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)
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

- Human Height: 1 m
- Vertebra: 10 mm
- Bone Implant Surface (mcB Art & Regenesis): 10 μm
- Bone - Nano Conventional (Surface): 100 μm
- Bone - Nano Biologically (Protein adsorption & signaling): 100 nm
- Human Height: 10 m

Most eukaryotic cells: osteoblasts, macrophages

Bone – Nano Conventional Vs Nano Biologically

Nanoscale Implant Surfaces Don’t Typically Mimic Nanoscale Bone

- Nanoscale Bone
- Nanoscale Titanium
- Nanotubular Titanium Oxide
- Nanoscale PEEK

Nano Structured Surfaces Increase Protein Binding Epitope Exposure

- Fibronectin on Nanoflat Surface (compressed morphology)
- Fibronectin on Nanorough Surface (spread morphology)
- Bone Nano Surface

Scale bars = 1 micron

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

PROCEDURES:
Pretreatment: chemical polishing using HF/HNO₃ mixture
Anodization: 0.5 or 1.5%HF
Voltage: 20V
Time: 20 min
Rinse and dry
Clean: acetone and ethanol
Sterilize

Annodization can Create a Consistent, Replicatable, Customized Nanotube Surface

Sketch of Anodization System

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, pus, 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 $1 \times 10^6$ 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

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 (2-DDCT method, baseline = week 1 expression at machined started surface).
Histological Sections at 3 and 8 Weeks

Machined (Nanoflat) at 3 weeks
70 nm TiO2 nanotubes at 3 weeks
Machine (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.

Bone to Implant Contact Varied by Nanofeature

Bone to Implant Contact (BIC)

Time after operation
The bars represent the mean ± 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 asterisk (**) shows a significant difference in comparison with all other groups in experiment (p < 0.05).

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

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

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, JI Abitbol, Rick Guyer

• U.S. National Institutes of Health Grant Number: 1 R43 AG049514
  Principal Investigator: Yao, Chang, JI Abitbol, Rick Guyer
  “Spinal Pseudoarthrosis Mitigation Using Nano Devices”

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Implant</th>
<th>Surface</th>
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</thead>
<tbody>
<tr>
<td>Machined PEEK</td>
<td><img src="image1" alt="Image" /></td>
<td><img src="image2" alt="Image" /></td>
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<tr>
<td>Subtractive Processes (Acids)</td>
<td><img src="image3" alt="Image" /></td>
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<tr>
<td>Additive Manufacturing (e-beam)</td>
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<td>Sprayed Particle Coatings</td>
<td><img src="image7" alt="Image" /></td>
<td><img src="image8" alt="Image" /></td>
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<td>Deeply Porous Scaffolds</td>
<td><img src="image9" alt="Image" /></td>
<td><img src="image10" alt="Image" /></td>
</tr>
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</table>

**Implant Durability: Abrasion Resistance of Sprayed Titanium Particle and Porous Titanium Scaffold Surfaces**

![Graph](graph.png)

*Percent Mass Loss (%) as a function of applied load. Data points are indicative of results from FortiCore scaffold only. Changes are made to the raw data for clarity. Note: Abrasion resistance is non-quantitative.*
Foundation Layer: Deeply Porous Titanium Scaffold (FortiCore®)

30x Magnification (Micron)

1,000x Magnification (Micron)

10,000x Magnification (Micron)

523 μm = Avg. Pore Size

60% = Pore Volume

750 microns = Depth of Porous Layer

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" analogy

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What about Titanium?

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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.

**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.
What About Fusion Assessment?

Porous Titanium Scaffold with PEEK Core

Porous Tantalum Implant

Titanium Implant

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 Shear Strength (MPa) Between Host Bone and PEEK or Allograft or Porous Titanium Scaffold after 5 weeks of Implantation

Shear Strength (MPa)

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.
Bone to Implant Contact Varied by Nanofeature

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 (**) shows a significant difference in comparison with all other groups in experiment (p < 0.05).

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

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Nanotube Surfaces

Nanoscale Design Features Adds NanoBiology to Biomechanics to
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A Abrasion Resistance of Porous Titanium Scaffold Foundation Layer
Compared to a Titanium Plasma Spray Control
DISCLOSURES

• NANOVIS

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
  – Nanosensors, TGA, 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®

30x Magnification (Macro)

300x Magnification (Macro)

1,000x Magnification (Micron)

10,000x Magnification (Micron)

123 μm = Avg. Pore Size
60% = Pore volume
750 μm = Depth of porous ingrowth layer

523 μm = Avg. Pore Size
60% = Pore volume
750 μm = Depth of porous ingrowth layer

% Mass Loss as a Function of Applied Load

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 machine, with the surface facing down. The half-cylinder has been placed in the specimen at a specified normal force and is cycled normal to the axis.

<table>
<thead>
<tr>
<th>Axial Load (N)</th>
<th>Avg Mass Loss</th>
<th>StDev Mass Loss</th>
<th>% Mass Loss</th>
<th>P value</th>
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<tbody>
<tr>
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