

Innovations In Osteobiologics

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Disclosures

- **Consultant**
 - **Innovasis**
 - **Titan Spine**
 - **K2M**
- **Royalties**
 - **Choice Spine**

Introduction

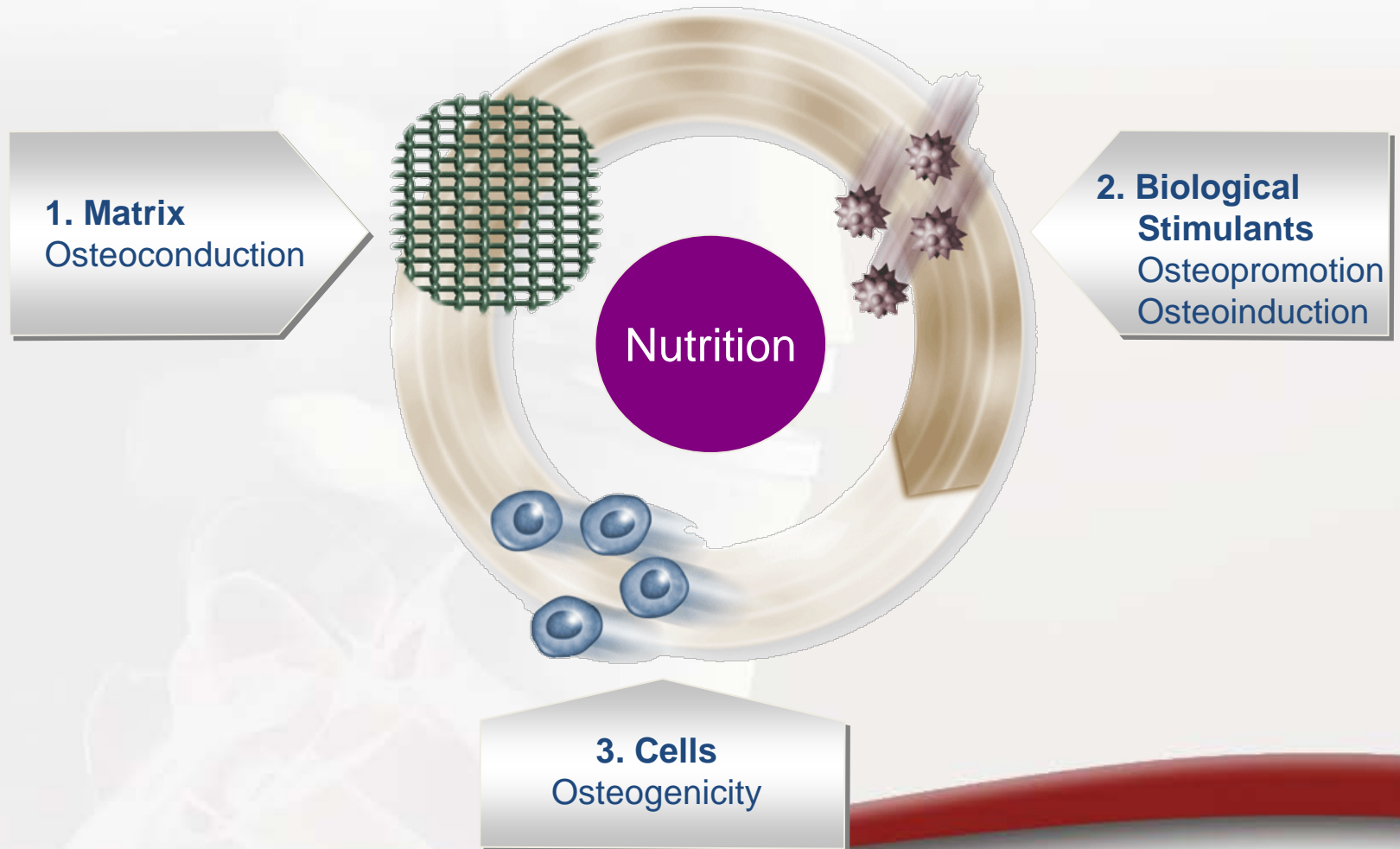
Fusion Is Important:

- **Axial pain**
- **Recurrence of radicular pain**
- **Instrumentation failure**
- **Complicated revisions**

BIOLOGIC OPTIONS

- **Autograft**
- **Allograft**
- **Demineralized Bone Matrix (DBM)**
- **Ceramics (TCP, HA, CaSO₄)**
- **Bone Morphogenetic Protein - 2 (rhBMP-2)**
- **Stem Cell Allografts**
- **Peptide enhanced allografts**

Key Ingredients for Bone Formation



Autograft



Potential advantages

- Gold standard for performance
- No disease transmission
- Histocompatible

Potential disadvantages

- Limited supply
- Second site morbidity (up to 20%)
- Increased OR time

Biological benefit

- Scaffold
- Cells
- Signal

grafton®



Optecure®
Optecure+ccc



on



Dynagraft



Accell 100™



OSSEOGRAFT (DBBM)



Optecure®



Texas Back Institute®

TABLE 2. Demographic Information

Demographic Information			
	Grafton	ICBG	P
Patients (n)	28	13	...
Age (yr)	64.3	65.3	0.3920*
Sex (M/F)	10/18	5/8	1.0000†
Education (n > HS)	26/28	13/13	1.0000†
Previous tobacco use (n)	8/28	7/13	0.1677†
Previous spine surgery	1/28	0/13	1.0000†
Diabetes	0/28	2/13	0.0951†
Alcohol use (any amount)	8/28	5/13	0.7197†

*Wilcoxon rank sum test.

†Fisher exact test.

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2-year fusion rates for grafton DBM and iliac crest groups

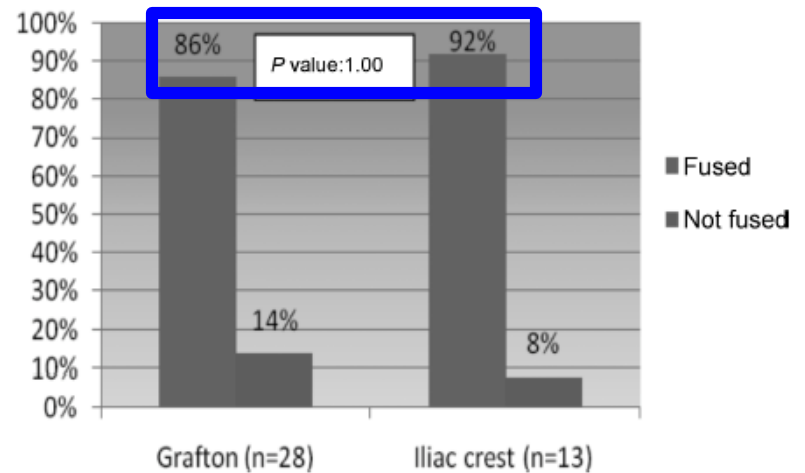


Figure 2. Overall radiographical fusion rates at 2 years. DBM indicates demineralized bone matrix.

DBM variability

ELISA measurements of BMP-2 in DBM

picogr/mg	Lot 1	Lot 2	Lot 3	CV%
Allomatrix	97.5	30.1	28.2	76
DBX	51.4	40.9	36.6	18
Dynagraft II gel	49.2	38.8	25.4	32
Dynagraft II putty	39.5	30.8	29.5	16
Grafton crunch	40.8	30.5	29.0	19
Grafton gel	85.6	33.6	20.2	74
Grafton putty	61.3	51.9	29.0	35
Intergro putty	89.7	50.5	33.0	50
Osteofil paste	120.6	48.4	28.4	74



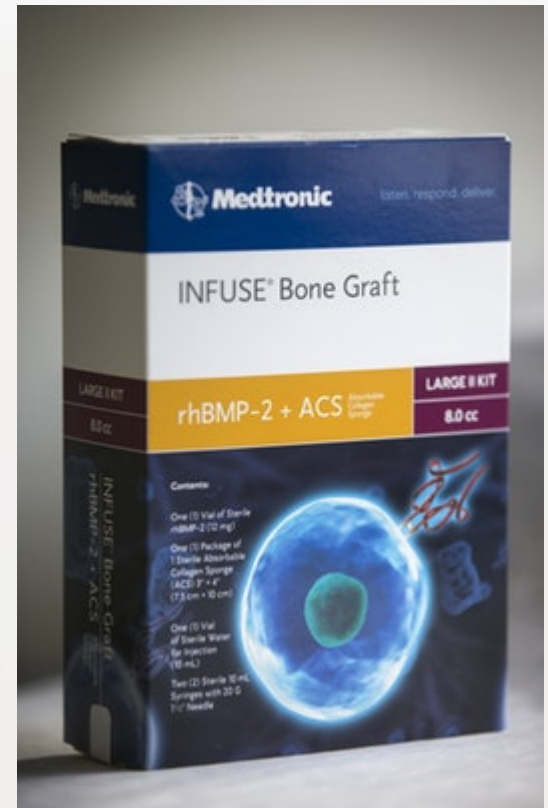
DBM Summary

- **Standards and Guidelines don't exist for the use of DBM in spine surgery**
- **Clinical evidence for Accell and Grafton:**
 - Equivalence to autograft as extender
- **More clinical research is needed**
- **Limited by amount of products on offer**



Bone Morphogenetic Protein

- **Works Great!!**
- **But....**



InFuse: Published/Presented Clinical Concerns

- Swelling/Dysphagia in ACDF
 - 23.2% complications (*Shield et al NASS 2005*)
 - 29% Infuse complications vs. 13% control (*Riew et al NASS 2005*)
- Post-op late radiculitis
 - Vaccaro, et. al. 2007 NASS, 8.4X increased incidence secondary to InFuse
- Ectopic bone formation
 - Approx 40% of Infuse leaks from the sponge after soaking 15 minutes (*Pradhan et al NASS 2005*)
 - Bone formation in the neuroforamen in 5 of 42 levels (*McClellan et al NASS 2005*)
 - PLIF with Infuse (*Alexander et al NASS 2002*)
- Osteoclastic Hyperactivity
 - Aggressive endplate remodeling in ACDF (*Pradhan et al NASS 2005*)
 - Osteolytic defects in 31 of 42 TLIF levels (*McClellan et al NASS 2005*)
 - 56% non-union Stand Alone ALIF – FRA, Implant failures (*Pradhan et al 51st ORS*)
- Poor results in Posterior Lumbar Fusion
 - 45% of patients were fused at 2 yr – instrumented PLF (*Dimar et al NASS 2005*)
 - PLF fusion rates Infuse = ICBG (only at 40 mg/level)

Graft Materials: Synthetics

Advantages

- No chance of disease transmission
- Can be engineered for better scaffolding properties
- Reduce 2nd site surgery
- Reduces OR time



Disadvantages

- Some versions difficult to use
- Resorption patterns variable
- Many versions not stand alone products



Graft properties

- Osteoconductive

Synthetic Bone Graft

- **Calcium phosphate based**
 - **Osteoconduction**
 - **Very slow biodegradation**
 - **May be prepared as ceramics**
 - **Tricalcium phosphate**
 - **Hydroxyapatite**
 - **No osteogenic or osteoinductive properties; framework only**

TABLE 3. Fusion Rates—Subgroup Analysis of BGE Materials

BGE Material	Studies (n)	Patients (n)	Pooled Fusion Rate (95% CI)	Pooled RR: Experiment vs. Control (95% CI)
TCP	3	130	95.1% (89.7%–100%)	0.98 (0.91–1.06)
CaSO ₄	2	96	75.0% (66.3%–83.7%)	0.68* (0.02–2.85)
HA and TCP	2	83	98.2% (94.7%–100%)	1.02 (0.95–1.09)
HA	2	58	76.9% (63.7%–90.1%)	0.82* (0.45–1.51)
Bioactive glass	1	40	85.0% (69.4%–100.6%)	0.94 (0.75–1.19)
Mineralized collagen with HA coating	1	25	80.0% (64.3%–95.7%)	0.95 (0.73–1.24)
BGE + LAG	7	316	86.9% (82.1%–91.7%)	0.97 (0.91–1.04)
BGE + BMA	3	77	76.6% (67.1%–86.1%)	0.80* (0.47–1.35)
BGE + LAG + BMA	1	39	95.0% (85.5%–100%)	1.00 (0.87–1.16)

*Higgins $I^2 > 50\%$ suggesting substantial heterogeneity.

calcium sulfate; HA, hydroxyapatite; BGE, bone graft extender; LAG, local

Pooled data the most successful fusion rates in comparison with ICBG

•β -TCP plus LAG

or

•β -TCP and HA plus LAG

Peptide Enhanced Allograft



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More than a
simple scaffold

i-FACTOR Peptide Enhanced Bone Graft Technology Platform

i-FACTOR Bone Graft is an advanced biologic that is supported with level I evidence, satisfies the highest regulatory imperatives, and provides a better cost/benefit ratio than engineered growth factors and cellular allografts.

[Animation](#)

[i-FACTOR Putty](#)

[Supplemental Information](#)

I-Factor

- **synthetic collagen fragment (P-15) bound to calcium phosphate particles**
- **P-15: synthetically derived 15-amino acid peptide found naturally in Type I human collagen**
- **“i-FACTOR Bone Graft facilitates and expedites the ingrowth of bone by promoting the migration of mesenchymal stem cells and other progenitor cells from surrounding tissue.”**

i-Factor Data

[Spine \(Phila Pa 1976\)](#). 2016 Jul 1;41(13):1075-83. doi: 10.1097/BRS.0000000000001466.

Efficacy of i-Factor Bone Graft versus Autograft in Anterior Cervical Discectomy and Fusion: Results of the Prospective, Randomized, Single-blinded Food and Drug Administration Investigational Device Exemption Study.

[Arnold PM](#)¹, [Sasso RC](#), [Janssen ME](#), [Fehlings MG](#), [Smucker JD](#), [Vaccaro AR](#), [Heary RF](#), [Patel AJ](#), [Goulet B](#), [Kalfas IH](#), [Kopjar B](#).

- Single Level ACDF Study
- Cortical Ring Allograft + LAG – 85.92% fusion at 1 year
- Cortical Ring Allograft + i-Factor Putty – 88.97% fusion at 1 year

Bioactive Glass Putty



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FIBERGRAFT®

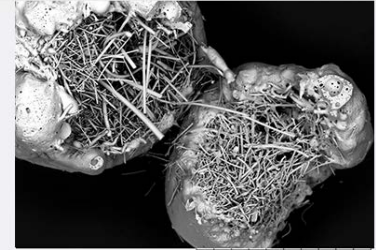
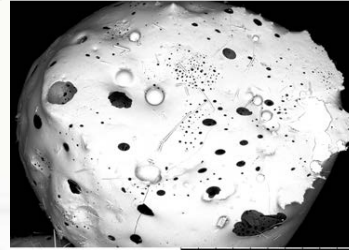
BG Putty

FIBERGRAFT® BG Putty is FIBERGRAFT® BG Morsels delivered through Prosidyen's proprietary bioactive carrier, OSSIGLIDE®.

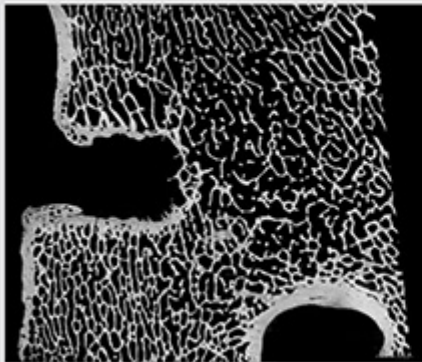


Fibergraft

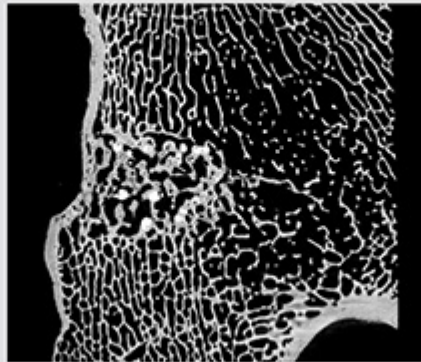
- Microspheres with internal structure promote osteoblast attachment/HA deposition
- Preclinical data impressive
- No published clinical articles



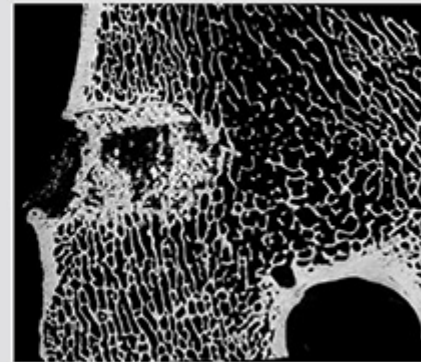
24 WEEKS



SHAM



FIBERGRAFT® BG MORSELS



COMPETITOR PRODUCT



Stem Cells for Fusion

- **Osteocel-Nuvasive**
- **Vivigen – Depuy/Synthes**
- **Bio-4 – Stryker**
- **Many, Many more**

Stem Cells

- **MSC numbers and health are unpredictable**
- **Varies with:**
 - **Age** [Sethe et al, Ageing Res Rev 2006](#); [Caplan, Clin Plastic Surg 1992](#)
 - **Gender** [Seebach et al, Calcif Tissue Int 2007](#)
 - **Aspiration/harvest technique and location** [Muschler et al, J Orthop Res 2001](#)
 - **Health of patient** [Seebach et al, Calcif Tissue Int 2007](#)
 - **Local vascularity** [Caplan, Cell Stem Cell 2008](#)

Clinical Study

Mesenchymal stem cell allograft as a fusion adjunct in one- and two-level anterior cervical discectomy and fusion: a matched cohort analysis

Steven J. McAnany, MD^a, Junyoung Ahn, BS^b, Islam M. Elboghday, BS^b,
Alejandro Marquez-Lara, MD^b, Nomaan Ashraf, MD,MBA^a, Branko Svovrlj, MD^a,
Samuel C. Overley, MD^a, Kern Singh, MD^b, Sheeraz A. Qureshi, MD, MBA^{a,*}

- **57 pts 1 or 2-level ACDF with PEEK cage, plate, and MSC (Osteocel, NuVasive)**
- **Compared with matched control group not receiving Osteocel (structural allograft, plate)**
 - **Groups similar on demographics and operative factors**

MSC for ACDF

- **Fusion rates:**
 - **MSC graft material: 87.7%**
 - **Control group: 94.7%**
- **Difference not statistically significant**

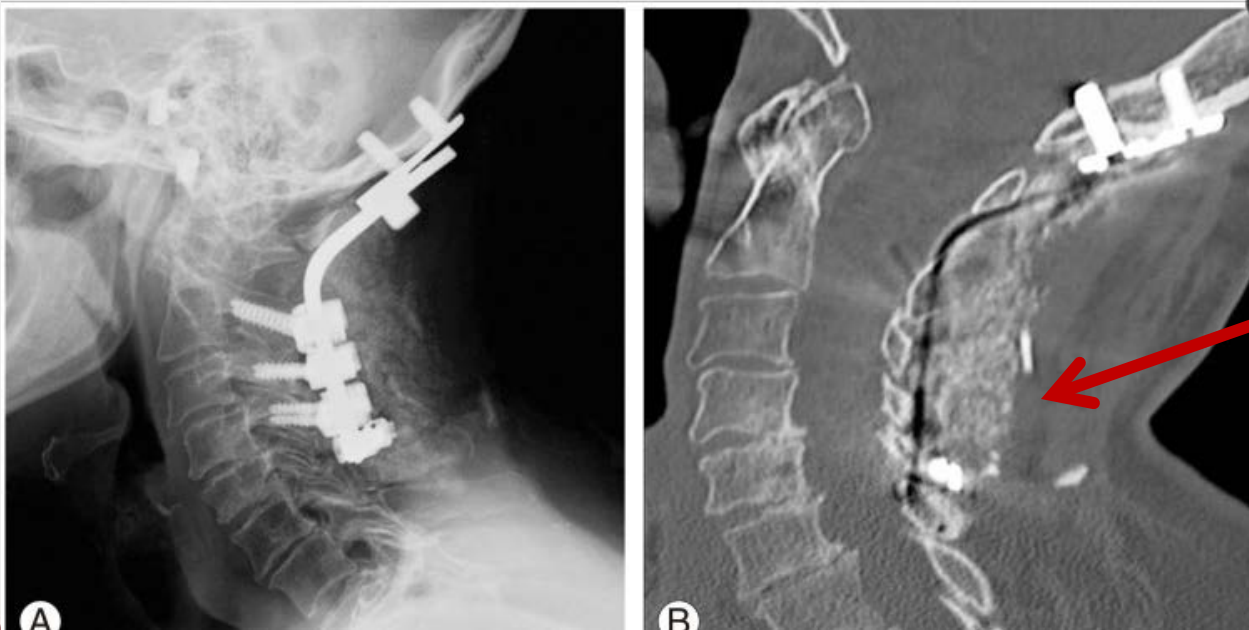
Vivigen

Asian Spine J. 2017 Jun;11(3):454-462. doi: 10.4184/asj.2017.11.3.454. Epub 2017 Jun 15.

Use of Allogenic Mesenchymal Cellular Bone Matrix in Anterior and Posterior Cervical Spinal Fusion: A Case Series of 21 Patients.

Divi SN¹, Mikhael MM^{1,2,3}.

- Case series
- Claimed 100% fusion for complex cervical cases...



Stem Cell Allograft for Fusion: Concerns

- **Is this better than allograft chips??**
- **Human tissue/allograft product**
- **Lack of compelling human clinical evidence**
- **Inferior handling properties**
- **Cost**