⁷¹ Other studies using ovine and porcine animal models have also shown HA-coated pedicle screws to have a higher screw pullout force threshold compared with untreated pedicle screws.^{67,70} They were also shown to have a superior osseointegration profile in canine and porcine osteoporosis models compared with untreated pedicle screws.^{72,73} Despite this, concerns remain regarding when the inevitable need for revision surgery arises in the setting of well-integrated, HA-coated polyaxial pedicle screws.

Carbon Fiber-Reinforced PEEK

Due to the metal-induced artifacts produced by standard titanium alloy pedicle screws on postoperative imaging, carbon fiber-reinforced PEEK (CF/PEEK) pedicle screws have been developed.⁷⁴ Because both carbon fiber and PEEK are radiolucent and have no magnetic properties, CF/PEEK pedicle screws help to minimize artifacts seen on both computed tomography and magnetic resonance imaging, thereby permitting a more thorough and accurate postoperative assessment of images.^{7,74,75} This feature plays an important role in detecting pseudarthrosis and adjacent segment disease and evaluating neural structures postoperatively.⁷⁴ Furthermore, the radiolucent feature of CF/PEEK pedicle screws can be of substantial benefit in spine tumor cases. The higher-quality images may help in dose calculations for radiotherapy planning. Additionally, CF/PEEK screws can also reduce the radiation scattering and tumor shielding caused by metallic implants.⁷⁵⁻⁷⁷ In a cadaveric study by Lindter et al,⁷⁴ investigators found no differences between the nonmetallic CF/PEEK pedicle screws and standard titanium pedicle screws with regard to screw loosening when subjected to cyclic craniocaudal loading. However, CF/PEEK pedicle screws are yet to be widely adopted due to their high cost and less availability compared with titanium.⁷⁸

Gold Nanoparticle Coating

Another relatively newer method of pedicle screw surface augmentation involves nanoparticle coating using metals such as gold or silver. Similar to the osseointegration exhibited by HA-coated pedicle screws,

gold nanoparticles have also been shown to increase osseointegration when applied to implant surfaces.⁷⁹⁻⁸¹ Gold nanoparticles act as osteogenic agents by inducing osteogenic differentiation of progenitor cells and by inducing activation of the p38 mitogen-activated protein kinase signaling pathway.^{79,82,83} The p38 mitogen-activated protein kinase pathway causes further upregulation of osteogenic genes essential for osteoblast differentiation, such as runt-related transcription factor 2 (RUNX2),⁸⁴ the gene that determines the osteoblast lineage from pluripotent mesenchymal stem cells.⁸³ Gold nanoparticles may be conjugated to the surface of titanium implants coated with 3-mercaptopropyl trimethoxysilane through gold-sulfur bonding.⁷⁹ In a study by Ko et al⁷⁹ using rabbit models, investigators demonstrated higher osseointegration parameters using pedicle screws doubly coated with gold nanoparticles compared with pedicle screws coated with HA. These findings suggest that implants coated with gold nanoparticles may be a valid alternative to HA-coated pedicle screws, particularly in patients with poor bone quality.

Silver Nanoparticle Coating

Silver nanoparticles can also be applied to the surface of pedicle screws, which is done either by silver plasma ion immersion or vapor deposition.⁸⁵ In addition to their biocompatible properties, silver nanoparticles have been shown to exert an antibacterial effect, which is achieved through the release of silver ions from soluble complexes, which generate reactive oxygen species that breakdown bacterial components.^{20,86} In a study by Hazer et al, investigators demonstrated that silver-impregnated pedicle screws had an antimicrobial effect against methicillin-resistant *Staphylococcus aureus*, especially in the inhibition of biofilm formation, in the lumbar spines of rabbit models.⁸⁷ The latter may represent a useful aspect of silver nanoparticle coating as hardware infection can be a life-threatening complication of spinal surgery.⁸⁸

CONCLUSION

In conclusion, implant surface technology has advanced significantly since the inception of the field. Substantial research in this area has led to a greater understanding of how various materials interact with native bone and tissue. In the field of spine surgery, interbody and pedicle screw surface materials play a crucial role in ensuring the success of spinal fusion procedures, and surgeons now have a range of options

Table. Advantages and disadvantages of implant surface technologies.

Surface Material	Advantages	Disadvantages
Interbody		
Titanium/HA-coated titanium/other surface-treated titanium	Strong biomechanical profile, biocompatible, and well studied	High stiffness increases risk of subsidence
Titanium-PEEK	Good fusion profile and radiolucent on imaging	Poor wear resistance, limited clinical data, and risk of delamination
PEEK	Radiolucent and biomechanical profile similar to native bone	Poor wear resistance, inferior fusion rate relative to auto/allograft, and fibrous scar formation
Silicon nitride	Low infection risk and good osseointegration	High cost, limited clinical data, and brittle
Tantalum	High fusion rate/biocompatibility	Radiopaque, difficult machining, and high cost
Pedicle Screws		
Roughened titanium	Improved osseointegration and pullout threshold	Lacking human clinical data
HA-coated screws	Improved osseointegration and pullout threshold	Lacking long-term randomized controlled trials
Carbon-fiber-PEEK	Radiolucent with reduced artifact in postoperative imaging	High cost and low availability; similar risk of loosening compared with traditional screws
Gold nanoparticle	Improved osseointegration	Lacking human clinical data
Silver nanoparticle	Decreased risk of infection	Lacking human clinical data

Abbreviations: HA, hydroxyapatite; PEEK, polyetheretherketone.

available to them (as summarized in Table) to enhance the integration of implants into surrounding tissues, reduce complications, and ultimately improve patient outcomes. Despite the advancements in this technology, the clinical data are relatively scarce and largely limited to laboratory studies or animal models. Long-term prospective clinical trials are required to further investigate the efficacy of these newer implant surface technologies. As researchers and surgeons continue to explore new options and refine existing techniques, we can expect to see continued advances in implant surface technology as additional research emerges.

REFERENCES

- Virk S, Qureshi S, Sandhu H. History of spinal fusion: where we came from and where we are going. *HSS J*. 2020;16(2):137–142. doi:10.1007/s11420-020-09747-7
- Hadra BE. Wiring of the vertebrae as a means of immobilization in fracture and Potts' disease. 1891. *Clin Orthop Relat Res*. 2007;460:11–13. doi:10.1097/BLO.0b013e318068692a
- Tarpada SP, Morris MT, Burton DA. Spinal fusion surgery: a historical perspective. *J Orthop*. 2017;14(1):134–136. doi:10.1016/j.jor.2016.10.029
- Desai SK, Brayton A, Chua VB, Luerssen TG, Jea A. The lasting legacy of Paul Randall Harrington to pediatric spine surgery: historical vignette. *J Neurosurg Spine*. 2013;18(2):170–177. doi:10.3171/2012.11.SPINE12979
- Warburton A, Girdler SJ, Mikhail CM, Ahn A, Cho SK. Biomaterials in spinal implants: a review. *Neurospine*. 2020;17(1):101–110. doi:10.14245/ns.1938296.148
- Hoppe S, Albers CE, Elfiky T, et al. First results of a new vacuum plasma sprayed (VPS) titanium-coated carbon/PEEK composite cage for lumbar interbody fusion. *J Funct Biomater*. 2018;9(1):23. doi:10.3390/jfb9010023
- Kurtz SM, Devine JN. PEEK biomaterials in trauma, orthopedic, and spinal implants. *Biomaterials*. 2007;28(32):4845–4869. doi:10.1016/j.biomaterials.2007.07.013
- Chen JW, Lim K, Bandini SB, et al. Controlling the surface chemistry of a hydrogel for spatially defined cell adhesion. *ACS Appl Mater Interfaces*. 2019;11(17):15411–15416. doi:10.1021/acsami.9b04023
- Khalili AA, Ahmad MR. A review of cell adhesion studies for biomedical and biological applications. *Int J Mol Sci*. 2015;16(8):18149–18184. doi:10.3390/ijms160818149
- Kuo TR, Chen CH. Bone biomarker for the clinical assessment of osteoporosis: recent developments and future perspectives. *Biomark Res*. 2017;5:18. doi:10.1186/s40364-017-0097-4
- Rao PJ, Pelletier MH, Walsh WR, Mobbs RJ. Spine interbody implants: material selection and modification, functionalization and bioactivation of surfaces to improve osseointegration. *Orthop Surg*. 2014;6(2):81–89. doi:10.1111/os.12098
- Deligianni DD, Katsala N, Ladas S, Sotiropoulou D, Amedee J, Missirlis YF. Effect of surface roughness of the titanium alloy Ti-6Al-4V on human bone marrow cell response and on protein adsorption. *Biomaterials*. 2001;22(11):1241–1251. doi:10.1016/s0142-9612(00)00274-x
- Shirazi-Adl A, Dammak M, Paiement G. Experimental determination of friction characteristics at the trabecular bone/porous-coated metal interface in cementless implants. *J Biomed Mater Res*. 1993;27(2):167–175. doi:10.1002/jbm.820270205
- Dos Santos MV, Elias CN, Cavalcanti Lima JH. The effects of superficial roughness and design on the primary stability of dental implants. *Clin Implant Dent Relat Res*. 2011;13(3):215–223. doi:10.1111/j.1708-8208.2009.00202.x
- Olivares-Navarrete R, Gittens RA, Schneider JM, et al. Osteoblasts exhibit a more differentiated phenotype and increased bone morphogenetic protein production on titanium alloy substrates than on poly-ether-ether-ketone. *Spine J*. 2012;12(3):265–272. doi:10.1016/j.spinee.2012.02.002
- Gittens RA, Olivares-Navarrete R, Cheng A, et al. The roles of titanium surface micro/nanotopography and wettability on the differential response of human osteoblast lineage cells. *Acta Biomater*. 2013;9(4):6268–6277. doi:10.1016/j.actbio.2012.12.002
- Salou L, Hoornaert A, Louarn G, Layrolle P. Enhanced osseointegration of titanium implants with nanostructured surfaces: an experimental study in rabbits. *Acta Biomater*. 2015;11:494–502. doi:10.1016/j.actbio.2014.10.017
- Krayenbühl N, Schneider C, Landolt H, Fandino J. Use of an empty, plasmapore-covered titanium cage for interbody fusion after anterior cervical microdiscectomy. *J Clin Neurosci*. 2008;15(1):11–17. doi:10.1016/j.jocn.2006.12.011

19. Kroppenstedt S, Gulde M, Schönmayr R. Radiological comparison of instrumented posterior lumbar interbody fusion with one or two closed-box plasmapore coated titanium cages: follow-up study over more than seven years. *Spine (Phila Pa 1976)*. 2008;33(19):2083–2088. doi:10.1097/BRS.0b013e31818448a9
20. Katsuura Y, Wright-Chisem J, Wright-Chisem A, Virk S, McAnany S. The importance of surface technology in spinal fusion. *HSS J*. 2020;16(2):113–116. doi:10.1007/s11420-020-09752-w
21. Tsuang F-Y, Li M-J, Chu P-H, Tsou N-T, Sun J-S. Mechanical performance of porous biomimetic intervertebral body fusion devices: an in vitro biomechanical study. *J Orthop Surg Res*. 2023;18(1):71. doi:10.1186/s13018-023-03556-4
22. Loh QL, Choong C. Three-dimensional scaffolds for tissue engineering applications: role of porosity and pore size. *Tissue Eng Part B Rev*. 2013;19(6):485–502. doi:10.1089/ten.TEB.2012.0437
23. Hacking SA, Bobyn JD, Tanzer M, Krygier JJ. The osseous response to corundum blasted implant surfaces in a canine hip model. *Clin Orthop Relat Res*. 1999;(364):240–253. doi:10.1097/00003086-199907000-00031
24. Zweymüller KA, Lintner FK, Semlitsch MF. Biologic fixation of a press-fit titanium hip joint endoprosthesis. *Clin Orthop Relat Res*. 1988;(235):195–206.
25. Vandrovcová M, Bačáková L. Adhesion, growth and differentiation of osteoblasts on surface-modified materials developed for bone implants. *Physiol Res*. 2011;60(3):403–417. doi:10.33549/physiolres.932045
26. Levy HA, Karamian BA, Yalla GR, Canseco JA, Vaccaro AR, Kepler CK. Impact of surface roughness and bulk porosity on spinal interbody implants. *J Biomed Mater Res B Appl Biomater*. 2023;111(2):478–489. doi:10.1002/jbm.b.35161
27. Frosch K-H, Barvencik F, Lohmann CH, et al. Migration, matrix production and lamellar bone formation of human osteoblast-like cells in porous titanium implants. *Cells Tissues Organs*. 2002;170(4):214–227. doi:10.1159/000047925
28. Lewis G. Properties of open-cell porous metals and alloys for orthopaedic applications. *J Mater Sci Mater Med*. 2013;24(10):2293–2325. doi:10.1007/s10856-013-4998-y
29. Fujibayashi S, Takemoto M, Neo M, et al. A novel synthetic material for spinal fusion: a prospective clinical trial of porous bioactive titanium metal for lumbar interbody fusion. *Eur Spine J*. 2011;20(9):1486–1495. doi:10.1007/s00586-011-1728-3
30. Wu S-H, Li Y, Zhang Y-Q, et al. Porous titanium-6 aluminum-4 vanadium cage has better osseointegration and less micromotion than a poly-ether-ether-ketone cage in sheep vertebral fusion. *Artif Organs*. 2013;37(12):E191–E201. doi:10.1111/aor.12153
31. Evans NT, Torstrick FB, Safranski DL, Guldborg RE, Gall K. Local deformation behavior of surface porous polyetherether-ketone. *J Mech Behav Biomed Mater*. 2017;65:522–532. doi:10.1016/j.jmbm.2016.09.006
32. Tsou H-K, Chi M-H, Hung Y-W, Chung C-J, He J-L. In vivo osseointegration performance of titanium dioxide coating modified polyetheretherketone using arc ion plating for spinal implant application. *Biomed Res Int*. 2015;2015:328943. doi:10.1155/2015/328943
33. Kim H-M, Himeno T, Kokubo T, Nakamura T. Process and kinetics of bonelike apatite formation on sintered hydroxyapatite in a simulated body fluid. *Biomaterials*. 2005;26(21):4366–4373. doi:10.1016/j.biomaterials.2004.11.022
34. de Groot K, Geesink R, Klein CP, Serekian P. Plasma sprayed coatings of hydroxylapatite. *J Biomed Mater Res*. 1987;21(12):1375–1381. doi:10.1002/jbm.820211203
35. Jing W, Zhang M, Jin L, et al. Assessment of osteoinduction using a porous hydroxyapatite coating prepared by micro-arc oxidation on a new titanium alloy. *Int J Surg*. 2015;24(Pt A):51–56. doi:10.1016/j.ijsu.2015.08.030
36. Ding M, Shi J, Wang W, Li D, Tian L. Early osseointegration of micro-arc oxidation coated titanium alloy implants containing Ag: a histomorphometric study. *BMC Oral Health*. 2022;22(1):628. doi:10.1186/s12903-022-02673-6
37. Kia C, Antonacci CL, Wellington I, Makanji HS, Esmende SM. Spinal implant osseointegration and the role of 3D printing: an analysis and review of the literature. *Bioengineering (Basel)*. 2022;9(3):108. doi:10.3390/bioengineering9030108
38. Brantigan JW, Steffee AD. A carbon fiber implant to aid interbody lumbar fusion. Two-year clinical results in the first 26 patients. *Spine (Phila Pa 1976)*. 1993;18(14):2106–2107. doi:10.1097/00007632-199310001-00030
39. Muthiah N, Yolcu YU, Alan N, Agarwal N, Hamilton DK, Ozpinar A. Evolution of polyetheretherketone (PEEK) and titanium interbody devices for spinal procedures: a comprehensive review of the literature. *Eur Spine J*. 2022;31(10):2547–2556. doi:10.1007/s00586-022-07272-1
40. Walsh WR, Pelletier MH, Bertollo N, Christou C, Tan C. Does PEEK/HA enhance bone formation compared with PEEK in a sheep cervical fusion model *Clin Orthop Relat Res*. 2016;474(11):2364–2372. doi:10.1007/s11999-016-4994-x
41. Johansson P, Jimbo R, Kjellin P, Currie F, Chrcanovic BR, Wennerberg A. Biomechanical evaluation and surface characterization of a nano-modified surface on PEEK implants: a study in the Rabbit Tibia. *Int J Nanomedicine*. 2014;9:3903–3911. doi:10.2147/IJN.S60387
42. Wu X, Liu X, Wei J, Ma J, Deng F, Wei S. Nano-TiO₂/PEEK bioactive composite as a bone substitute material: in vitro and in vivo studies. *Int J Nanomedicine*. 2012;7:1215–1225. doi:10.2147/IJN.S28101
43. McGilvray KC, Easley J, Seim HB, et al. Bony ingrowth potential of 3D-printed porous titanium alloy: a direct comparison of interbody cage materials in an in vivo ovine lumbar fusion model. *Spine J*. 2018;18(7):1250–1260. doi:10.1016/j.spinee.2018.02.018
44. Wong KL, Wong CT, Liu WC, et al. Mechanical properties and in vitro response of strontium-containing hydroxyapatite/polyetheretherketone composites. *Biomaterials*. 2009;30(23–24):3810–3817. doi:10.1016/j.biomaterials.2009.04.016
45. Kim IY, Sugino A, Kikuta K, Ohtsuki C, Cho SB. Bioactive composites consisting of PEEK and calcium silicate powders. *J Biomater Appl*. 2009;24(2):105–118. doi:10.1177/0885328208094557
46. Ma R, Tang T. Current strategies to improve the bioactivity of PEEK. *Int J Mol Sci*. 2014;15(4):5426–5445. doi:10.3390/ijms15045426
47. Barkarmo S, Wennerberg A, Hoffman M, et al. Nano-hydroxyapatite-coated PEEK implants: a pilot study in rabbit bone. *J Biomed Mater Res A*. 2013;101(2):465–471. doi:10.1002/jbm.a.34358
48. Han C-M, Lee E-J, Kim H-E, et al. The electron beam deposition of titanium on polyetheretherketone (PEEK) and the resulting enhanced biological properties. *Biomaterials*. 2010;31(13):3465–3470. doi:10.1016/j.biomaterials.2009.12.030
49. Ha SW, Gisep A, Mayer J, Wintermantel E, Gruner H, Wieland M. Topographical characterization and microstructural interface analysis of vacuum-plasma-sprayed titanium and

- hydroxyapatite coatings on carbon fibre-reinforced poly(etheretherketone). *J Mater Sci Mater Med*. 1997;8(12):891–896. doi:10.1023/a:1018562023599
50. Chan JL, Bae HW, Harrison Farber S, Uribe JS, Eastlack RK, Walker CT. Evolution of bioactive implants in lateral interbody fusion. *Int J Spine Surg*. 2022;16(S1):S61–S68. doi:10.14444/8237
51. Torstrick FB, Safranski DL, Burkus JK, et al. Getting PEEK to stick to bone: the development of porous PEEK for interbody fusion devices. *Tech Orthop*. 2017;32(3):158–166. doi:10.1097/BTO.0000000000000242
52. Cheng A, Humayun A, Cohen DJ, Boyan BD, Schwartz Z. Additively manufactured 3D porous Ti-6Al-4V constructs mimic trabecular bone structure and regulate osteoblast proliferation, differentiation and local factor production in a porosity and surface roughness dependent manner. *Biofabrication*. 2014;6(4):045007. doi:10.1088/1758-5082/6/4/045007
53. Agarwal R, González-García C, Torstrick B, Guldberg RE, Salmerón-Sánchez M, García AJ. Simple coating with fibronectin fragment enhances stainless steel screw osseointegration in healthy and osteoporotic rats. *Biomaterials*. 2015;63:137–145. doi:10.1016/j.biomaterials.2015.06.025
54. Oest ME, Dupont KM, Kong H-J, Mooney DJ, Guldberg RE. Quantitative assessment of scaffold and growth factor-mediated repair of critically sized bone defects. *J Orthop Res*. 2007;25(7):941–950. doi:10.1002/jor.20372
55. Clemow AJ, Weinstein AM, Klawitter JJ, Koeneman J, Anderson J. Interface mechanics of porous titanium implants. *J Biomed Mater Res*. 1981;15(1):73–82. doi:10.1002/jbm.820150111
56. Bal BS, Rahaman MN. Orthopedic applications of silicon nitride ceramics. *Acta Biomater*. 2012;8(8):2889–2898. doi:10.1016/j.actbio.2012.04.031
57. Anderson MC, Olsen R. Bone ingrowth into porous silicon nitride. *J Biomed Mater Res A*. 2010;92(4):1598–1605. doi:10.1002/jbm.a.32498
58. Du X, Lee SS, Blugan G, Ferguson SJ. Silicon nitride as a biomedical material: an overview. *Int J Mol Sci*. 2022;23(12):6551. doi:10.3390/ijms23126551
59. Kato H, Nakamura T, Nishiguchi S, et al. Bonding of alkali- and heat-treated tantalum implants to bone. *J Biomed Mater Res*. 2000;53(1):28–35. doi:10.1002/(sici)1097-4636(2000)53:1<28::aid-jbm4>3.0.co;2-f
60. Hu G, Zhu Y, Xu F, et al. Comparison of surface properties, cell behaviors, bone regeneration and osseointegration between nano tantalum/PEEK composite and nano silicon nitride/PEEK composite. *J Biomater Sci Polym Ed*. 2022;33(1):35–56. doi:10.1080/009205063.2021.1974812
61. Sinclair SK, Konz GJ, Dawson JM, Epperson RT, Bloebaum RD. Host bone response to polyetheretherketone versus porous tantalum implants for cervical spinal fusion in a goat model. *Spine (Phila Pa 1976)*. 2012;37(10):E571–E580. doi:10.1097/BRS.0b013e318240f981
62. Fernández-Fairen M, Sala P, Dufoo M, Ballester J, Murcia A, Merzthal L. Anterior cervical fusion with tantalum implant: a prospective randomized controlled study. *Spine (Phila Pa 1976)*. 2008;33(5):465–472. doi:10.1097/BRS.0b013e3181657f49
63. Sandén B, Olerud C, Johansson C, Larsson S. Improved bone-screw interface with hydroxyapatite coating: an in vivo study of loaded pedicle screws in sheep. *Spine (Phila Pa 1976)*. 2001;26(24):2673–2678. doi:10.1097/00007632-200112150-00008
64. Wu Z, Gong F, Liu L, et al. A comparative study on screw loosening in osteoporotic lumbar spine fusion between expandable and conventional pedicle screws. *Arch Orthop Trauma Surg*. 2012;132(4):471–476. doi:10.1007/s00402-011-1439-6
65. Weiser L, Huber G, Sellenschloh K, et al. Insufficient stability of pedicle screws in osteoporotic vertebrae: biomechanical correlation of bone mineral density and pedicle screw fixation strength. *Eur Spine J*. 2017;26(11):2891–2897. doi:10.1007/s00586-017-5091-x
66. El Saman A, Meier S, Sander A, Kelm A, Marzi I, Laurer H. Reduced loosening rate and loss of correction following posterior stabilization with or without PMMA augmentation of pedicle screws in vertebral fractures in the elderly. *Eur J Trauma Emerg Surg*. 2013;39(5):455–460. doi:10.1007/s00068-013-0310-6
67. Upasani VV, Farnsworth CL, Tomlinson T, et al. Pedicle screw surface coatings improve fixation in nonfusion spinal constructs. *Spine (Phila Pa 1976)*. 2009;34(4):335–343. doi:10.1097/BRS.0b013e318194878d
68. de Kater EP, Sakes A, Edström E, Elmi-Terander A, Kraan G, Breedveld P. Beyond the pedicle screw—a patent review. *Eur Spine J*. 2022;31(6):1553–1565. doi:10.1007/s00586-022-07193-z
69. Schwartz Z, Raz P, Zhao G, et al. Effect of micrometer-scale roughness of the surface of Ti6Al4V pedicle screws in vitro and in vivo. *J Bone Joint Surg Am*. 2008;90(11):2485–2498. doi:10.2106/JBJS.G.00499
70. Sandén B, Olerud C, Larsson S. Hydroxyapatite coating enhances fixation of loaded pedicle screws: a mechanical in vivo study in sheep. *Eur Spine J*. 2001;10(4):334–339. doi:10.1007/s005860100291
71. Sandén B, Olerud C, Petré-Mallmin M, Larsson S. Hydroxyapatite coating improves fixation of pedicle screws. A clinical study. *J Bone Joint Surg Br*. 2002;84(3):387–391. doi:10.1302/0301-620x.84b3.12388
72. Hasegawa T, Inufusa A, Imai Y, Mikawa Y, Lim T-H, An HS. Hydroxyapatite-coating of pedicle screws improves resistance against pull-out force in the osteoporotic canine lumbar spine model: a pilot study. *Spine J*. 2005;5(3):239–243. doi:10.1016/j.spinee.2004.11.010
73. Ohe M, Moridaira H, Inami S, Takeuchi D, Nohara Y, Taneichi H. Pedicle screws with a thin hydroxyapatite coating for improving fixation at the bone-implant interface in the osteoporotic spine: experimental study in a porcine model. *J Neurosurg Spine*. 2018;28(6):679–687. doi:10.3171/2017.10.SPINE17702
74. Lindtner RA, Schmid R, Nydegger T, Kenschake M, Schmolz W. Pedicle screw anchorage of carbon fiber-reinforced PEEK screws under cyclic loading. *Eur Spine J*. 2018;27(8):1775–1784. doi:10.1007/s00586-018-5538-8
75. Eicker SO, Krajewski K, Payer S, Krätzig T, Dreimann M. First experience with carbon/PEEK pedicle screws. *J Neurosurg Sci*. 2017;61(2):222–224. doi:10.23736/S0390-5616.16.03260-4
76. Rapallino MV, Cupello A, Hydén H. Direct evidence for the presence of GABAA receptors on the cytoplasmic side of the deiters' neurone membrane. *Brain Res*. 1988;462(2):350–353. doi:10.1016/0006-8993(88)90563-x
77. Nevelsky A, Borzov E, Daniel S, Bar-Deroma R. Perturbation effects of the carbon fiber-PEEK screws on radiotherapy dose distribution. *J Appl Clin Med Phys*. 2017;18(2):62–68. doi:10.1002/acm2.12046
78. Laux CJ, Hodel SM, Farshad M, Müller DA. Carbon fibre/polyether ether ketone (CF/PEEK) implants in orthopaedic oncology. *World J Surg Oncol*. 2018;16(1):241. doi:10.1186/s12957-018-1545-9

79. Ko W-K, Kim SJ, Heo DN, et al. Double layers of gold nanoparticles immobilized titanium implants improve the osseointegration in rabbit models. *Nanomedicine*. 2020;24:102129. doi:10.1016/j.nano.2019.102129
80. Takanche JS, Kim J-E, Kim J-S, et al. Chitosan-gold nanoparticles mediated gene delivery of C-Myb facilitates osseointegration of dental implants in ovariectomized rat. *Artif Cells Nanomed Biotechnol*. 2018;46(sup3):S807–S817. doi:10.1080/21691401.2018.1513940
81. Weng H-A, Wu C-C, Chen C-C, Ho C-C, Ding S-J. Preparation and properties of gold nanoparticle-electrodeposited titanium substrates with Arg-Gly-Asp-Cys peptides. *J Mater Sci Mater Med*. 2010;21(5):1511–1519. doi:10.1007/s10856-010-4026-4
82. Yi C, Liu D, Fong C-C, Zhang J, Yang M. Gold nanoparticles promote osteogenic differentiation of mesenchymal stem cells through P38 MAPK pathway. *ACS Nano*. 2010;4(11):6439–6448. doi:10.1021/nn101373r
83. Li J, Li JJ, Zhang J, Wang X, Kawazoe N, Chen G. Gold nanoparticle size and shape influence on osteogenesis of mesenchymal stem cells. *Nanoscale*. 2016;8(15):7992–8007. doi:10.1039/C5NR08808A
84. Komori T. Regulation of proliferation, differentiation and functions of osteoblasts by Runx2. *Int J Mol Sci*. 2019;20(7):1694. doi:10.3390/ijms20071694
85. Qin H, Cao H, Zhao Y, et al. In vitro and in vivo antibiofilm effects of silver nanoparticles Immobilized on titanium. *Biomaterials*. 2014;35(33):9114–9125. doi:10.1016/j.biomaterials.2014.07.040
86. Li W, Xu D, Hu Y, Cai K, Lin Y. Surface modification of titanium substrates with silver nanoparticles embedded sulfhydrylated chitosan/gelatin polyelectrolyte multilayer films for antibacterial application. *J Mater Sci Mater Med*. 2014;25(6):1435–1448. doi:10.1007/s10856-014-5190-8
87. Hazer DB, Sakar M, Dere Y, Altinkanat G, Ziyal MI, Hazer B. Antimicrobial effect of polymer-based silver nanoparticle coated pedicle screws: experimental research on biofilm inhibition in rabbits. *Spine (Phila Pa 1976)*. 2016;41(6):E323–E329. doi:10.1097/BRS.0000000000001223
88. Casper DS, Zmistowski B, Hollern DA, et al. The effect of postoperative spinal infections on patient mortality. *Spine (Phila Pa 1976)*. 2018;43(3):223–227. doi:10.1097/BRS.0000000000002277

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