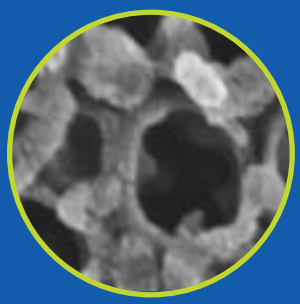
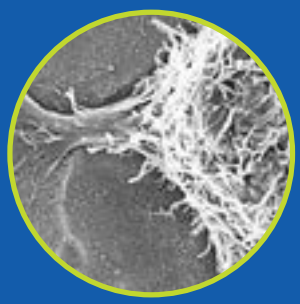
NANOVIS®

Nanotechnology

Designed to enhance osseointegration and reduce bacterial colonization





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NANOVIS®

Nanotechnology designed to accelerate osseointegration and reduce bacterial colonization

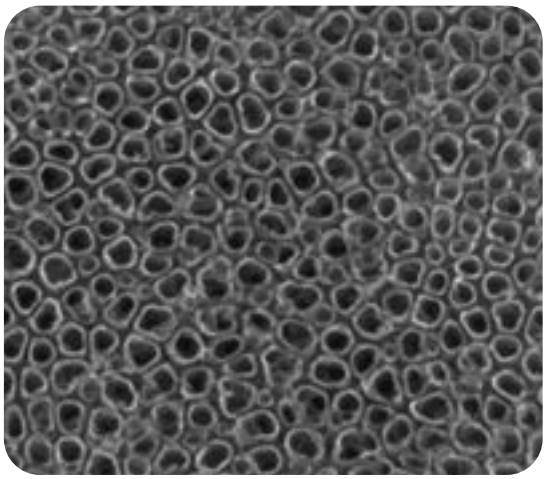
Nanovis® is a pioneering surface technology-driven company committed to addressing unmet clinical needs and developing innovative solutions. Their flagship nanoVIS Ti™ Surface Technology is making waves in the spine, orthopedic, and dental industries, particularly for its unique nanotechnology designation with the FDA, aimed at enhancing bone-to-implant osseointegration. Other noted benefits include reducing bacterial colonization when introduced to our nano surface.

Nanovis® can help you integrate market leading nanotechnology into your pedicle screw portfolio

Enhance your pedicle screw portfolio with our nanoVIS Ti™ Surface Technology

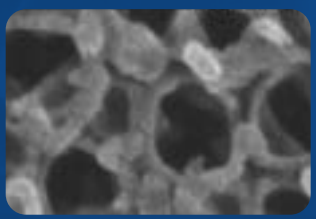
What is nanotechnology?

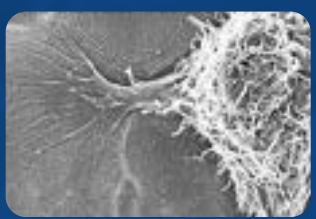
Nano means small. How small? We usually consider technology to be 'nano' when it's less than 100 nanometers. But how big is a nanometer? While the average man stands at about 1,750,000,000 nanometers tall, his hair is about 50,000 nanometers thick and his red blood cells are about 7,000 nanometers in diameter. It's hard to imagine things much smaller than that, but the proteins that make up your cells and the tissues surrounding them are about 1-100nm. In other words, the human body is full of natural nanotechnology. The nanotechnology that we build today has a lot of uses. There are lighter-than-air aerogels and computer chips that can fit on your pinky nail and customized molecules that can aid in drug delivery. There are also bioactive nanosurfaces that can help the body heal better around an implant. Nano might be small, but it can make a big difference.



What is **Nanovis'** nanotechnology?

Nanovis' FDA cleared nanosurface has two main components: titanium dioxide nanotubes and a thin calcium phosphate layer. The nanotubes are the main driver of the surface technology. They are designed to have an average diameter of 70nm to accelerate healing around an implant. The increased surface area gives space for protein attachment, and the size and shape of the nanotubes mimic the natural structures found in bone or soft tissue. Together, these factors encourage cells to differentiate and quickly lay down mineralized extracellular matrix.





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nanoVIS Ti™ Surface Technology At-a-Glance

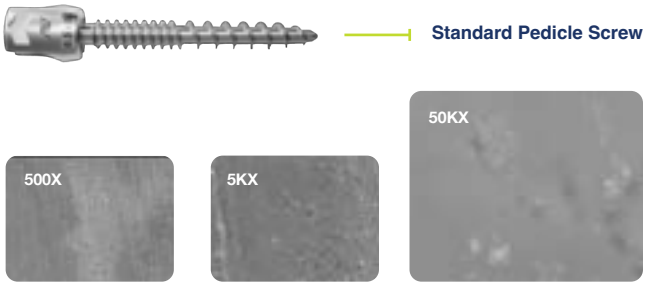
Nanotechnology Designation with comparative surface data showing Mesenchymal Stem Cell and Osteoblast mineralization, on-label

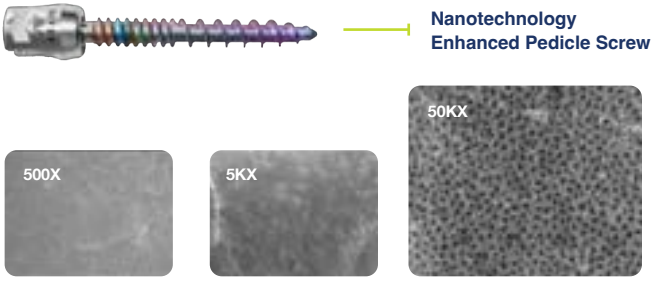
Faster and more consistent osseointegration coupled with increased micro vascularization reduces bacterial colonization

Multiple 510k clearances and process validations on both CP Ti and Ti alloys

ISO 13485:2016 compliant controlled QMS process operated by Nanovis

Sales force and surgeon excitement with increased technology pricing and market share wins





Real-Life Application

TODD BONVALLET, MD

Atlanta, Georgia

"As a spine surgeon, my primary goal is to achieve the best possible outcomes for my patients. One of the challenges we face in spinal surgery is the risk of pseudoarthrosis, or the failure of bone fusion to occur as intended. This can result in continued pain and instability, and may require additional surgery to correct.

To address this challenge, I have incorporated Nanovis' bone-growth Nanotechnology to support rapid bone growth on and through the fusion construct. While I am not a technology expert, I have been impressed with the results in the interbody space the last 3 years, and the last 18 months on pedicle screws.

The nanotubes seem to promote rapid osseointegration, or the formation of new bone tissue, around the implant sites, leading to faster and more complete fusion.

Every patient is unique and the risk of pseudoarthrosis is not always predictable preoperatively. However, I believe that using the latest technology available can help reduce the risk of complications and improve the overall success rate of spinal surgeries. I am excited about the potential benefits of Nanovis' technology for supporting rapid bone growth and fusion, and will continue to use it in my practice as part of my ongoing commitment to achieve the best possible outcomes for my patients."

Common Problems Associated with Pedicle Screws

Image Source

Problem: Loosening

The term “aseptic loosening” refers to the loosening of an implant from native bone without infection or trauma complications. Excessive motion where the bone and implant interface causes aseptic loosening. It is one of the most common reasons for implant failure and often results in revision spine surgery. Loosening is enhanced by poor bone quality and pull-out forces created by long fusion constructs (deformity).

Our Solution

Titanium implants enhanced with nanoVIS Ti™ Surface Technology accelerate osseointegration between the implant surface and bone. With rapid establishment of bone approximated to the implant substrate, micromotion is reduced, substantially lessening the chance of aseptic loosening.

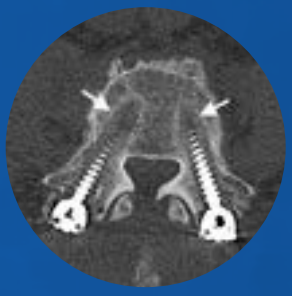


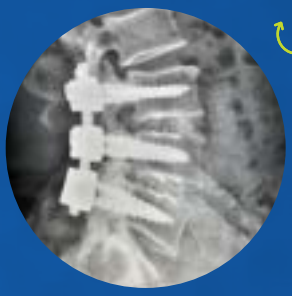
Image Source

Problem: Infection

Implants can fail due to a decline in systemic health, bacterial accumulation or trauma. In cases of bacterial colonization, perioperative contamination is a significant risk factor. Infections cause several problems, including inflammation, that jeopardize pedicle screw stability.

Our Solution

Titanium implants enhanced with nanoVIS Ti™ Surface Technology catch osteogenic proteins that encourage rapid attachment of mature osteocytes and stem cells. The attached cells are driven to accelerate the calcification of extra cellular matrix, resulting in bone proliferation over the implant surface. Increased occupation of the surface by host bone reduces available surface area for bacterial colonization. Additionally, the accompanying increase in micro vascularization allows the body’s immune system to respond naturally to potential bacterial threats. Managing wound care and supporting spinal fusion procedures with antibiotics can also prevent implant failure due to infection.



Problem: Implant Longevity

There are many reasons why pedicle screws fail early or long-term, chief among them being poor osseointegration. Proper placement, bone growth, and maintenance of an aseptic environment safeguard the pedicle screw and its longevity in patients.

Our Solution

nanoVIS Ti™ Surface Technology improves the already excellent lifespan of titanium implants. Its advanced nanotechnology is a permanent surface proven in orthopedic applications to trigger osseointegration of bone-to-implant, reducing the colonization of bacteria. When a properly placed pedicle screw is correctly supported by rapid bone formation, issues that cause pedicle screws to fail are avoided, increasing longevity.

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Clinical and Commercial Solution for Titanium Implants

CLINICAL VALIDATION

- This product demonstrates the requirements for nanotechnology.
- These nanotube arrays have been shown to increase and accelerate calcified extracellular matrix production in vitro.
- Human Osteoblasts: statistically significantly superior calcified extracellular matrix production compared to other surface technologies.
- Human Mesenchymal Stem Cells: statistically significantly superior calcified extracellular matrix production compared to other surface technologies.

IFU for Nano FortiFix™ Pedicle Screws.

DESCRIPTION

Nano FortiFix® (C) is a posterior pedicle screw system consisting of rods, polyaxial pedicle screws, cross connectors and fasteners in a variety of sizes to accommodate differing anatomic requirements. The implants are manufactured from alloys (Ti6Al4V ELI per ASTM F136 and CoCr per ASTM F1537). The Nano FortiFix® (C) pedicle screws are provided sterile with a nanosurface. All components except for the nanosurfaced screws are sold non-sterile.

The Nano FortiFix® (C) pedicle screw has a micro- and nano-roughened surface that demonstrates the requirements for nanotechnology. The surface of the nano screw threads has been deliberately manipulated to produce nanoscale dimensions which exhibit specific properties. These threads are electrochemically treated to possess a controlled nanotopography composed of nanotube arrays having a pore size diameter between 30-90 nanometers. Calcium and phosphate are incorporated into the nanotube surface. These nanotube arrays have been shown to increase and accelerate calcified extracellular matrix production in vitro[1] (Figure 1 and Figure 2).

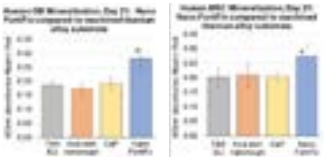

Figure 1 In vitro osteoblast (OB, left) and mesenchymal stem cell (MSC, right) mineralization on material surfaces. *Nano FortiFix nanosurface compared to "as machined" Ti6Al4V ELI substrate without further treatment (Ti64 ELI), with Acid etch nanorough surface and with Calcium Phosphate (CaP), p<0.0001 for both cells.

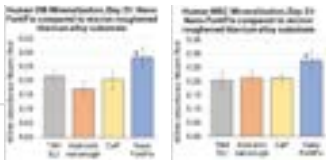

Figure 2 In vitro osteoblast (OB, left) and mesenchymal stem cell (MSC, right) mineralization on material surfaces. *Nano FortiFix nanosurface compared to "micron roughened" Ti6Al4V ELI substrate without further treatment (Ti64 ELI), with Acid etch nanorough surface and with Calcium Phosphate (CaP), p<0.0001 for both cells.
In vitro performance may not be representative of clinical performance.

INDICATIONS

The Nano FortiFix® System is intended to provide immobilization and stabilization of spinal segments in skeletally mature patients as an adjunct to fusion in the non-cervical spine for the following indications: DDD (defined as back pain of discogenic origin with degeneration of the disc confirmed by history and radiographic studies), spinal stenosis, spondylolisthesis, spinal deformities (i.e., scoliosis, kyphosis, and/ or lordosis), trauma (i.e., fracture or dislocation), tumor, pseudarthrosis and/or failed previous fusion. The Nano FortiFix® System can be used in an open approach or a percutaneous approach with MIS instrumentation.

CONTRAINDICATIONS

- The presence of infections localized to the site of implantation such as open wound, abscess or erythema.
- Evidence of active systemic infection such as fever or leukocytosis.
- The presence of tumors or congenital abnormalities which would preclude the potential benefit of spinal implant surgery.
- Inadequate soft tissue at the intended operative site such that appropriate wound closure may not be possible.
- Suspected or documented allergy or intolerance to the implant material.
- Pregnancy.
- Patients who are occupationally or recreationally subject to heavy lifting, twisting, bending, stooping, or repetitive motions that would produce excessive loads leading to implant failure or failure to achieve bony union.
- Patients with conditions that impede their ability to comply with appropriate postoperative management and activity restrictions. These conditions include but are not limited to intellectual disabilities, alcoholism, substance use disorders and mental instability.
- Patients with diminished bone quality arising from degenerative diseases such as metabolic disorders, active malignancy or postoperative or therapeutic radiation.
- Any patient in which implant utilization would interfere with anatomical structures or expected physiological performance.
- Any case where the implant components selected for use would be too large or too small to achieve a successful result.
- Any condition not described in the indications for use.

WARNINGS

- The Nano FortiFix® nano screws are sterile. Resterilization of the implant component is not permitted. Do not clean and/or resterilize sterile screws. Do not use if package is opened or damaged or if expiration date has passed.
- All Nano FortiFix® implants are single use only. These must never be reused or reimplanted. Even though the device appears undamaged, it may have small defects

[1] Data on file, available from Nanovis Spine.

COMMERCIAL VALIDATION

- On-label marketing for superior positioning and marketing to drive new surgeon conversions, provider approvals, and technology price premiums.
- Surface on a surface story. Great way to further enhance/differentiate with a nano surface on a micron-roughened or macro porous 3D printed surface.
- Surgeon engagement at a scientific and innovation level creating opportunities for studies, papers, podium presentations, etc.
- Sales force excitement! Advanced implant technology to take share and grow business.

Technology Validation

nanoVIS Ti™ SURFACE TECHNOLOGY

REGULATORY VALIDATION

1ST

FDA clearance with **Nanotechnology** designation on Ti pedicle screws

#1

FDA **Nanotechnology** designation on (9) device systems referencing (1) master file

MANUFACTURING VALIDATION

OVER

18,000

Implants manufactured with nanoVIS Ti™ Surface Technology

MARKET VALIDATION

39% - 95%

Average price premium on technology **enabled** implants

Interbodies

Currently in development agreement on spinal interbodies with **TOP 10** spine company

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Our Leadership

Nanovis® has a strong executive leadership team with **80+ years** of experience in medical devices and innovation.

BRIAN EMERICK

Chairman

Founded Nanovis® in 2006 and Micropulse, Inc. in 1988, as well as incubating several other technology companies.

BRIAN MORE

CEO

Has been with Nanovis® in various roles since its founding in 2008. With over 20 years of medical device experience helping lead the growth of Micropulse, as well as the creation of five other related portfolio companies, Brian brings deep experience in manufacturing, operations, corporate governance, strategy and business development.

JEFF SHEPHERD

Chief Commercial Officer

Joined Nanovis® in 2014 and has nearly two decades of product sales and commercialization experience. Jeff has been instrumental in commercializing nanoVIS Ti Surface Technology™ in spine and leading business development efforts in spine, orthopedics, and dental. Prior to Nanovis, Jeff was a Regional Sales Director for Codman, a division of Johnson & Johnson, where he was responsble for over $100mm in revenue.

JEFF FORBES

Vice President of Business Development

Joined Nanovis® in 2015 and has over 30 years of medical device sales and sales management experience. Jeff has played an important role in formalizing strategy in the spine segment. He has also connected the company to KOL's in multiple specialties of spine and orthopedics. Prior to Nanovis, Jeff was a regional sales manager for Synthes, now Depuy-Synthes a division of Johnson and Johnson, where he was responsible for the Mid-Atlantic U.S.

KREIGH WILLIAMS

Director of Technology

Joined Nanovis® in 2023 and has over 12 years' experience as an engineer, leader, and innovator in medical devices. He has a proven track record of taking products and technologies from initial concept to market in a high-growth startup environment. Prior to Nanovis, Kreigh played a pivotal role in building a company focused on a porous material technology.

DAVID DETWILER, PHD

Principle Research Scientist

Came on board with Nanovis® in 2014. He brings deep scientific research and development experience. In his role, he has become an industry leader in nanosurface technology and its biological response within the human body.

JOE ROTH

Director of Operations

Has been with Nanovis® since 2020 and previously was the company's quality manager. Joe has nearly two decades of manufacturing and quality experience.

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FDA Nanotechnology Designation

Nanovis® has (5) 510K clearances with FDA nanotechnology designation. To achieve this, the following four criteria were satisfied. The responses are specific language out of our label.

1. Material or end product is engineered and not incidental to have certain dimensions or exhibit certain properties.

The surface of the screw threads has been deliberately manipulated to produce nanoscale features that exhibit specific biologic properties to drive bone growth.

2. The material or end product uses or contains or involves the use of materials that address the questions above.

Nanotubes qualify as a nanostructured material per the nanotechnology designated 510(k) clearances.

3. Demonstrate that at least one external dimension, or an internal or surface structure, in the nanoscale range (approximately 1 nm to 100 nm but up to 1000 nm may be acceptable).

These threads are electrochemically treated to possess a controlled nanotopography composed of nanotube arrays having an average pore diameter of 70nm.

4. Show that properties or phenomena are attributable to the nanoscale dimension(s) based on your intended application.

These nanotube arrays have been shown to increase and accelerate calcified extracellular matrix production in vitro.

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Resources

1. **The Effect of Paraspinal Muscle Degeneration on Distal Pedicle Screw Loosening Following Corrective Surgery for Degenerative Lumbar Scoliosis** | May 2020
   https://journals.lww.com/spinejournal/abstract/2020/05010/the_effect_of_paraspinal_muscle_degeneration_on.11.aspx#:~:text=In%20conclusion%2C%20degeneration%20of%20paraspinal,fusion%20had%20no%20this%20influence.
2. **Prevalence and Risk Factors of Iliac Screw Loosening After Adult Spinal Deformity Surgery** | Sept 2017
   https://journals.lww.com/spinejournal/abstract/2017/09010/prevalence_and_risk_factors_of_iliac_screw.7.aspx
3. **Pullout Strength of Pedicle Screws Following Redirection After Lateral or Medial Wall Breach** | Sept 2018
   https://journals.lww.com/spinejournal/abstract/2018/09010/pullout_strength_of_pedicle_screws_following.2.aspx
4. **Comparing rates of early pedicle screw loosening in posterolateral lumbar fusion with and without transforaminal lumbar interbody fusion** | May 2020
   https://pubmed.ncbi.nlm.nih.gov/32387295/
5. **Preoperative Hounsfield Units Predict Pedicle Screw Loosening in Osteoporotic Patients Following Short Segment Lumbar Fusion** Apr 2024
   https://journals.lww.com/spinejournal/abstract/9900/preoperative_hounsfield_units_predict_pedicle.626.aspx
6. **Vertebral Bone Quality Score as a Predictor of Pedicle Screw Loosening Following Surgery for Degenerative Lumbar Disease** Dec 2023
   https://journals.lww.com/spinejournal/fulltext/2023/12010/vertebral_bone_quality_score_as_a_predictor_of.2.aspx
7. **The Usefulness of Trabecular CT Attenuation Measurement at L4 Level to Predict Screw Loosening After Degenerative Lumbar Fusion Surgery** | May 2022
   https://journals.lww.com/spinejournal/abstract/2022/05150/the_usefulness_of_trabecular_ct_attenuation.8.aspx
8. **Implant Microbial Colonization Detected by Sonication as a Cause for Spinal Device Failure** | Nov 2021
   https://journals.lww.com/spinejournal/abstract/2021/11010/implant_microbial_colonization_detected_by.14.aspx
9. **High frequency of low-virulent microorganisms detected by sonication of pedicle screws: a potential cause for implant failure** May 2019
   https://thejns.org/spine/view/journals/j-neurosurg-spine/31/3/article-p424.xml?rskey=hyfjNr&result=8
10. **Impaction grafting of lumbar pedicle defects: a biomechanical study of a novel technique for pedicle screw revision** | Nov 2022
    https://thejns.org/spine/view/journals/j-neurosurg-spine/38/3/article-p313.xml?rskey=AUk14M&result=16

Real-Life Application

WADE CEOLA, MD, FAANS

Fayetteville, Arkansas

"I have been using Nanovis' nanotechnology enhanced cervical cages for several years. I have seen superior outcomes with the nano enhanced interbody cages with adherence of the bone generally within one month. In comparison to traditional PEEK cages, I see a definite improvement in the cages bonding into the bony endplates. I have not had to perform an additional fusion or revision on an anterior cervical since the introduction of Nanovis' nanotechnology enhanced cages.

In this case, I believe the nanotechnology enhanced pedicle screws assisted with early bone ongrowth, which in turn improved healing and stronger fixation. I preferred the nano enhanced pedicle screws over fenestrated screws with methyl methacrylate due to the significant hardeningof the vertebral bodies with PMMA and risk of adjacent segment fracture. The Nanovis FortiFix pedicle screws functioned flawlessly, and I am verypleased with the outcome in this patient."

ALAN MCGEE JR, MD

Fort Wayne, Indiana

"Working up and managing a patient with prior surgery and pseudoarthrosis, as well as infection, can be a daunting task. Patients will have to deal with the comorbidities associated with multiple surgeries as well as persistent pain and disability to address these issues. Given the complication profile as well as additional levels of instability, ensuring a high-quality surgical plan is a must.

Having the ability to incorporate Nanovis' bone growth nanotechnology to ensure rapid bone growth and solid osseous fusion has been extremely beneficial to my practice as well as my patient's outcomes.

By utilizing the nano pedicle screws' large diameter and length to bridge the SI joints, I am confident I will obtain a solid SI joint arthrodesis as well as a solid base for my long construct fusions. From a radiographic standpoint I can closely monitor the patient's rapid progression of fusion with noting the new bone tissue around the implants.

For challenging cases that are more at risk for pseudoarthrosis, such as revisions, infections, multiple comorbidities, as well as long construct fusions, I feel confident using Nanovis nanotechnology to ensure the best outcomes for my patients."

DOUGLAS PAHL, MD

Columbus, Georgia

"While certain procedures may hold less risk in terms of potential negative outcomes, it is important to note that complications can occur in any patient unexpectedly. This reality highlights the importance of consistently accessing advanced technology with the potential to improve my patients' chances for achieving excellent outcomes.

Since 2018, I have incorporated Nanovis surface technologies into my practice and have managed the full gamut of patient pre-operative co-morbidities and complications. From 1-level cervical fusions to multi-level lumbar revisions in patients with very poor bone quality, Nanovis' proprietary nanotube technology has worked very well in my practice with no known implant failures with over 1200 nanotechnology-enhanced implants in patients to date. While it may be tempting to reserve its use solely for complex or high-risk cases, I have chosen to implant their technology consistently, and my patients have done very well."