# CAN NANO TREATED SURFACES ENHANCE FUSION?

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## DISCLOSURES

- SAB; K2M, Osprey, Nanovis, Clariance, Vertera, St Theresa
- Royalties; Osprey, K2M, Nanovis
- Stock ownership; Surgical Ventures, Vertera, Morphogeny, Amedica, Surgifile, Paradigm, St. Theresa
  (all <1%)

## PEEK

- PEEK
  - Abundant
  - Relatively cheap
  - Radiolucent
  - Modulus of Elasticity close to bone
  - Concern due to high non-union rates
  - Caused many to seek alternatives (titanium)


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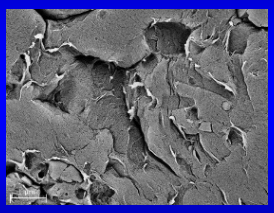
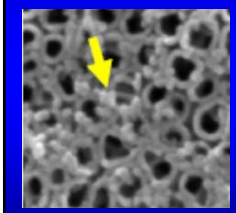
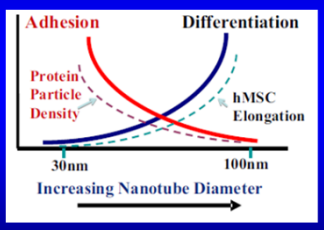
## PEEK



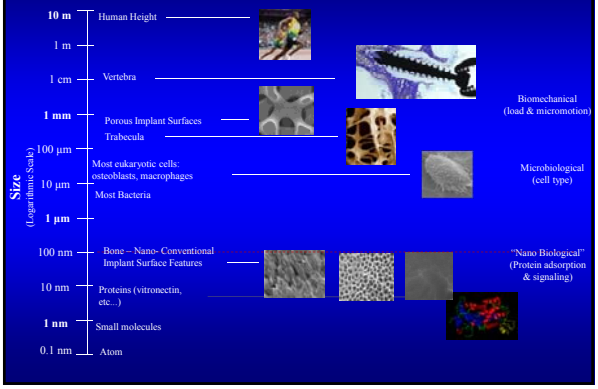
Nanotechnology: National Institutes of Health-
"Control of matter at a length scale of approximately 1 - 100 nanometers, where novel properties and functions occur because of the size."



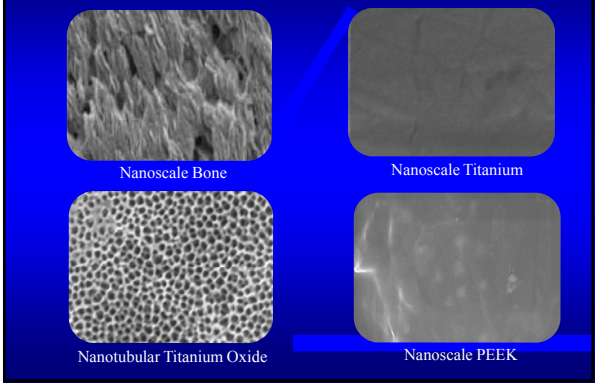



Oh et al. 2009, PNAS

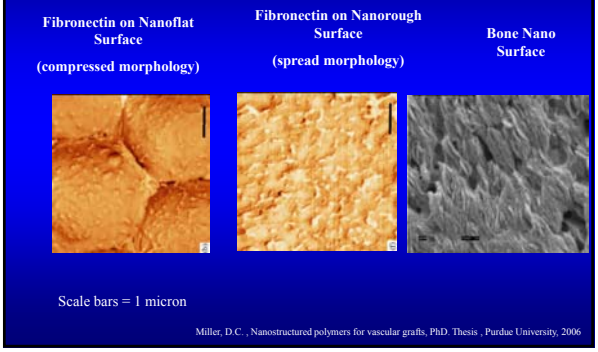
## Nanoscale Design Features Adds NanoBiology to Biomechanics to Achieve Biomechanical Fixation




## Nanoscale Implant Surfaces Don't Typically Mimic Nanoscale Bone

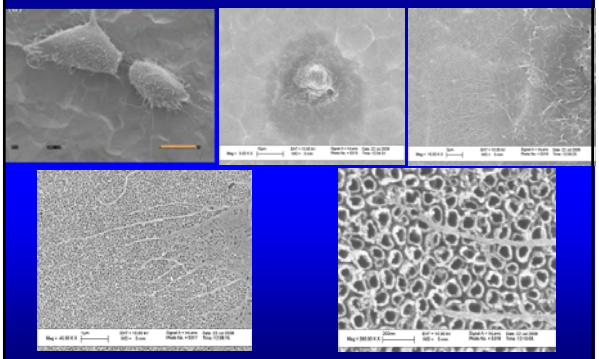



## Nano Structured Surfaces Increase Protein Binding Epitope Exposure



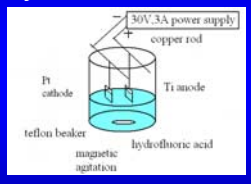

Miller, D.C. , Nanostructured polymers for vascular grafts, PhD. Thesis , Purdue University, 2006

## Osteoblast Morphology and Filopodia Attachment Conventional (Flat) Ti ELI vs. Physiologic Nanosurfaces



## Annodization can Create a Consistent, Replicatable, Customized Nanotube Surface

**Sketch of Anodization System**




**PROCEDURES:**

**Pretreatment: chemical polishing using $HF/HNO_3$ mixture**

**Anodization: 0.5 or 1.5%HF**

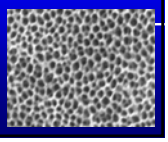
**Voltage: 20V**

**Time: 20 min**

**Rinse and dry**

**Clean: acetone and ethanol**

**Sterilize**



## Race to the surface: Bacteria or Tissue: Rhode Island VA Abutment Study: Anodized Ti Implant After 28 Days

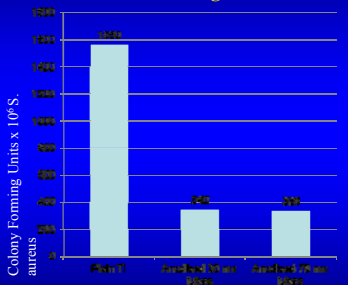
Unanodized Ti (Nanoflat)

Anodized Ti (Nanotubes)

Infection, puss, no skin attachment

Skin attachment, no infection

## Race to the Surface: Bacteria Colonization of nanotube surfaced titanium and conventional (nano-flat) titanium. Guinea Pig S. aureus Challenge



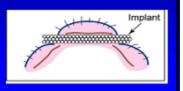
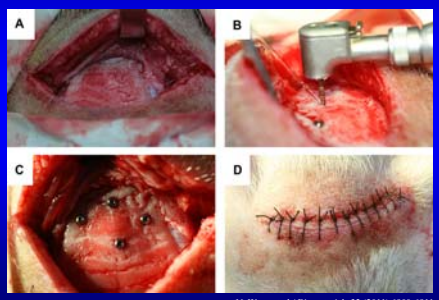



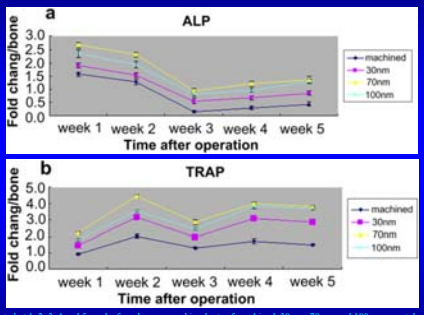

Figure: Preliminary data of *S. aureus* colony forming units on various Ti rods inserted into the skin of pigs, inoculated with 1 x $10^6$ *S. aureus*, recovered for 7 days. Data = mean +- SEM; N = 3; * p < 0.01 compared to plain titanium and ** p < 0.01 compared to anodized titanium alone.

## Porcine Calvaria Model Comparing Conventional (Nanoflat) Ti6AL4V pins and TiAL4V with 30, 70, and 100 nm Diameter Nanotube Surfaces




N. Wang et al./ Biomaterials 32 (2011) 6900-6911

## Gene Expression Markers of Bone Growth

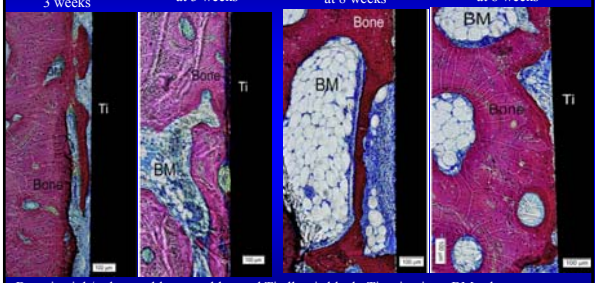



Total RNA was isolated at 1, 2, 3, 4 and 5 weeks from bone around implants of machined, 30 nm, 70 nm and 100 nm nanotubes. The temporal pattern of expression levels for (a) ALP, (b) TRAP is shown as fold change (2DDCT method, baseline =week 1 expression at machined implant surface).

N. Wang et al./ Biomaterials 32 (2011) 6900-6911

## Histological Sections at 3 and 8 Weeks

Machined (Nanoflat) at 3 weeks | 70 nm TiO2 nanotubes at 3 weeks | Machined (Nano flat) at 8 weeks | 70 nm TiO2 nanotubes at 8 weeks




Bone is pink/red, osteoblasts are blue and Ti alloy is black, Ti = titanium, BM = bone marrow.

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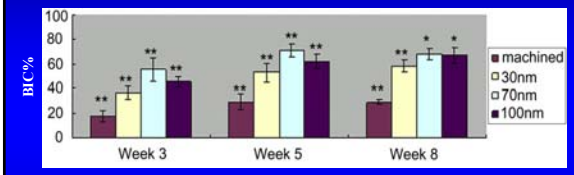
## Bone to Implant Contact Varied by Nanofeature

**Bone to Implant Contact (BIC)**




**Time after operation**

The mean values with SD (error bars) of bone-implant contact (BIC) over the total implant length for all implant surfaces at 3, 5 and 8 weeks after implantation. Asterisk (*) shows a significant difference in comparison with machined implant ($p < 0.05$). Double asterisks (**) show a significant difference in comparison with all other groups in experiment ($p < 0.05$).

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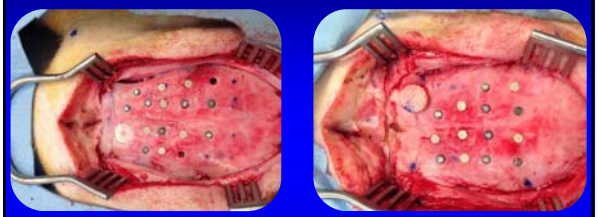
## Comparative Study of Fixation Strength. Porcine Calvaria Pin Removal Model.

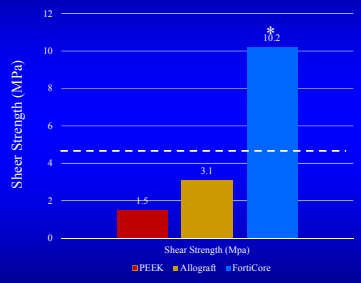


- Groups Compared: Novel Porous Titanium Scaffold, Allograft, PEEK
- Model: Pig skull, 5 weeks
- Endpoint: push out strength (Mega Pascales, MPa)

Guyer, Abitbol, Szpalski, Gunzberg

## Direct Comparison of Sheer Strength (MPa) Between Host Bone and PEEK or Allograft or Porous Titanium Scaffold after 5 weeks of Implantation

Data=Mean±STDEV. Data were assessed for significance using Student's t-tests. *p<0.01.

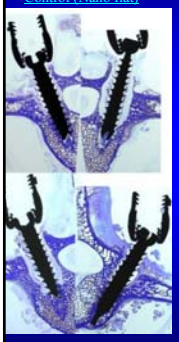



4.5 MPa, Shear Strength of Porcine Vertebral Trabecular Bone N=3, p<0.05.

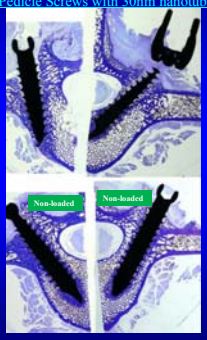
The fixation/bone attachment strength at 5 weeks was stronger than that of mature porcine vertebral trabecular bone.

## Putting it Together in Challenging Biomechanics: 3 Month Ovine Pseudoarthrosis Model

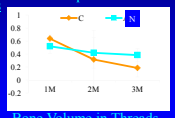
Control (Nano flat)



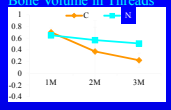
Pedicle Screws with 30nm nanotubes



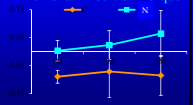

Bone-Implant Contact




Bone Volume in Threads



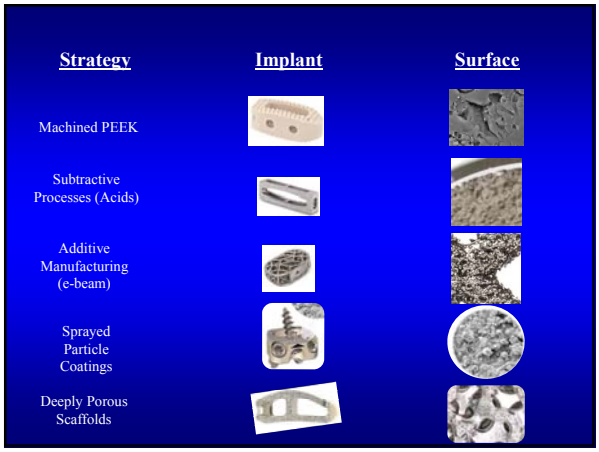

Δ=Removal–Insertion Torque

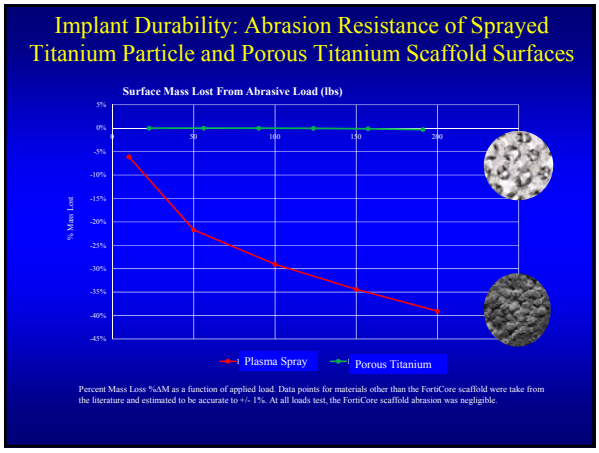



## Nanotube Surfaced Pedicle Screws to Delay or Prevent Pseudoarthrosis Complications? – Pedicle Screw Loosening

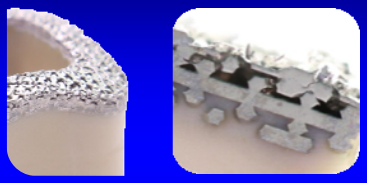
- Ovine Pilot Study used to Structure FDA targeted study
- Non fusion, posterolateral fixation screws & rods only
- Time points: 1, 2, and 3 months
- Histology & mechanical attachment

- U.S. National Institutes of Health Grant Number: 1 R43 AR066979-01A1
  Principal Investigator: Yao, Chang, JJ Abitbol, Rick Guyer
  "Durable Biomechanical Stabilization of Spinal Fusion Segments Despite Pseudoarthrosis Using Spinal Implants with Nano and Micron Porous Hierarchical Structures in a Novel Non-Union Model"
- U.S. National Institutes of Health Grant Number: 1 R43 AGO49514
  Principal Investigator: Yao, Chang, JJ Abitbol, Rick Guyer
  "Spinal Pseudoarthrosis Mitigation Using Nano Devices"

Foundation Layer: Deeply Porous Titanium Scaffold (FortiCore®)

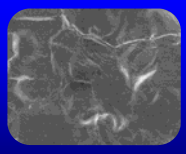


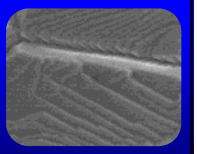


523 µm = Avg. Pore Size

60% = Pore Volume

750 microns = Depth of Porous Layer





30x Magnification (Macro)

1,000x Magnification (Micron)

10,000x Magnification (Micron)

# SUMMARY

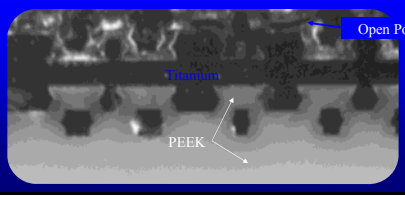
- Nano flat surfaces seem to lack characteristics to promote ingrowth and fixation
- Recent animal studies appear encouraging that Nano treated surfaces enhance bone ingrowth and fixation
- Not all surfaces are Nano (<100nm)

# THANK YOU

## What About Coating PEEK with Titanium? Implant Manufacturing and Durability:

Titanium Particles Sprayed on PEEK

PEEK Injection molded into titanium scaffold "rebar in concrete" strategy




## What about Titanium?

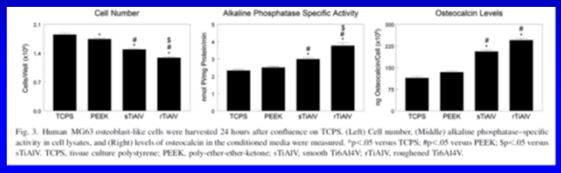



Fig. 3. Human MG63 osteoblast-like cells were harvested 24 hours after confluence on TCPS. (Left) Cell number, (Middle) alkaline phosphatase–specific activity in cell lysates, and (Right) levels of osteocalcin in the conditioned media were measured. *p<.05 versus TCPS; #p<.05 versus PEEK; §p<.05 versus sTiAlV. TCPS, tissue culture polystyrene; PEEK, poly-ether-ether-ketone; sTiAlV, smooth Ti6Al4V; rTiAlV, roughened Ti6Al4V.

Olivares-Navarrete, et al, The Spine Journal 12 (2012) 265-272,

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Eur Spine J. 2013 Jul;22(7):1539-46.

**Comparison of titanium and polyetheretherketone (PEEK) cages in the surgical treatment of multilevel cervical spondylotic myelopathy: a prospective, randomized, control study with over 7-year follow-up.**

Chen Y 1, Wang X, Lu X, Yang L, Yang H, Yuan W, Chen D.

**RESULTS:**

At the final follow-up, the clinical outcomes including JOA score, NDI score, and the excellent and good rates of clinical outcomes in the PEEK group were better than those in the titanium group. More loss of the Cobb angles and the intervertebral height was observed in the titanium group, resulting in the radiological parameters in the titanium group becoming inferior to the PEEK group at the final follow-up. Cage subsidence rates were 34.5 and 5.4% in the titanium and PEEK groups, respectively. Fusion was observed in all patients of two groups at the final follow-up. Two patients presented with cage dislocation without clinical symptoms in the titanium group.

**CONCLUSIONS:**

In surgical treatment of multilevel CSM, PEEK cage is superior to titanium cage in maintenance of intervertebral height and cervical lordosis, resulting in better clinical outcomes in the long-term follow-up.

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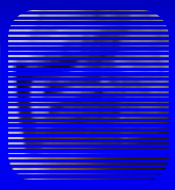
## What About Fusion Assessment?

Titanium Implant

Porous Tantalum Implant



Porous Titanium Scaffold with PEEK Core

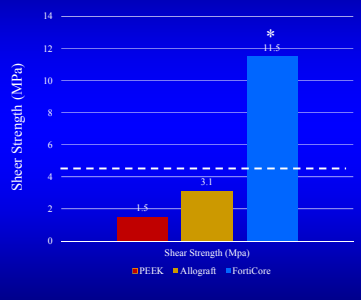
## Comparative Study of In growth into Porous Titanium Scaffolds: Canine OsseoIntegration Model

- Population
  - 8 Animals, Unilateral Implantation
  - 6 Stems with Micron Porous -Ti Scaffold
  - 2 Control Stems (Conventional BFX)

Void Space Occupied by Bone 12 Weeks after Implantation: THR 24-58% porous titanium scaffold ~75%.

Data on File, Nanovis Spine, LLC

## Direct Comparison of Sheer Strength (MPa) Between Host Bone and PEEK or Allograft or Porous Titanium Scaffold after 5 weeks of Implantation

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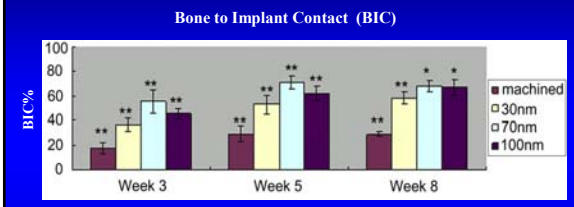


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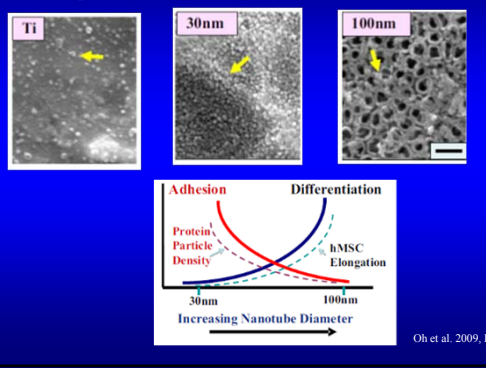
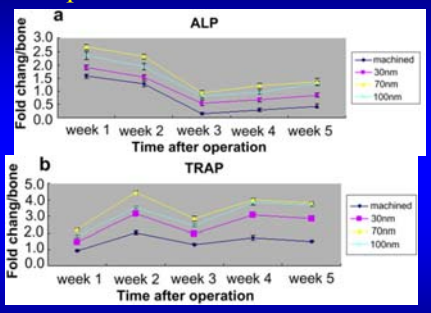
N. Wang et al./ Biomaterials 32 (2011) 6900-6911

## Adjust Nanotube Sizes (Sub 100nm) to Tune Protein Spacing Mediated Stem Cell Differentiation




Oh et al. 2009, PNAS

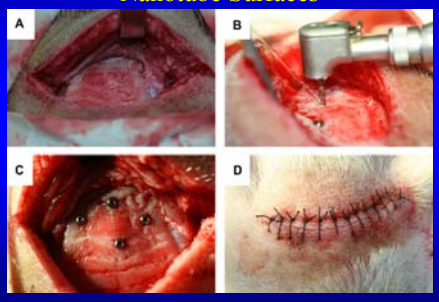
## Gene Expression Markers of Bone Growth




Total RNA was isolated at 1, 2, 3, 4 and 5 weeks from bone around implants of machined, 30 nm, 70 nm and 100 nm nanotubes. The temporal pattern of expression levels for (a) ALP, (b) TRAP is shown as fold change (2DDCT method, baseline ¼week 1 expression at machined implant surface).

N. Wang et al./ Biomaterials 32 (2011) 6900-6911

## Porcine Calvaria Model Comparing Conventional (Nanoflat) Ti6AL4V pins and TiAL4V with 30, 70, and 100 nm Diameter Nanotube Surfaces

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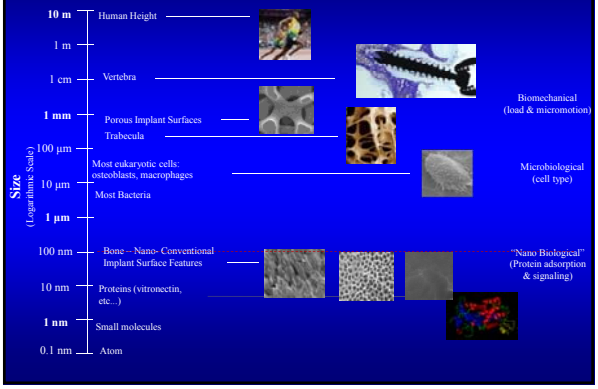
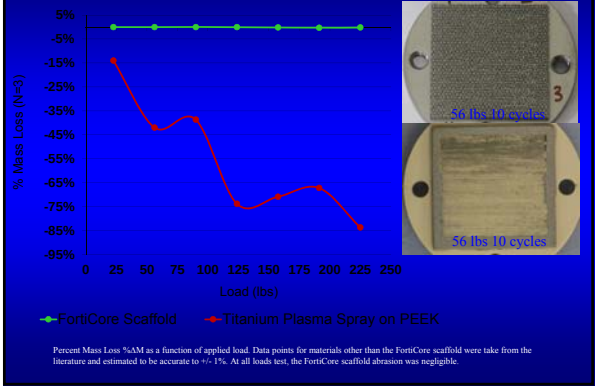
## Nanoscale Design Features Adds NanoBiology to Biomechanics to Achieve Biomechanical Fixation



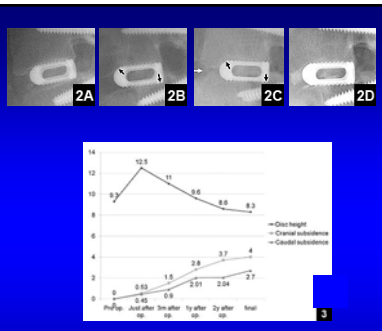

## Abrasion Resistance of Porous Titanium Scaffold Foundation Layer Compared to a Titanium Plasma Spray Control




Percent Mass Loss %ΔM as a function of applied load. Data points for materials other than the FortiCore scaffold were take from the literature and estimated to be accurate to +/- 1%. At all loads test, the FortiCore scaffold abrasion was negligible.

# DISCLOSURES

- NANOVIS




**Subsidence of Metal Interbody Cage After Posterior Lumbar Interbody Fusion With Pedicle Screw Fixation**
Yasuaki Tokuhashi, MD; Yasumitsu Ajiro, MD; Natsuki Umezawa, MD
•**Orthopedics**
•April 2009 - Volume 32 · Issue 4

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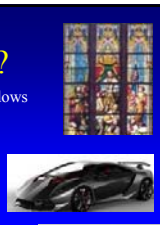
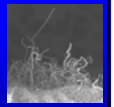
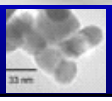
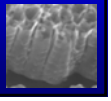
# What about Nanotechnology?

- Pigments in Medieval stained glass windows
- Water resistant fabrics
- Ultra low weight materials (bike frames, tennis rackets, Lamborghini's, etc…)
- Invisibility surfaces (light diffracting nanotubes - ( picture not available)



- Nanostructured organ regeneration scaffolds
- Tissue Growth Nanosensors
- Nanoparticles
  - Sunscreen- $TiO_2$ nanoparticles
  - Targeted drug delivery
  - Solubilizing agents for hydrophobic drug delivery
- Nanosurface Porous Scaffolds?



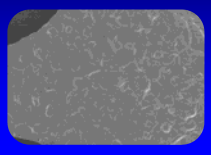
## Deeply Porous Titanium Scaffold with an injection molded PEEK Core. Product Family Trademark is FortiCore®

523 µm = Avg. Pore Size

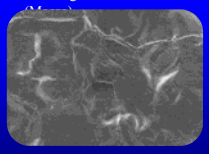
60% = Pore volume

750 microns = Depth of porous ingrowth layer

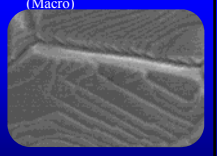
30x Magnification



300x Magnification (Macro)

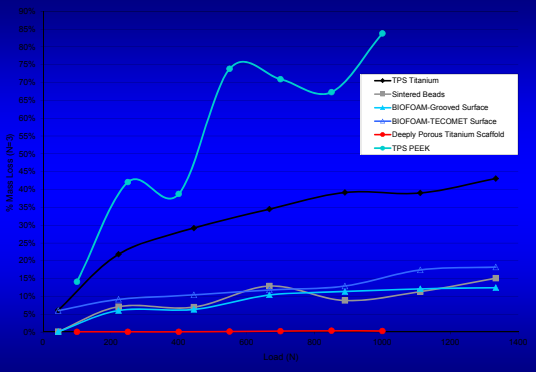


1,000x Magnification (Micron)



10,000x Magnification (Micron)

## % Mass Loss as a Function of Applied Load

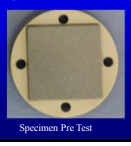



Percent Mass Loss % as a function of applied load. Data points for materials were taken from Biofoam technical monograph. Writ Medical. 2009. At all loads tested, abrasive wear of TPS PEEK was higher than that for other porous scaffolds.

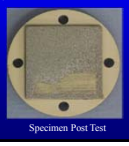
## Surface Durability Subject to Abrasive Forces:

- Abrasion resistance tested using FDA "Guidance Document for Testing Orthopedic Implants with Modified Metallic Surfaces Apposing Bone or Bone Cement"
- 10 Cycles at a specified normal force
- Travel in one direction was 25 mm
- 3 samples tested at each load

Abrasion Test Setup. The abrasion specimen is fixed to the top of the test maching, with the surface facing down. The half-cylinder has been pushed into the specimen at a specified normal force and is cycled normal to its axis.



Specimen Pre Test



Specimen Post Test

# Results

| | TPS PEEK % Mass Loss | | Deeply Porous Titanium Scaffold % Mass Loss | | P value |
|---|---|---|---|---|---|
| Axial Load (N) | Avg | StDev | Avg | StDev | P value |
| 100 | 14.0% | 13.4% | -0.02% | 0.002% | 0.1442 |
| 250 | 42.0% | 24.1% | -0.02% | 0.014% | 0.0392 |
| 400 | 38.6% | 19.4% | -0.02% | 0.002% | 0.0267 |
| 550 | 73.8% | 5.5% | 0.03% | 0.057% | 0.0001 |
| 700 | 70.8% | 12.9% | 0.14% | 0.146% | 0.0007 |
| 850 | 67.2% | 9.8% | 0.29% | 0.300% | 0.0003 |
| 1000 | 83.7% | 9.1% | 0.19% | 0.193% | 0.0001 |