Technological Advancements in Spinal Fusion Implants: A Summary of the Current Scientific and Clinical Research on Titanium Engineered Surfaces

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Background

Lumbar interbody fusion is commonly performed by inserting an implant into the disc space. Interbody fusions are beneficial because they result in high fusion rates, maintain spinal alignment, and allow for indirect decompression of the neuroforamen.¹ Currently, the two most commonly used implants are made of polyether ether ketone (PEEK) or allograft bone. Threaded titanium (Ti) cages were used in the past, but many surgeons became concerned about challenges with imaging the fusion around titanium as well as subsidence, and their use declined. These implants were previously used as threaded “stand-alone” constructs (no pedicle screw fixation). This was shown to be mechanically inferior and led to more clinical failures due to surgical technique rather than the implant material.

A new class of Ti implants with nano-roughened (micron-level) surface modifications have been shown to induce greater osteoblast differentiation of culture stem cells than PEEK.² There is an emerging trend in spine surgery to move away from plastic interbody fusion spacers. This trend has stimulated an expanding clinical and scientific interest in the surface technology of acid-etched titanium spinal implants. The purpose of this article is to review the scientific literature surrounding these unique titanium engineered surfaces and discuss the clinical outcomes to date.

Titanium alloys have been extensively studied in the dental literature and have a well-established history of use. Basic science studies have shown that titanium, especially with roughened nano-surface (micron-level) properties, creates a favorable bone-implant contact surface and superior osseointegration with the surrounding bone.³,⁴,⁵ In vitro experiments comparing the responses of immature osteoblasts to roughened and smooth titanium surfaces conclude that the differentiation of the cells is greater when the surface has an engineered texture with micron-scale (10⁻⁶) roughness. This is the scale on which the mesenchymal stem cells are stimulated.

Dual acid etching processes applied to the surface of Ti has been shown to stimulate local, physiologic bone morphogenetic protein (BMP) production, transforming growth factor beta (TGF-β), and vascular endothelial growth factor (VEGF), all of which promote a natural osteogenic environment and may facilitate bone integration with the implant surface.³,⁴ This is a novel concept that has not been previously examined in the spinal fusion clinical application.

![Figure 1. Laser Microscopy Images and Average-Roughness (Sa) Values of PEEK (A), sTiAlV/Smooth Titanium (B), and rTiAlV/Roughened Titanium (C) Surfaces of 644 × 644 Micron Field.](image-url)
Basic Science

The scientific evidence supporting the physiologic benefits of acid-etched titanium is strong. Gittens et al. published a paper in 2013 which demonstrated human mesenchymal stem cells reacted favorably to nano-texturing (10^{-9} level) the surface of titanium.\(^6\) The cell cultures preferentially expressed strong osteoblastic differentiation as well as increased levels of VEGF. Furthermore, Olivares-Navarrete and co-authors reported their data in two published studies. They compared nano-textured Ti to PEEK and found that the Ti showed significant upregulation in factors associated with bone formation and angiogenesis, both critical for successful fusion. PEEK and smooth Ti both demonstrated inferior results.\(^3\) In their other paper, Olivares-Navarrete et al. demonstrated statistically significant upregulation of BMP-2, BMP-4 and BMP-7, with nano-textured Ti.\(^2\) The PEEK results showed no upregulation of these important bone-forming factors. Summarizing these studies, it is clear that modifying the surface structure to a micron/nano-level can create an osteogenic environment in the host bone. This may enhance bone formation and implant stability, fostering bone ingrowth without exogenous growth factors.

Clinical Applications

Titanium is the most commonly implanted medical material. It is the standard implant material of choice for trauma plates and screws, total joint implants, pedicle screws, among others. It is biocompatible and MRI compatible.

Dental surgeons and total joint surgeons have long been interested in the surface technology of their implants in order to drive osseous integration.\(^5,7\) This is a relatively new but exciting area of increased focus in spine surgery. Acid-etched Ti pedicle screws have shown superior pull-out strength compared to standard screws due to improved bone-screw integration.\(^4\)

PEEK (polyether ether ketone) is a polymer plastic material that has been used commonly by spine surgeons as an option for interbody fusions. This material has no intrinsic capacity to bond to bone and does not elicit a favorable response in the host bone. Therefore, a strong biologic catalyst chemical such as bone morphogenetic protein (BMP) is commonly used to create a fusion with PEEK. BMP, however, has been associated with some concerning complications such as ectopic bone growth and nerve inflammation.\(^8\) It is
also expensive compared to alternative biologic bone graft extenders, so its use is being restricted by many hospitals and insurance carriers.

Titanium with micron (nano) scale surface treatments is gaining substantial ground with spine surgeons looking to move away from PEEK or strongly inflammatory biologics. Titan Spine, LLC, (Mequon, WI) is the only company that manufactures titanium fusion implants with this proprietary surface technology.

Clinical Investigations

In 2013, Dr. Girasole and his co-authors published a retrospective review of 82 patients who underwent transforaminal lumbar interbody fusions (TLIF) using a Titan Endoskeleton implant. All patients had local bone graft plus an allograft bone extender (Osteo-Sponge®; Bacterin International, Belgrade, Montana). Patients were divided into two cohorts with one studied at 6 months and the other at 12 months after surgery.

Fine-cut CT scans were reviewed by an independent radiologist, and fusion results were calculated using a grading scale. At 6 months, the fusion rate was 93.2%; at 12 months, the fusion rate was 97.4%. There were no surgical complications and no device-related complications. The authors compared their results with many other published articles and concluded that their results compared equally well.

Our institution, SpineCare Medical Group, has presented data on two clinical investigations looking at the results of anterior lumbar interbody fusions (ALIF) using the Titan Endoskeleton TA® implant.
The first is a clinical outcomes study of 77 patients enrolled prospectively with 24 month post-operative follow up results.\textsuperscript{10} All patients underwent ALIF with a standard dose (3 mg/fusion level) of Infuse\textsuperscript{®} (Medtronic, Inc.) as the biologic bone graft substitute. Pedicle screw fixation was used in 94\% of the cases with 6\% having a stand-alone ALIF. Clinical outcomes (Oswestry Disability Index: ODI; Visual Numerical Scale: VNS 0-10) were measured at 6, 12, and 24 months.

One of the most compelling results was that the functional improvement was rapidly noticed by the patients by 6 months, and these results held without decline at both 12 and 24 months. Meaningful clinical improvements, ODI $>15$ points and VNS $>3$ points, were noted in the majority of the patients. There were no device related complications.

Another area of key interest to surgeons considering using titanium interbody devices is radiographic fusion assessment. Many express concerns about the
accuracy of CT scans due to problems of scatter and artifact. Previously published reports on this issue have generally focused on older technologies using paired, threaded, smooth titanium devices.\textsuperscript{11–14} These devices had smaller apertures for bone graft and a much greater problem with artifact.

My co-authors and I decided to investigate the interobserver reliability of CT scans in assessing fusion criteria in ALIF patients with these new titanium interbody implants (Titan Spine, LLC).\textsuperscript{15} Thirty-three patients (56 spinal fusion segments) underwent random CT scans as part of the protocol for the clinical outcomes study discussed above. Scans were performed at 6, 9, and 12 months to look for any variability in fusion rates at different times. The images were sent to two independent radiologists blinded to outcomes to assess for fusion variables.

The interobserver agreement for the overall study was 88% (agreement on 345/394 data points). No difference was noted between patient CT results among the patients studied at 6, 9, or 12 months. Interobserver reliability for fusion formation was 77% agreement between the radiologists. Overall fusion rates were 94%. In conclusion, the titanium implant studied demonstrated minimal artifact, minimal subsidence, and easily visualized trabecular bone. The investigators concluded that radiographic fusion criteria can be reliably assessed using CT scans with a high degree of interobserver agreement.

![Figure 7. Overall Fusion Grades: Grade 5: Definitely Fused; Grade 4: Probably Fused; Grade 3: Indeterminate; Grade 2: Probably Not Fused; Grade 1: Definitely Not Fused.](image)

Success Story of a Spinal Champion

The Spinal Research Foundation is focused on patient care, advocacy, and promoting scientific research to improve the outcomes of spinal care. It is always very special for the surgeons and our staff to see patients directly benefit from these scientific advancements. An example of such a patient is RR.

RR was a competitive adult athlete, doing triathlons and endurance events until he injured his back. As a teacher and parent, RR found that he couldn’t even play with the kids at home or on the playground at school. He struggled for over a year with debilitating back pain and nerve pain into his leg. After his evaluation, I diagnosed him with spinal in-

![Figure 8. Spinal Champion RR and Dr. Slosar shake hands after the SRF We’ve Got Your Back Race hosted by SpineCare Medical Group in September 2013.](image)
stability (spondylolisthesis) as well as a separate disc herniation injury at the next level. My recommendation was fusion of both discs with the Titan interbody implants.

Within five days after surgery, RR was up and able to move the way patients do when they are closer to four weeks after an operation. He entered a walking race at 3 months after surgery, but RR couldn’t resist and ran it without pain, never looking back. He later participated in the 2013 San Francisco We’ve Got Your Back Race that benefits the Spinal Research Foundation and ran 4.2 miles without a problem (5 months post-op), finishing 1st in his age group.

RR is a Spinal Champion: an inspiration to his doctors, his family, and his friends.

Conclusion

Over the past eight years, there have been significant scientific advancements with acid-etched titanium (nano-textured) spinal implants. Most importantly, the remarkable basic science data generated in the laboratory is carrying over into the surgical and clinical side of care. Advances in surgical techniques and implants benefit patients when applied carefully and accurately. The clinical results outlined in this review paper are very encouraging, offering us and our patients a step forward; closer to achieving successful outcomes for even more of our patients in the future.

REFERENCES


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Dr. Slosar is an orthopedic spine surgeon and President of SpineCare Medical Group in Daly City, CA. He is also the Medical Director of the Spine Care Institute of San Francisco, Co-Director of the San Francisco Spine Institute Surgical Fellowship training program, and Director of Surgical Research. He has authored over 20 original articles in peer-reviewed journals and several book chapters, serves as an editorial board member for multiple medical journals, and has given numerous podium presentations at national and international meetings. Dr. Slosar is a member of the The International Society for the Study of Lumbar Spine, the American Academy of Orthopaedic Surgery, the North American Spine Society, and additional local and state medical societies. His current research interests include minimally invasive surgical techniques, spinal motion-preservation technology, and implant surface technologies.