Hyun Bae, MD

Professor of Surgery
Department of Surgery
Director of Education
Cedars Spine Center

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
Paradigm Shift

Bone Cells (Osteoblasts and Osteocytes) are the preferred cell types for bone repair. 2,3,4,5,6
**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. SMAST, July 2013.

**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

---

**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

---

**The Spine Journal**

Available online: 29 February 2016

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 Molony, MD, 1 Mohammed N. Younis, MD, 1 Islam M. Elshigebly, 2 Alejandro Mercue-Lari, MD, 1, 3 Neuman Ahamat, MD, MABA, 1, 3 Darbco Sowry, MD, 1, 2 Samuel D. Oliver, MD, 1, 2 Kamin Singh, MD, 1, 2 Sherrin Guness, MD, MBA, 1

*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
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...

 Porto 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.

Power of Nano

<table>
<thead>
<tr>
<th>Constant Volume 1 cm^3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Area = 6 x (10 nm)^2 x 1,000,000^2 = 600,000,000 cm^2 or 6000 km^2</td>
</tr>
</tbody>
</table>
Surface area 6000 km²

- Great Salt Lake 3000 to 6000 km²
- Manhattan 58 km²
- Los Angeles 1200 km²

Human Stem Cell on nanoLOCK™ surface

Up-regulate Osteoblasts - TGF-β1, BMP-2,4,7

TCPS = Tissue Culture Polystyrene
sTi = Smooth Titanium
rTi = Roughened Titanium (Micro scale)
Hierarchy of Implant Surface Topography

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

**Image courtesy of Barbara D. Boyan, PhD**

**Nano Unlocks**

Unlocks the Alpha 2 Beta 1 integrin to start cellular transcription.
The Stryker Spine Tritanium PL Cage is an intervertebral body fusion device indicated for use with autograft and/or allogenic bone graft comprised of cancellous and/or corticocancellous bone graft when used as an adjunct to fusion in patients with degenerative disc disease (DDD) at one level or two contiguous levels from L2 to S1.

**Tritanium In-Growth Technology**
- Designed for in-growth
- Empowered by expertise

**3-D Printing**
- Tritanium PL Cage
- Engineered for stability
- Developed to minimize subsidence
- Designed to allow visualization

**Specifications**
- **Material:** Ti Alloy Ti6Al4V
- **Porous Surface**
  - **Porosity:** mean 60%
  - **Pore size:** 100–700µm; mean 438µm
- **Sizing**
  - **Height:** 7–14mm
  - **Width:** 9 and 11mm
  - **Length:** 23 and 28mm
  - **Lordosis:** 0 and 6° (oblique for 28mm)

**Histology**
- Pre-Clinical Study
- Sagittal View
- Cranial vertebra
- Caudal vertebra
- **Pre-op** in an ovine model
- 16 weeks post-op

*Correlation to humans has not been established or demonstrated.*
COHERE™ Cervical Cage Product Line

Increased Cell Proliferation

Increased Osteogenic Differentiation

Not all Porosities are the same
How Bones Heal

Fibers provide connectivity for bones to heal

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.

FIBERGRAFT™ IN-VITRO BIOACTIVITY TEST

3 day FIBERGRAFT™ in SBF at 37°C
Cell Proliferation Study

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

12M Follow up

12mont 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.

```
ABM
```

"ABM" is Anorganic Bone Mineral (Natural Hydroxyapatite)

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

**Primary Outcomes and Responder Analysis**

<table>
<thead>
<tr>
<th>Primary Outcome</th>
<th>i-FACTOR Bone Graft vs Autograft</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fusion Success</td>
<td>89.0% vs 78.0% (p = 0.0382)</td>
</tr>
<tr>
<td>NDI Success</td>
<td>93.7% vs 89.0% (p = 0.0004)</td>
</tr>
<tr>
<td>Neurological Success</td>
<td>97.5% vs 93.0% (p = 0.0001)</td>
</tr>
<tr>
<td>Safety Success</td>
<td>68.8% vs 85.8% (p = 0.0001)</td>
</tr>
<tr>
<td>Overall Success</td>
<td>93.0% vs 95.4% (p = 0.8814)</td>
</tr>
</tbody>
</table>

Black p values non-inferiority test
Red p value superiority test
* Safety: no difference in re-operations at index level Fisher's exact test for superiority

**THANK YOU!!!