

BioV™ Bioactive Glass with DBM Putty



A novel implant that combines two active elements in one easy to use product to concentrate, stimulate and proliferate the formation of new bone.

BioV Bioactive Glass with DBM Putty is the only commercially available implant that harnesses the biologic properties of both demineralized allograft bone and bioactive glass into one easy to deliver option.



A GLOBAL EXTREMITY COMPANY

BioV™ Bioactive Glass with DBM Putty Monograph



When implanted into a bony defect, BioV Bioactive Glass with DBM Putty provides the components necessary for new bone growth: an osteoconductive scaffold, osteoinductive power to influence host mesenchymal cells towards osteoprogenitor lineage and the creation of an environment where bone cells can thrive¹. Autologous blood can easily be mixed into the various formulations in order to further bolster the graft with viable osteogenic and angiogenic cells as well as native growth factors.

The dual mechanism of action provided by the DBM and Bioglass components works on the principle of **concentrate**, **stimulate** and **proliferate**. The osteoinductive properties of demineralized bone increases the concentration of osteoprogenitor cells present at the site², the osteostimulative properties of bioglass stimulate the formation of mature osteoblasts³, and together they create an environment for the rapid proliferation of new bone⁴.

Key Features of BioV Bioactive Glass with DBM Putty:

- 33% demineralized cortical bone powder for osteoinductive signaling
- 33% bioactive glass for rapid graft adhesion to the defect site and acceleration of the osteogenic process³
- A porcine gelatin carrier to encapsulate the osteopromotive components into an easily

handled void filler

- carrier resists irrigation so graft stays in the surgical site
- shelf-stable at room temperature
- quickly hydrates at the time of surgery to ensure the viability of inductive proteins within the demineralized bone⁵
- Processed to achieve a sterility assurance level (SAL) of 10⁻⁶
- Each lot of DBM is tested to ensure osteoinductivity

Indications for Use:

BioV Bioactive Glass with DBM Putty is indicated to be gently placed in bony voids or gaps of the skeletal system that are not intrinsic to the stability of the bony structure (i.e., the extremities, pelvis and posterolateral spine). These defects may be surgically created osseous defects or osseous defects created from traumatic injury to the bone. BioV Bioactive Glass with DBM Putty must be used with autograft as a bone graft extender in the posterolateral spine. The product provides a bone graft that remodels into the recipient's skeletal system.

BioV Bioactive Glass with DBM Putty has a history of safe and effective clinical use. Biocompatibility and testing and in vitro bench testing was conducted to evaluate the biological safety and performance characteristics of the device formulation. The performance of BioV Bioactive Glass with DBM Putty in the extremities and posterolateral spine was evaluated in vivo.

CONCENTRATE - with the osteoinductive properties of demineralize bone

Demineralized bone is a commonly utilized bone graft substance because of its widely accepted osteoinductive properties. The demineralization process exposes the latent Bone Morphogenic Proteins (BMP's) present within allograft bone. Upon implantation, these BMP's stimulate the conversion of host mesenchymal stem cells into bone forming osteoblasts^{6,7}. The active conversion process results in an increased concentration of osteoprogenitor cells in the area of the demineralized graft.

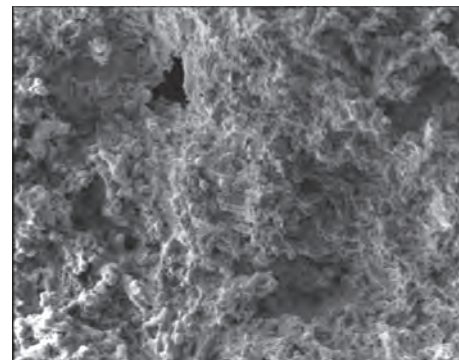


Fig 1: A 500x SEM of demin. bone powder, demonstrating powder maintains the osteoconductive surface of mineralized bone.

- Demineralization process exposes natural morphogenic proteins in the bone matrix, making them available for osteogenesis⁸.
- Allograft bone is sourced from a non-profit, AATB Certified tissue bank.
- Each lot of DBM is individually tested to ensure osteoinductive potential.

STIMULATE - with the osteo-stimulative effects of Bioactive glass

The History of Bioactive Glass

Developed over 30 years ago, Bioactive glass is the first man-made material to form a direct chemical bond with bone. It is also the first man-made material to exert a positive effect on osteoblastic differentiation and osteoblast proliferation³. Years of testing, pre-clinical and clinical work have proven the safety and efficacy of Bioglass in a clinical setting⁹. Further studies have demonstrated equivalent rates of bone growth for Bioglass particles and for autograft, and reported rapid proliferation of bone in contact with Bioglass particles¹⁰. Because of its proven clinical benefits, Bioglass-only implants are currently available under a number of different brand names. BioV Bioactive Glass with DBM Putty the only product that provides the benefits of Bioglass in conjunction with the osteoinductive properties of a demineralized bone powder.

Behavior Upon Implantation

When Bioglass is introduced to an aqueous environment such as body fluids, there is an immediate dissolution process and ion exchange with the host environment. This results in a silica-rich gel layer on the surface of each Bioglass particle and an increase of ions, specifically P and Ca, in the localized area. The silica-rich layer rapidly mineralizes into hydroxyapatite and chemically bonds to host bone. The increased concentration of P and Ca then activate gene expression in osteoprogenitor cells that give rise to

enhanced bone regeneration¹¹.

The Osteostimulative Effects of Bioglass

- *Enhanced marrow cell differentiation* - Researchers concluded that the dissolution products specific to the type of Bioglass found in Bioactive Glass with DBM Putty “provided a favorable situation for the differentiation of marrow cells to differentiate into osteoblast-like cells and a large amount of mineralized tissue formation”¹.
- *Increased concentration of critical growth factors* - Human osteoblasts showed a 290% increase in IGF-II expression when exposed to the dissolution products of Bioglass compared to control groups. IGF-II is a known inducer of osteoblast proliferation¹².
- *Greater population of osteoblasts* - In the same study as above, osteoblast cultures exposed to Bioglass dissolution products showed a 155% increase in population over those grown in the control medium¹².
- *Faster development of complex mineralization* - Osteoprogenitor cells in the presence of Bioglass showed evidence of complex bone nodule formation in as little as 6 days whereas the control group showed no such growth after 12 days. Researchers concluded that “Bioglass has the ability to stimulate the growth and osteogenic differentiation of human primary osteoblasts”².

PROLIFERATE - the synergistic effect of demineralized bone and Bioglass

- Increased Bone Formation -

Clinical work has demonstrated the synergistic effect of the combined DBM and bioglass found in BioV Bioactive Glass with DBM Putty. When compared against other commercially available DBM pastes, BioV Bioactive Glass with DBM Putty showed greater levels of new bone formation, higher concentrations of osteoblasts and an increased presence of bone marrow¹³.

- Greater proliferation of osteoblastic activity - The combination of DBM and Bioglass found within BioV Bioactive Glass with DBM Putty lead to greater bone formation by stimulating osteoblast activity. Alkaline phosphatase is a key marker that indicates levels of osteoblastic activity. Clinical work has shown that AP levels are greater when osteoblasts are exposed to BioV Bioactive Glass with DBM Putty than when exposed to either DBM or Bioglass in isolation (Fig 2)¹⁴.

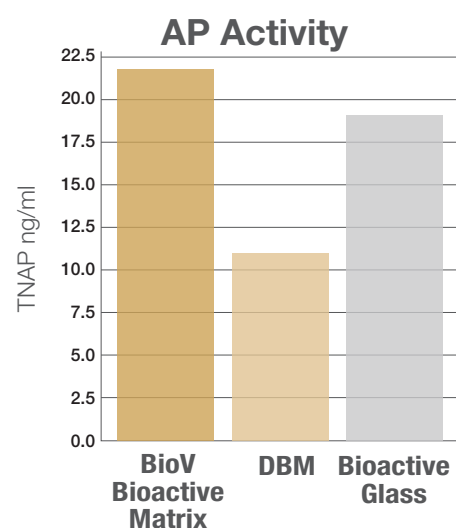


Fig 2: Graph of Alkaline - Phosphatase activity demonstrates the more robust osteoblast activity in the presence of BioV Bioactive Glass with DBM Putty

BioV™ Bioactive Glass with DBM Putty

REFERENCES

1. Bosetti M, Cannas M. The Effect of Bioactive Glasses on Bone Marrow Stromal Cells Differentiation. *Biomaterials*, 2005 (26): 3873-3879
2. Boyan BB, McMillan J, Lohman CH, Ranly DM, Schwartz Z. Bone Graft Substitutes: Basic Information for Successful Clinical Use with Special Focus on Synthetic Bone Graft Substitutes. In: Laurencin CT, editor. *Bone Graft Substitutes: ASTM*; 2003. p 231-259
3. Xynos ID, Hukkanen, MVJ et al. Bioglass 45S5 Stimulates Osteoblast Turnover and Enhances Bone Formation In Vitro: Implications and Applications for Bone Tissue Engineering. *Calcified Tissue International* (2000) 67 p 321-329
4. Kirk TJ, Ritter G et al. Radiographic and Histologic Comparison of © DBM and a Bioactive Glass in a Rabbit Spinal Fusion Model. Abstract on file at Amend Surgical
5. Han B, Yang Z, Nimni M. Effects of moisture and temperature on the osteoinductivity of demineralized bone matrix. *J Orthop Research* 2005 Jul;23(4):855-61. Epub 2005 Jan 19.
6. Khan et al. The Biology of Bone Grafting. *J Am Acad Orthop Surgery*, 2005, 13 p 77-86
7. Han et al. Quantitative and Sensitive In Vitro Assay for Osteoinductive Activity of Demineralized Bone Matrix. *J Orthop Research*, 2003, Jul:21(4): 648-54
8. Mulliken JB, Kaban LB, Glowacki J. Induced Osteogenesis-The Biological Principle and Clinical Applications. *J Surg Res*, 1984, 37(6): 487-496
9. Wheeler DL, et al. Effect of Bioactive Glass Particle Size on Osseous Regeneration of Cancellous Defects. *J Biomed Mater Res*, 1998, 41(4): p 527-33
10. Krishnan V, Lakshmi T. Bioglass: A Novel Biocompatible Innovation. *J Advan Pharm Technical Res*, 2013, Apr-Jun; 4(2): 78-83
11. Gerhardt LC, Boccaccini A, Bioactive Glass and Glass-Ceramic Scaffolds for Bone Tissue Engineering. *Materials*, 2010, (3): 3867-3910
12. Xynos I, Edgar A et al. Ionic Products of Bioactive Glass Dissolution Increase Proliferation of Human Osteoblasts and Induce Insulin-like Growth Factor II mRNA Expression and Protein Synthesis. *Biochemical and Biophysical Research Comm.*, (2000) 276: 461-465
13. NanoFuse White Paper, Data on file at Amend Surgical.
14. Kirk JF. Osteoconductivity and Osteoinductivity of NanoFuse DBM. *Cell Tissue Bank* DOI 10. 1007/s10561-012-9297-1



A GLOBAL EXTREMITY COMPANY