Actifuse/Osteoamp/Stem Cell Products

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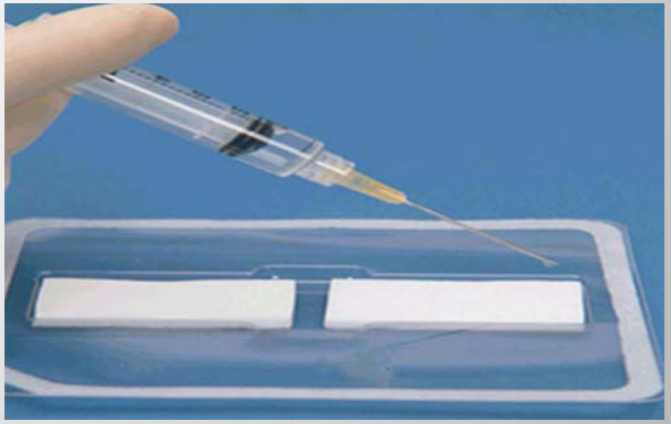
The quest to replace autograft/RhBMP...

- Autograft
  - Donor site morbidity
    - Pain
    - Infection
    - Fracture
  - Volume
  - Quality depends on patient

- rhBMP
  - Cost
  - Ectopic bone formation
  - Seroma
  - ?cancer risk

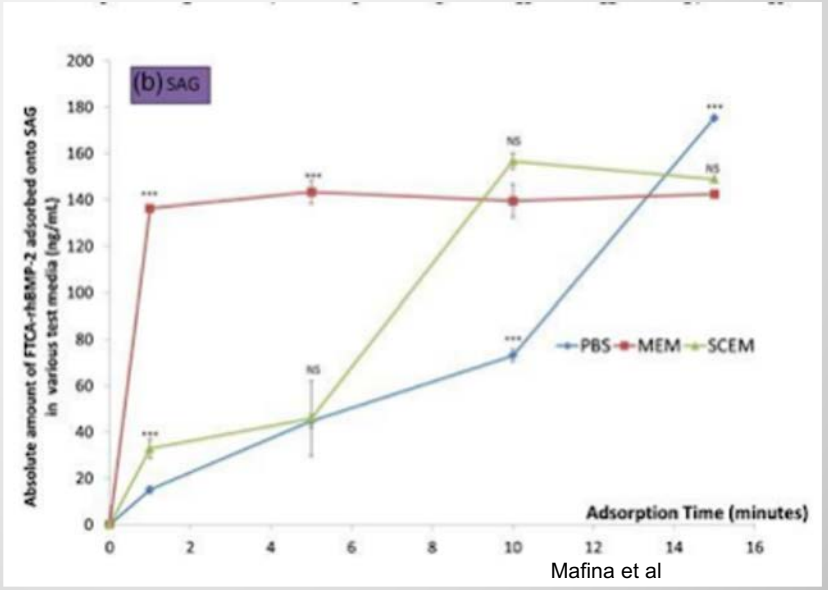


Actifuse - bone graft substitute

- Baxter
  - Floseal, Tisseal
- Bone void filler, “resorbs and is replaced by bone during the healing process”
  - Non-structural
- Silicate-substituted HA granules suspended in a resorbable alkylene oxide
  - 0.8% silicon by weight - similar to natural bone polymer matrix
- “Osteostimulative”
  - Macro/micro-porous structure - 80% porosity to mimic cancellous bone
  - Silicate substitution process - attracts and stimulates OPCs and MSCs

Actifuse

- Fluorescent-labeled rhBMP-2
- Silicate-substituted (0.8% Si) HA in multiple mediums
- >50% of rhBMP-2 in medium was adsorbed onto SA granules at 15 min
    - vs. 30% for HA granules



Mafina et al

Actifuse - SiCaP

- Licina et al
- Comparison of Actifuse v. rhBMP-2 (InFUSE)
- Posterolateral lumbar fusions in adults with DDD
- 9/9 v. 8/9 at 12 months
- Less back pain at 6 weeks, QOL higher at 6 months

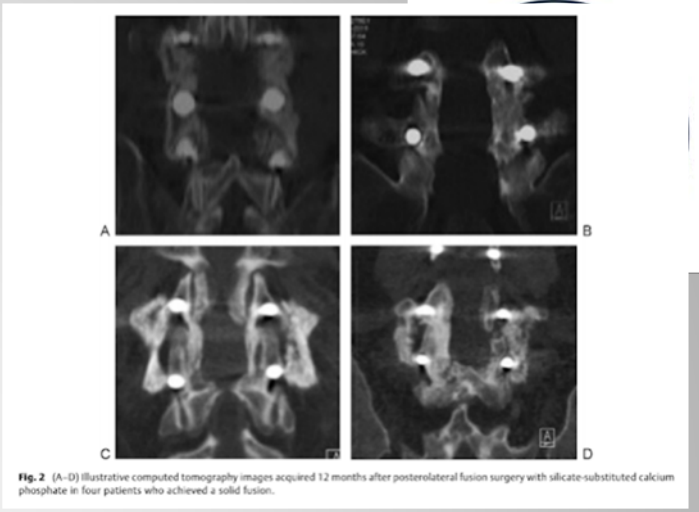


Fig. 2 (A–D) Illustrative computed tomography images acquired 12 months after posterolateral fusion surgery with silicate-substituted calcium phosphate in four patients who achieved a solid fusion.

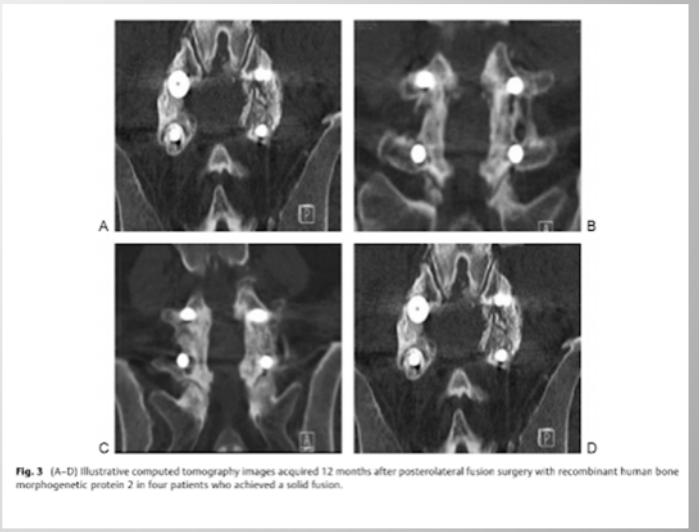
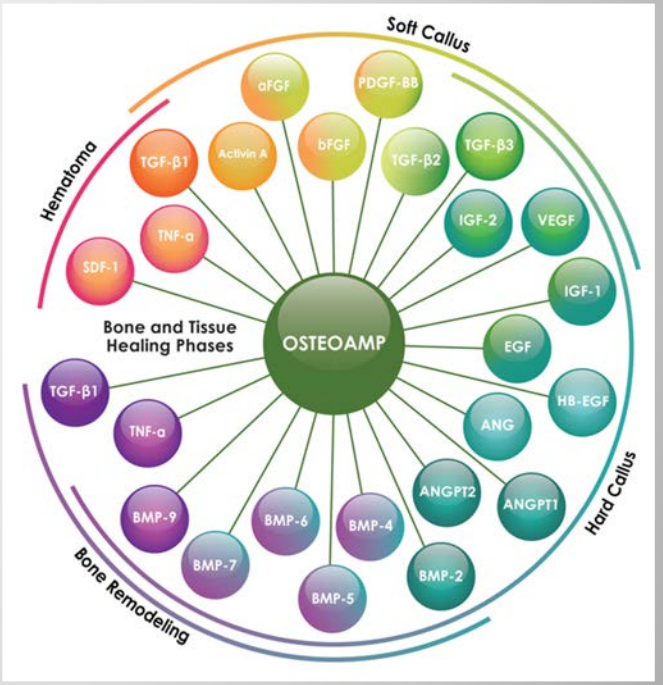


Fig. 3 (A–D) Illustrative computed tomography images acquired 12 months after posterolateral fusion surgery with recombinant human bone morphogenetic protein 2 in four patients who achieved a solid fusion.

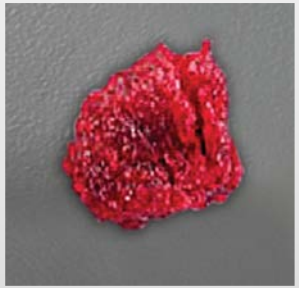
OsteoAMP

- Bioventus Surgical
  - Previously Advanced BIologics
  - Signafuse (biphasic CaP)
- Osteo Allogeneic Morphogenetic Proteins
- “Retain up up to 23 natural growth factors that support bone formation.”
- Granules, putty, sponge, fibers



OsteoAMP

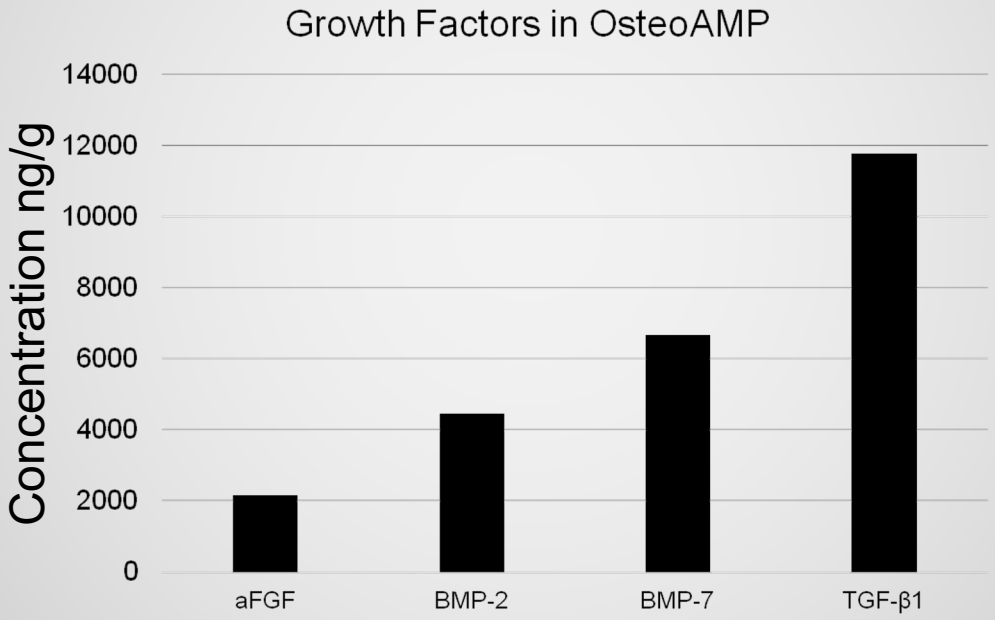
- “A unique, differentiated bone graft”
- Proprietary process utilizes the bone and growth factor rich bone marrow from the donor bone
- High levels of a heterogeneous array of naturally occurring growth factors to better support bone healing
  - BMP-2, BMP-7, TGF-β1. aFGF, VEGF, ANG1



The OsteoAMP Process

- Differs from traditional allograft processing in the following ways:
  - Debride/Clean soft tissue off of bone.
  - Other allografts wash away growth factor rich bone marrow. OsteoAMP retains the growth factor rich bone marrow.
  - Cut or grind into desired format.
  - Expose to proprietary solution.
  - Naturally occurring growth factors are retained.
  - Demineralize sponge and putty formats.
  - Other allografts, especially many of the DBMs, are combined with a carrier for handling properties. OsteoAMP is 100% allogeneic bone (including marrow).
  - Cleaning and sterilization process that renders the bio-implant sterile.
  - Lyophilize (freeze-drying) and package.
  - Expose to a low-dose of gamma irradiation.
  - Distribute.

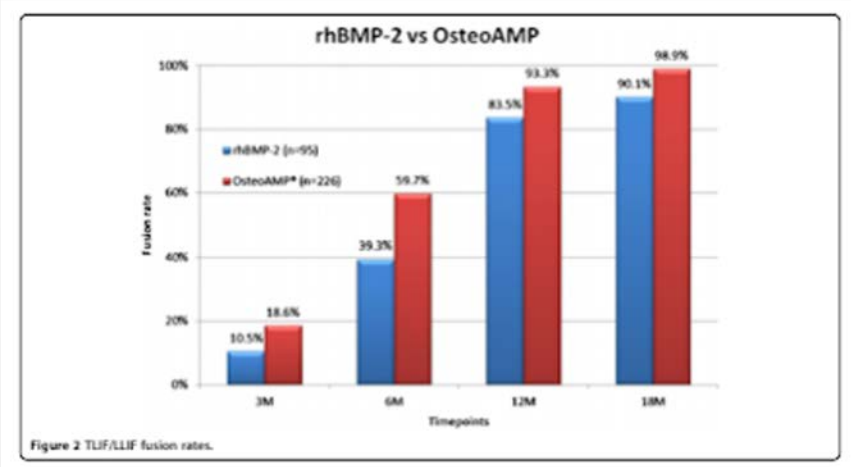
Array of growth factors in OsteoAMP



RPT-000327 Report on Growth Factor Concentrations in Bone and Bone Marrow Aspirate, December 3, 2010, Advanced Biologics, LLC. Data from a single lot of OsteoAMP sponge product.

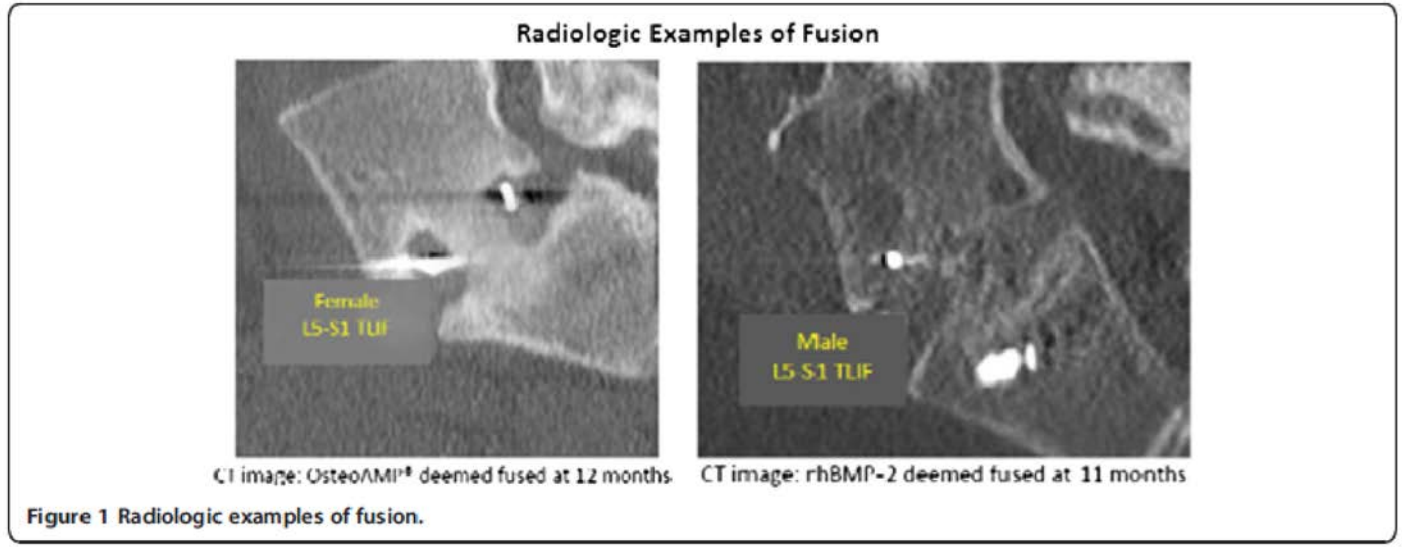
Clinical Data

- Yeung et. al (2014) - 285 pts with cervical and lumbar fusion and 98% fusion at 12 months.
- Field et. al (2014) - 184 pts cervical fusion with 100% fusion at 18 months.
- Roh et. al (2013) - 321 pts with lumbar interbody fusion: 98% fusion better than BMP-2 with less complications.



Competing interests: Authors JR, CY, and JF are unpaid consultants for Advanced Biologics and hold shares in the company. TM is an unpaid consultant for Advanced Biologics. An acquisition of the OsteoAMP product was made by Bioventus after the time of publication. JR, CY and JF have no financial ties to Bioventus.

Lumbar CT images: OsteoAMP vs. rhBMP-2



Roh et al

Stem Cells

- Mesenchymal (bone-forming)
  - Osteogenic factors
- Extreme variability in acquisition, application
- Source:
  - BMA - <0.1% MSCs
    - Isolation and expansion probably required before implantation*
- Require scaffold +/- growth factors
- Many studies underway, but still a paucity of reliable data
- Cost?

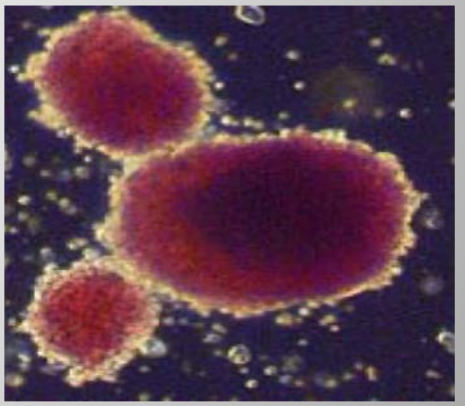


Table 4. Clinical Studies in Spinal Fusion Displaying Fusion Rates Across Studies.

Study	No. of Patients	Approach	End Point	Assessment	Conditions (if Available)	Fusion (%)
Prospective, multicenter, nonrandomized						
Eastlack et al (2014)[57]	182	ACDFP; 1-2 levels	24 mo	CT	Osteocel + PEEK interbody cage and anterior plating	1 level: 92 Overall: 87
Prospective clinical, nonrandomized						
Gan et al (2008)[61]	41	Posterior spinal fusion for DDD or TLF	24 mo	CT	Enriched BMA + βTCP	95.1
Retrospective chart review						
Hostin et al (2013)[62]	22	AIBF	12 mo	CT	Col + BMA in carbon fiber cage	87
Ammerman et al (2013)[56]	23	MITLIF	12 mo	X-ray	Osteocel + DBM	91.3
McAfee et al (2013)[65]	25	XLIF	24 mo	CT	Autograft/Osteocel	85
Caputo et al (2013)[64]	30	XLIF	12 mo	CT	Osteocel + DBM	89.6
Tohmeh et al (2012)[59]	40	XLIF	12 mo	FGX (39) or CT (1)	Osteocel + DBM	90.2
Kerr et al (2011)[58]	52	360 fusion, ALIF, TLIF	5-8 mo	X-ray and CT	Osteocel	92.3
Systematic review						
Khashan et al. (2013)[55]		Comparing BMA with ICBM or LBG				
1 Kitchel (2006), randomized controlled	25	PLF and IF	24 mo	CT	Col + BMA ICBG	80 84
2 Neen et al (2006), prospective case control	50	PLF/TLF/360	24 mo	X-ray	Col/HA + BMA: ICBG	IF 85, PLF 93 IF 92, PLF 93
3 Niu et al (2009), prospective cohort	21	PLF	24 mo	CT	LGB + BMA ICBG	85.7 90.5
4 Vaccaro et al (2007), prospective cohort	73	PLF	24 mo	X-ray	DBM + BMA ICBG	63 67
5 Bansal et al (2009), prospective cohort	30	PLF	12 mo	CT	HA + TCP + BMA ICBG	100 96
6 Morro-Barrero et al (2007) prospective cohort	35	PLF	24 mo	X-ray	BCP + BMA LBG	88 80
7 Taghavi et al (2010), retrospective cohort	62	PLF	24 mo	X-ray	Col + BMA LBG	100 100

Abbreviations: AIB, anterior interbody fusion; ACDFP, anterior cervical discectomy and fusion with plating; BMA, bone marrow aspirate; BCP, biphasic calcium phosphates; Col, collagen; DBM, demineralized bone matrix; DDD, degenerative disc disease; FGX, fluoroscopy-guided level-by-level radiography; HA, hydroxyapatite; ICBG, iliac crest bone graft; LBG, local bone graft; PLF, posterolateral fusion; TCP, tricalcium phosphate; XLIF, extreme lateral interbody fusion.

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References

- Mafina MK, Sullivan AC, Hing KA. Use of a Fluorescent Probe to Monitor the Enhanced Affinity of rh-BMP-2 to Silicated-Calcium Phosphate Synthetic Bone Graft Substitutes Under Competitive Conditions. Materials in Science and Engineering. Materials for Biologic Applications, 80, 207-212 2017.
- Yeung C, Field J, Roh J. “Clinical Validation of Allogeneic Morphogenetic Protein: Donor Intervariability, Terminal Irradiation and Age of Product is not Clinically Relevant.” *Journal of Spine*. 2014; 3(3).
- Field J, Yeung C, Roh J. “Clinical Evaluation of Allogeneic Growth Factor in Cervical Spine Fusion.” *Journal of Spine*. 2014; 3(2).
- Roh JS, Yeung CA, Field JS, McClellan RT. “Allogeneic morphogenetic protein vs. recombinant human bone morphogenetic protein-2 in lumbar interbody fusion procedures: a radiographic and economic analysis. ” *Journal of Orthopaedic Surgery and Research*. 2013; 8:49.
- Licina P, Coughlan M, Johnston E, Pearcy M. Comparison of Silicate-Substituted Calcium Phosphate (Actifuse) with Recombinant Human Bone Morphogenetic Protein-2 (Infuse) in Posterolateral Instrumented Lumbar Fusion. Global Spine Journal. 2015; 5(6): 471–478.
- Robbins MA, Haudenschild DR, Wegner AM, Klineberg EO. Stem Cells in Spinal Fusion. Global Spine Journal. 2017, Vol. 7(8) 801-810.