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Disclosures

- Depuy- Consultant
- Stryker- Consultant
- Nuvasive- Consultant
- Prosidyan- SAB and CMO, Royalties

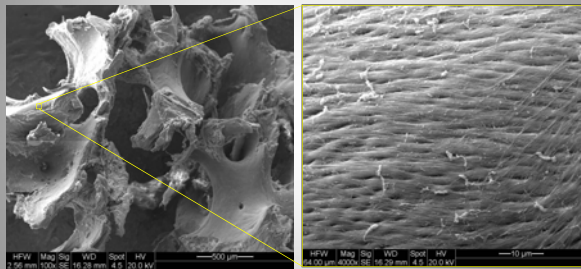
New therapies for spinal fusions

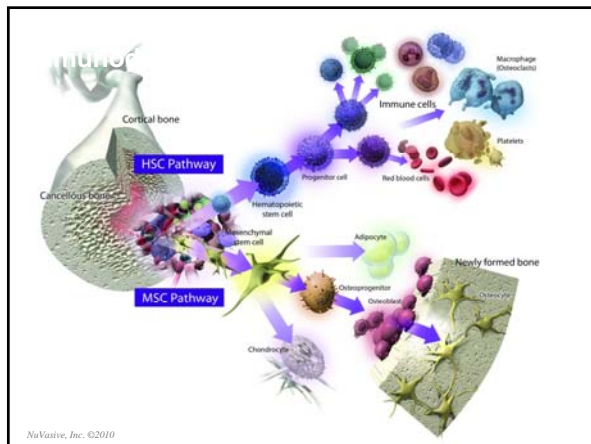
Cells, Molecules and Surfaces"

Stem Cell Enhanced Allograft

- Osteocell Plus-- Nuvasive
- Trinity Evolution-- Orthofix
- Cellentra-- BioMet

SEM Analysis of Osteocel Plus 100 X and 4000 X





ViviGen[®] Cellular Bone Matrix
The right cells. The right time.

LifeNec Health[®]
Strong. Unbreakable. Right. Where it counts.

ViviGen is a registered trademark of LifeNec Health

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DBUSP/N0715049_0715

Paradigm Shift

Bone Cells (Osteoblasts and Osteocytes) are the preferred cell types for bone repair^{2,3,4,5,6}

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BIO4[®]
BONE GRAFT SUBSTITUTE

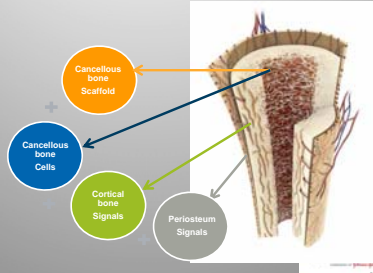
BIO4
NCTD 81403906
NCTD 70002
NCTD 814042017

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BIO⁴ – Next Generation

- BIO⁴ is processed from allograft donor bone using proprietary methods
- BIO⁴ includes all components of natural bone: cancellous bone containing endogenous cells and cortical bone, and periosteum



10 DRUGSPL02150049 0715

Cellular Allograft in Anterior Cervical Discectomy and Fusion (ACDF)

Evaluation of Clinical and Radiographic Outcomes from a Prospective Multi-center Study

Robert Eastlack¹, Christopher R. Brown², Craig Meyer³. IMAST. July 2013.
¹Scriptis Clinic, La Jolla, CA ²Duke University Medical Center, Durham, NC ³Columbia Orthopaedic Group, Columbia, MO

BACKGROUND

- Prospective, multicenter trial (17 sites)
- 249 levels (182 patients)
 - 1- (63%) or 2- (37%) level ACDF (C3-T1)
- 2 year follow-up with radiograph and CT data
- Data reviewed by 3 independent spine surgeon reviewers

SUMMARY OF RESULTS

- **Single Level:** 95% fusion (<3° ROM on F/E); 92% fusion (CT)
- **Two Level:** 89% fusion (<3° ROM on F/E); 83% fusion (CT)
- **All Levels:** 92% fusion (<3° ROM on F/E); 87% fusion (CT)
- 93% patient satisfaction scores

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The Spine Journal

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In Press, Accepted Manuscript — Note to users

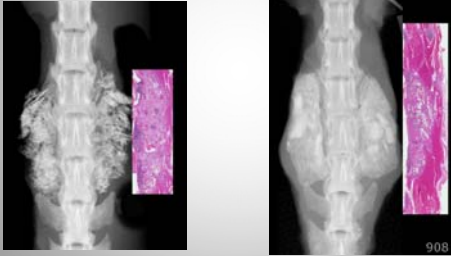


Mesenchymal Stem Cell Allograft As A Fusion Adjunct In One And Two Level Anterior Cervical Discectomy And Fusion: A Matched Cohort Analysis

Steven McAnany, MD¹, Mohamed N.B. Nouredin, MD², Islam M. Elboghady², Alejandro Marquez-Lara, MD², Noman Ashraf, MD, MBA¹, Branko Svorinji, MD¹, Samuel Overley, MD¹, Kern Singh, MD², Sheeraz Qureshi, MD, MBA¹

Show more

MSC Allograft vs DBM



Advantages

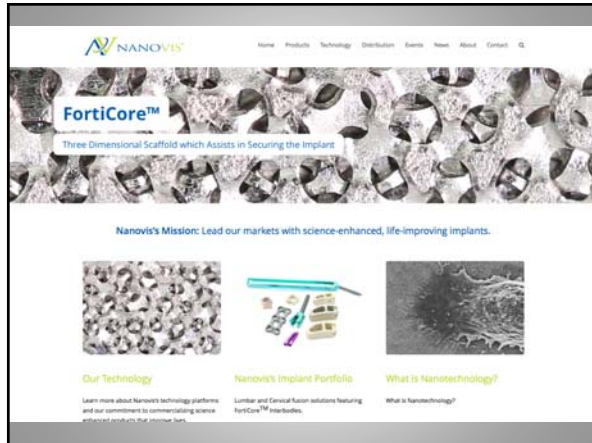
It's a good source of allograft

Good Safety Profile

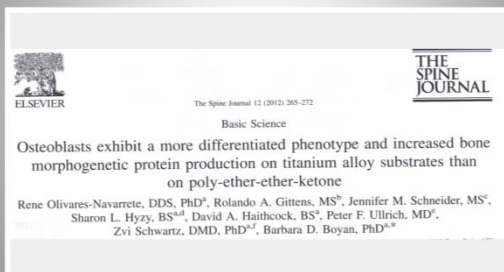


PEEK vs. Titanium

- Titanium
 - Widely used across all many Bone applications
 - Bio-compatible
 - Compatible with MRI and CT
 - Bone ingrowth directly onto surface of some Implants (surface dependent)
 - (Re-) Emerging as a reliable material for spine fusion



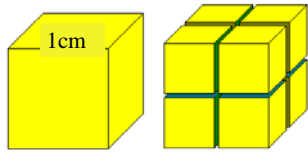
Ti Surface



Nanotechnology

- How small is nano
- One nanometer is a billionth of a meter, or 10^{-9} of a meter. Here are a few illustrative examples:
 - A sheet of newspaper is about 100,000 nanometers thick
 - On a comparative scale, if a marble were a nanometer, then one meter would be the size of the Earth

Power of Nano: Surface-to-Volume Comparisons...

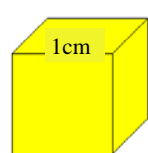


Volume is constant
 $1 \text{ cm} \times 1 \text{ cm} \times 1 \text{ cm} = 1 \text{ cm}^3$

- Neglecting spaces between the smaller boxes, the volumes of the box on the left and the boxes on the right are the same but the surface area of the smaller boxes added together is much greater than the single box.

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Power of Nano



Area = $6 \times 1 \text{ cm}^2 = 6 \text{ cm}^2$



Area = $6 \times (1/2 \text{ cm})^2 \times 8 = 12 \text{ cm}^2$



10 nm

Constant Volume 1 cm^3

Area = $6 \times (10 \text{ nm})^2 \times 1,000,000^3 = 600,000,000 \text{ cm}^2$ or 6000 km^2

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Surface area 6000 km²



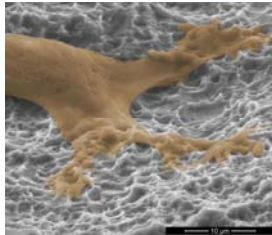
- Great Salt Lake 3000 to 6000 km²



- Manhattan 58 km²
- Los Angeles 1200 km²

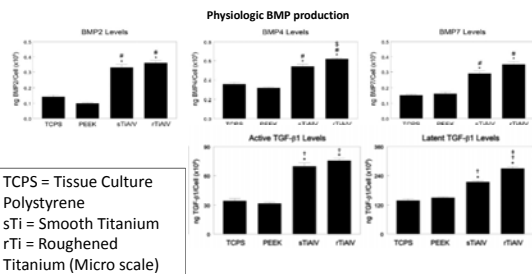
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Human Stem Cell on nanoLOCK™ surface



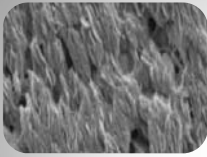
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Up-regulate Osteoblasts - TGF-B1, BMP-2,4,7

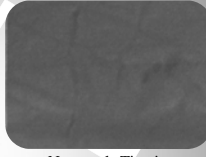


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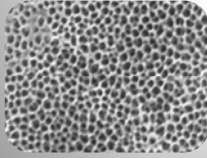
Nanoscale Mimics Nanoscale Bone



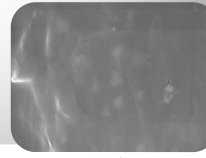
Nanoscale Bone



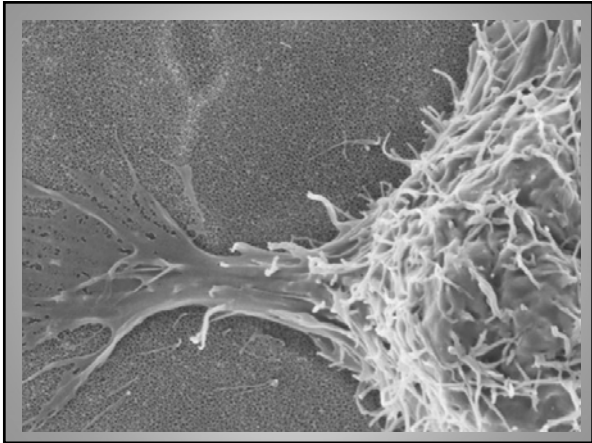
Nanoscale Titanium

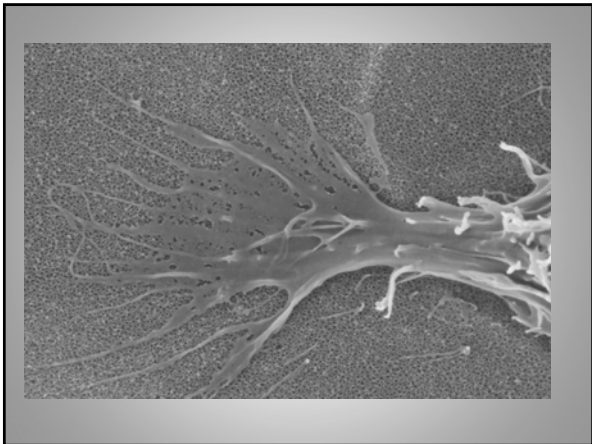


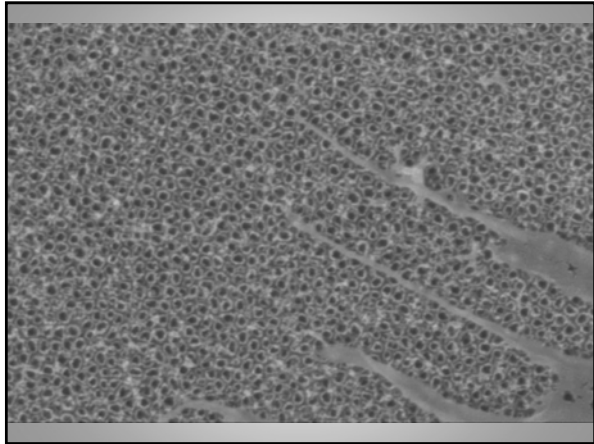
Nanotubular Titanium Oxide



Nanoscale PEEK







Hierarchy of Implant Surface Topography

- Macro level (10^{-3} m)
- Micro level (10^{-6} m)
- Nano level (10^{-9} m)

Biochemical Influence Barrier

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Nano-Unlocks

the Alpha 2 Beta 1 Integrins to start cellular transcription.

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Image courtesy of Barbara D. Boyan, PhD

3-D Printing

Titanium PL Cage
featuring **Titanium In-Growth Technology!**



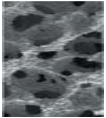


Titanium In-Growth Technology!

- Designed for **in-growth!**
- Empowered by **experience!**

Titanium PL Cage

- Created to allow **visualization!**
- Developed to **minimize subsidence!**
- Engineered for **stability!**




1. 100% Ti6Al4V
2. 100% Ti6Al4V
4. 100% Ti6Al4V
5. 100% Ti6Al4V

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TITR1302

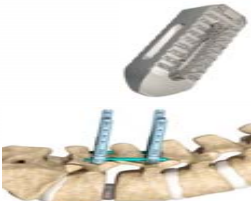
Titanium PL Cage specifications



Material
Ti-Alloy TR60AF

Porous Surface Parameters:
Porosity: mean 60%, ±3
Pore size: 100-700µm mean 63µm³

Straps
Height: 7-14mm
Width: 9 and 11mm
Length: 25 and 28mm
Loadline: (Open End) (Edge or 2mm)




1. 100% Ti6Al4V
2. 100% Ti6Al4V
4. 100% Ti6Al4V
5. 100% Ti6Al4V


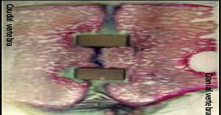

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TITR1302

Pre-clinical Study¹ Histology*



Sagittal View



FEKA Cage **TR Prime Sprayed FEKA Cage** **Titanium PL Cage**

16 weeks post-op in an ovine model!

*Ovine data obtained independent of the present study.

1. SPM, S40; STYMER 0015
2. SPM, S40; STYMER 0015
4. SPM, S40; STYMER 0015
5. SPM, S40; STYMER 0015

TITR1302

COHERE™ Cervical Cage Product Line

Increased Cell Proliferation

Material	EdU Incorporation (Counts)
Smooth PEEK	~10000
PEEK Score	~30000
Ti-6Al-4V	~5000

Increased Osteogenic Differentiation

Material	Calcium (µg)
Smooth PEEK	~10
PEEK Score	~80
Ti-6Al-4V	~10

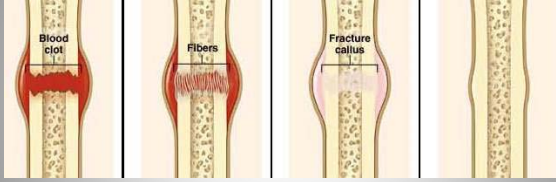
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Not all Porosities are the same

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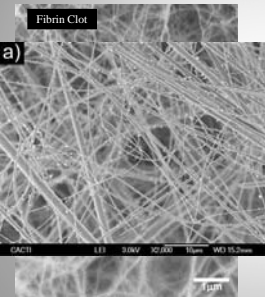
How Bones Heal



Fibers provide connectivity for bones to heal

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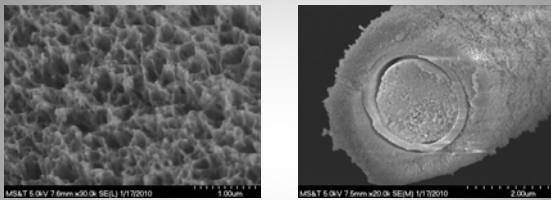
Sentinel Healing-Fibrin Clot



- In situ catalytic conversion of fibrinogen to fibrin by thrombin to form cross-linked fibrin matrix
- Fiber mediated healing
- Basic mechanism for all connective tissue healing.

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FIBERGRAFT™ IN-VITRO BIOACTIVITY TEST



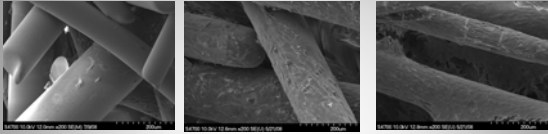
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day

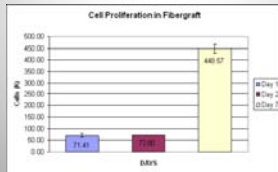
FIBERGRAFT™ in SBF at 37°C

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Cell Proliferation Study



Laboratory Tests Show Rapid Growth of Bone Forming Cells on Bioactive Glass Fibers

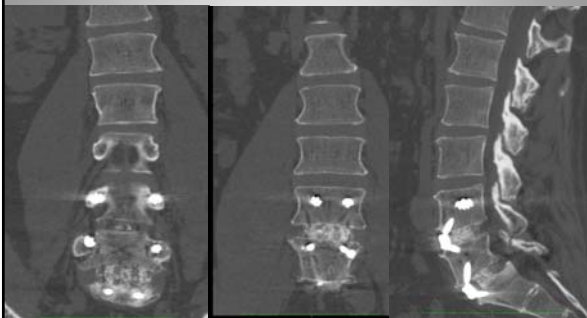


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12M Follow up



12month CT Follow up



i-FACTOR "Peptide Enhanced" Bone Graft*

Mechanism of Action: "Attract - Attach - Activate"

i-FACTOR Bone Graft will
Attract anchorage
 dependent osteogenic cells
 that **Attach** to P-15, **Activate**
 and form bone

Osteogenic Cell

"ABM" is Anorganic Bone Mineral (Natural Hydroxyapatite)

P-15

"P-15" is a Fifteen Amino Acid Synthetic Analog of the Cell-Binding Domain of Human Type I Collagen

ABM

* Investigational Device, not approved for use in the United States

CERAPEDICS
 Enhancing the Science of Bone Repair

