The case for nanoLOCK™ technology in spinal fusion.

A compelling story supported by in vivo and in vitro data.

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Dr. Barrett Woods has performed several hundred lumbar fusions utilizing the Medtronic interbody fusion devices with Titan nanoLOCK™ surface technology. There has been a proliferation of literature describing the advantages of the nanoLOCK™ surface in stimulating an osteogenic cellular response when compared to PEEK or smooth titanium surfaces[1,3,4,6,8,12, †, ‡]. In this article, Dr. Woods summarizes these foundational basic science publications that support nanoLOCK™ technology. Additionally, he shares the results of a recent multi-center retrospective study and provides his insights as to how the technology has made a positive impact on his practice and patient outcomes.

The story

The story leading to the emergence of nanoLOCK™ surface technology in spinal fusion is compelling. Initially, I was somewhat skeptical of using titanium interbody implants due to concerns of subsidence, and modulus of elasticity differences between titanium implants and vertebral bodies. Over time, these myths have been debunked, and the power of the bioactive surface technology and the concept of biomimicry could be appreciated. The concept behind nanoLOCK™ technology is the replication of osteoclastic pits to stimulate optimized cellular responses, leading to bone formation. At the foundation of this concept are several compelling in vitro studies which identified optimal substrate and surface topography to elicit this cellular response.[1-10]

1. Bio active surface: nanoLOCK™ basic science updates†

1.1 A peer-reviewed article on biomimetic surface topographies concluded that modifications to fusion implant surfaces, especially those engineered to resemble osteoclastic resorption pits, have evidence showing that these surfaces are bio active, specifically that they promote bone formation and osseous integration.[11]

1.2 Cellular adhesion to the surface of an implant is an essential component to initiate a desirable bio-active cascade and minimize the chance for biofilm formation. The more quickly and reliably mesenchymal stem cells (MSCs) can attach to the surface, and subsequently differentiate into osteoblasts, the more quickly bone growth and osteointegration may occur. The nanoLOCK™ surface demonstrated increased adhesion kinetics compared to PEEK and smooth titanium.[12] **(Figure 1)**

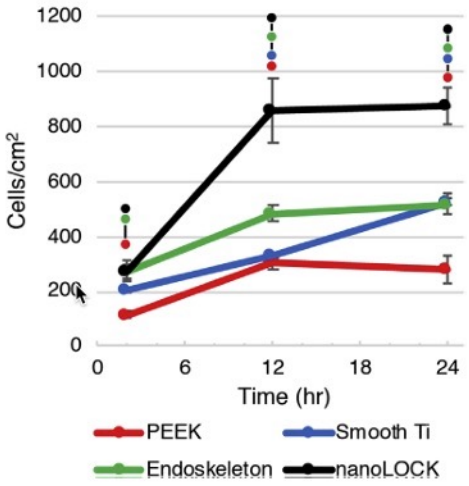

Figure 1.

MSC cellular differentiation into osteoblasts was highest, and occurred most rapidly, in the nanoLOCK™ surface compared to peak and smooth titanium. This was demonstrated by increased alkaline phosphatase **(ALP)** production, an early marker of bone formation, which then transitioned to high concentrations of osterix **(OSX)**, a marker of mature bone formation.[12] These data demonstrate MSC adhesion and differentiation on nanoLOCK™ was dramatically improved compared to the other surfaces including smooth titanium and PEEK.

1.3 Arguably one of the most important recent publications is focused on the ability of the surface to drive cellular differentiation and create a microenvironment surrounding the implant that is osteoinductive. Berger, et al., performed a 2-stage cellular assay analyzing PEEK, smooth titanium, and the nanoLOCK™ surfaces.[13] Next, they implanted demineralized bone matrix (DBM) saturated with the cellular products that were produced during the initial phase of the study. The nanoLOCK™ substrate impregnated with the DBM produced more ectopic bone formation compared to control groups in a mouse muscle pouch model. This *in vivo* experiment strongly supports that the cellular products created by the nanoLOCK™ surface result in signaling factors which create an osteoinductive microenvironment. **(Figure 2)**

† Not necessarily indicative of clinical outcomes

‡ $p < 0.05$ for all referenced studies

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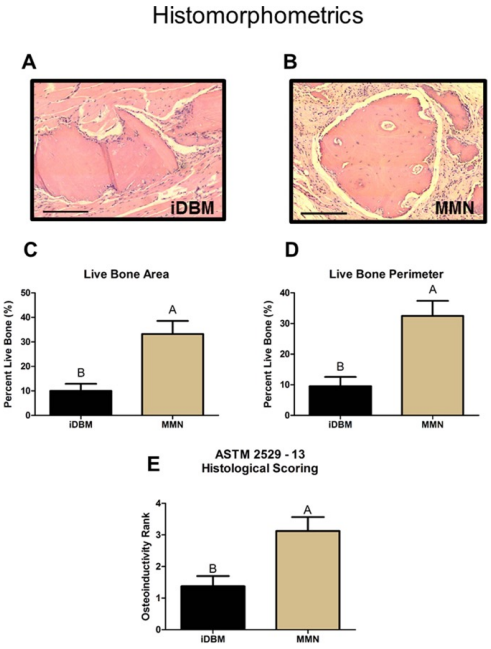


Figure 2. Histological analysis of new bone formation ectopically. (A) and (B) Representative histological images of the H&E staining for both the (A) iDBM and the (B) MMNTM groups. (C) Quantification of the live bone area using quantitative histomorphometry. (D) Quantification of the live bone perimeter using quantitative histomorphometry. (E) Ranked scoring of each sample according to an adapted ASTM Standard 2529–13 (standard guide for in vivo evaluation of osteoinductive potential for materials containing demineralized bone). Black arrows mark areas of live bone with cells populating lacunae. Black lines are scale bars at 1 mm. Groups not sharing letters are significantly different at $p < 0.05$.
iDBM: Inactive Demineralized Bone Matrix
MMN: Micro Macro Nano (nanoLOCK) surface

2. Bio active surface: clinical updates

The nanoLOCK™ technology first became available to surgeons in 2015. I adopted the technology in 2016 and have to date placed several hundred cervical and lumbar implants with excellent clinical results. We recently published a multi-center retrospective study in which 124 patients received an anterior cervical discectomy fusion (ACDF) using the nanoLOCK™ cervical fusion implant.[14] Two groups were included in the study. The first group included 55 patients who received two-level fusions, while 69 patients in the second group had three- or four- level fusions. Fusion rates, need for supplemental posterior fixation and complications were evaluated at various time points.

Our results showed that at three months there was a higher rate of osseous fusion in the two-level cohort compared to the three and four level group. However, at six months, both groups showed statistically similar fusion rates and there were no differences in clinical outcomes between groups. **(Figure 3)**.

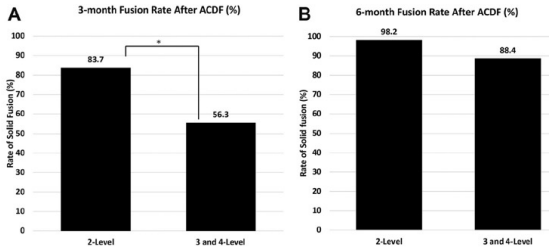
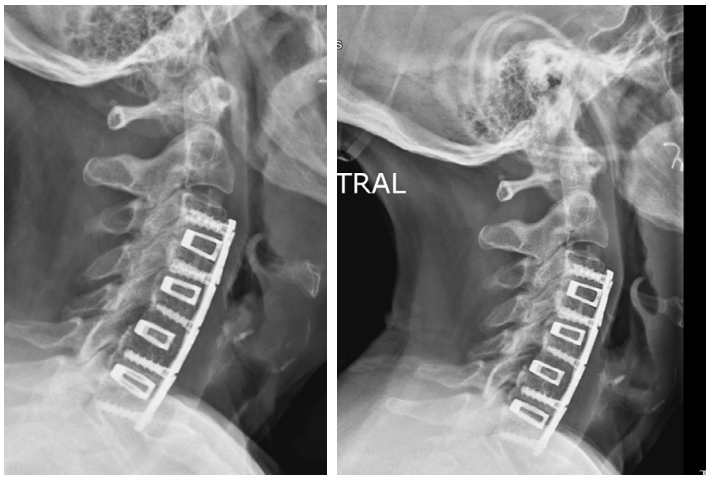


Figure 3: Graphic representation of fusion rates at (A) 3 and (B) 6 months for both the 2-level and 3- or 4-level groups. Asterisks and a denotes statistical significance. ACDF: anterior cervical discectomy fusion.

None of the 124 patients required supplemental posterior fixation. **(Figure 4)** We concluded that when the nanoLOCK™ cervical fusion implant was used with plate fixation in multi-level cases posterior fixation was not routinely needed in the population studied.

The future of surface technology

The efficacy of the nanoLOCK™ surface technology has been illustrated when using interbody constructs. Now this technology is being offered as an option to enhance pedicle screw fixation. Medtronic is offering surgeons the newly released CD Horizon™ ModuLex™ nanoLOCK™ shanks which implement nano surface topography on the threads and shaft of the screw. A recent animal study demonstrated increased extraction force and improved fixation for screws with nanoLOCK™ surface technology compared to anodized screws.[15]



Figures 4: Radiographs of a 4-level ACDF at (A) 3 months and (B) 6 months postoperatively.

Conclusion

The *in vivo* and *in vitro* data supporting nanoLOCK™ surface technology are compelling, and my clinical experience with these products has been very positive. As my clinical practice has evolved, I have performed more minimally invasive procedures and have been very happy with the clinical results achieved with the nanoLOCK™ surface technology. I would recommend all surgeons evaluate these products.

Barrett Woods, M.D.
Dr. Woods is a paid consultant by Medtronic

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Indications

Endoskeleton™ TC Interbody System devices including those with macro-, micro-, and nano-roughened surface textured features are indicated for use for anterior cervical interbody fusion in skeletally mature patients with cervical disc degeneration and/or cervical spinal instability, as confirmed by imaging studies (radiographs, CT, MRI), that results in radiculopathy, myelopathy, and/or pain at multiple contiguous levels from C2 to T1. The Endoskeleton™ TC Interbody System is indicated to be used with supplemental fixation cleared by the FDA for use in the cervical spine and autograft bone, allograft bone comprised of cancellous and/or corticocancellous bone, demineralized allograft with bone marrow aspirate, or a combination thereof.

The CD Horizon™ spinal system with or without Sextant™ instrumentation is intended for posterior, non-cervical fixation as an adjunct to fusion for the following indications: degenerative disc disease (defined as back pain of discogenic origin with degeneration of the disc confirmed by history and radiographic studies), spondylolisthesis, trauma (i.e., fracture or dislocation), spinal stenosis, curvatures (i.e., scoliosis, kyphosis, or lordosis), tumor, pseudarthrosis, and/or failed previous fusion.

Consult instructions for use at this website www.medtronic.com/manuals.

Risks

Implant migration.
Breakage of the device(s).
Foreign body reaction to the implants including possible tumor formation, auto immune disease, and/or scarring.
Pressure on the surrounding tissues or organs.
Infection.

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15. Animal study data on file. Animal results are not necessarily indicative of human clinical performance.

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