Products manufactured by Bone Solutions, Inc., distributed by Alliant Biotech, LLC.
www.alliantbiotech.com
2140 Oak Industrial Drive NE
Grand Rapids, MI 49505
888-307-1144

Mg BONESOLUTIONS

MAGNESIUM-BASED ORTHOPEDIC TECHNOLOGIES

DISTRIBUTOR TRAINING MANUAL

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PRODUCT OVERVIEW

The orthopedic technologies from Bone Solutions are fast-setting Magnesium-based bone substitutes that remodel into bone over time through creeping substitution.

LOW VISCOSITY | MEDIUM VISCOSITY | HIGH VISCOSITY

Ready in 30 Seconds | Moldable/ Injectable | Cohesive/ Adhesive | Drillable/ Settable | Radiopaque

COMPOSITION

Bone Solutions orthopedic products (Mg OSTEO technologies) are made from a fully synthetic, pre-measured blend of magnesium, phosphates, and a proprietary solution.

MAGNESIUM BENEFITS

Magnesium is critical for bone health and development. Approximately 60% of Magnesium in the body resides in the bones, contributing to the structural development of bone and playing a key role in the absorption and regulation of calcium. Magnesium also controls the active transport of calcium across cell membranes and deficiency can contribute to osteoporosis.

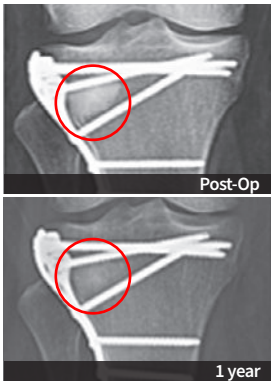
Magnesium increases proliferation of marrow stromal cells, **enhances mineralization** of the extracellular matrix and stimulates proteins for enhanced bone regeneration.[1] Additionally, it improves attachment and **growth of osteoblasts**, and initiates apatite layer formation on scaffolds, as well as **new bone formation** through the scaffold.[2]

References:

1. Yoshizawa et at. Magnesium ion stimulation of bone marrow stromal cells enhances osteogenic activity, stimulating the effect of magnesium allow degradation. Acta Biometer. 2014; 10(6): 2834-42.4
2. Wong et al. Engineered polycaprolactone-magnesium hybrid biodegradable porous scaffold for bone tissue engineering. Materials International. 2014; 24: 561-567.
3. S. Magister, J. Kolaczko, A. Sattar et al., Clinical parameters and radiographic resorption of a novel magnesium based bone void filler, Injury.
4. Lapine Posterolateral Fusion and Condyle Defect Models. Internal study. Results on file at Bone Solutions, Inc.
5. Am J Vet Res. 2009; 70 (8) 964-972. Hirvinen LJ, Litsky AS, Samii VF, Weisbrode SE, Bertone AL
6. Orthopaedic Research Society 2006; Chicago, IL. Bertone A, DeMaria M, Johnson A, Weisbrode S, Kowaleski M

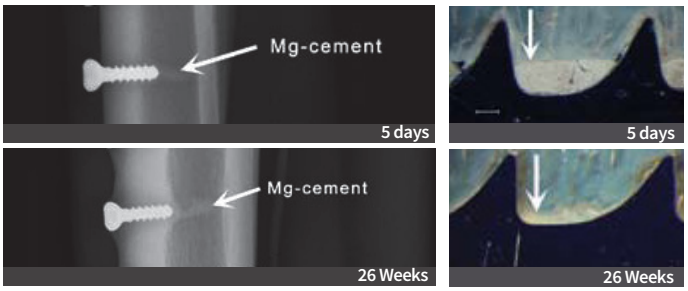
STUDY DATA

Bone Remodeling:
Study 1 - In a radiographic review of 18 patients, the average grade of resorption was 3.6 ±0.6 at 1 year. This demonstrates clinically relevant resorption, and structural support in challenging bone voids.[3]



Histology from a separate study further demonstrates bone remodeling through creeping substitution.[4]

Bone Mineral Density:
Study 2 - When compared to a calcium-based product, Mg OSTEO Technologies showed a 24% increase in bone mineral density adjacent to the screw.[5]



REGULATORY INFORMATION

Cleared by FDA 510(k)	K071004, K192674, K161568, K234013
Regulation Number	21CFR 888 3045
Classification Product Code	MQV, OIS

PACKAGING SPECIFICATIONS

Latex	Not made with natural rubber latex
Storage	Store at room temperature
Shelf Life	36 Months
Sterilization	Gamma irradiation
Sterile	Yes
Single-Use	Yes
MRI Safe	Yes
Dimensions	26cm (l) x 21cm (w) x 8cm (h)

MATERIAL SPECIFICATIONS

Setting Temperature	98°F (37° C)
Compressive Strength	36MPa at 48 hours

Biocompatibility
Mg OSTEOCRETE has been evaluated to be biologically safe to use. The materials that comprise this product have been used clinically for many years. The product has been extensively tested in *in vitro* and *in vivo* settings, and follow the requirements of EN ISO 10993-1.

INDICATIONS

Mg OSTEOCRETE is intended for bony voids or defects of the extremities, intervertebral disc space, posterolateral spine, and pelvis that are not intrinsic to the stability of the bony structure. These defects may be surgically created osseous defects or osseous defects created by traumatic injury to the bone.

Mg OSTEOCRETE can be used as an adjunct to conventional rigid hardware fixation by supporting the bone fragments during the surgical procedure only in the extremities and pelvis. Once the material has set, it acts as a temporary support medium and is not intended to provide structural support during the healing process.

Mg OSTEOCRETE is intended to be placed into bony voids either before or after final fixation. It is resorbed and replaced with bone during the healing process and must be used with morselized autograft bone at a ratio of 1:1 by volume with an intervertebral body fusion device and in the posterolateral spine. **Mg OSTEOCRETE** is not intended to treat large defects that in the surgeon's opinion would fail to heal spontaneously.

Part Number	Description
44-050-00-BSI	Mg OSTEOCRETE – Full Kit – 5cc
44-100-00-BSI	Mg OSTEOCRETE – Full Kit – 10cc
44-150-00-BSI	Mg OSTEOCRETE – Full Kit – 15cc

Kit Contents: 5cc Mg Powder, High Viscosity Solution (30-Second Putty), Medium Viscosity Solution, Mixing Syringe, Funnel, Basin, Spatula & 4.2mm Cannula/Pusher, Mechanical Advantage

Part Number	Description
44-050-00-STR	Mg OSTEOCRETE – Basic Kit – 5cc
44-100-00-STR	Mg OSTEOCRETE – Basic Kit – 10cc
44-150-00-STR	Mg OSTEOCRETE – Basic Kit – 15cc

Kit Contents: 5cc Mg Powder, High Viscosity Solution (30-Second Putty), Medium Viscosity Solution, Basin, Spatula

REGULATORY INFORMATION

Cleared by FDA 510(k)	K071004, K192674, K161568, K234013
Regulation Number	21CFR 888 3045
Classification Product Code	MQV, OIS

PACKAGING SPECIFICATIONS

Latex	Not made with natural rubber latex
Storage	Store at room temperature
Shelf Life	36 Months
Sterilization	Gamma irradiation
Sterile	Yes
Single-Use	Yes
MRI Safe	Yes
Dimensions	26cm (l) x 21cm (w) x 8cm (h)

MATERIAL SPECIFICATIONS

Setting Temperature	98°F (37° C)
Compressive Strength	36MPa at 48 hours

Biocompatibility
Mg OSTEOINJECT has been evaluated to be biologically safe to use. The materials that comprise this product have been used clinically for many years. The product has been extensively tested in *in vitro* and *in vivo* settings, and follow the requirements of EN ISO 10993-1.

INDICATIONS

Mg OSTEOINJECT is intended for bony voids or defects of the extremities, intervertebral disc space, and pelvis that are not intrinsic to the stability of the bony structure. These defects may be surgically created osseous defects or osseous defects created by traumatic injury to the bone.

Mg OSTEOINJECT can be used as an adjunct to conventional rigid hardware fixation by supporting the bone fragments during the surgical procedure only in the extremities and pelvis. Once the material has set, it acts as a temporary support medium and is not intended to provide structural support during the healing process.

Mg OSTEOINJECT is intended to be placed into bony voids either before or after final fixation. It is resorbed and replaced with bone during the healing proces and must be used with morselized autograft bone at a ratio of 1:1 by volume with an intervertebral body fusion device. **Mg OSTEOINJECT** is not intended to treat large defects that in the surgeon's opinion would fail to heal spontaneously.

Part Number	Description
44-050-00-INJ	Mg OSTEOINJECT – 5cc
44-100-00-INJ	Mg OSTEOINJECT – 10cc

Kit Contents: Mg Powder Pouch, Low Viscosity Solution, Mixing Syringe, Funnel, 4.2mm Cannula & Pusher, Mechanical Advantage

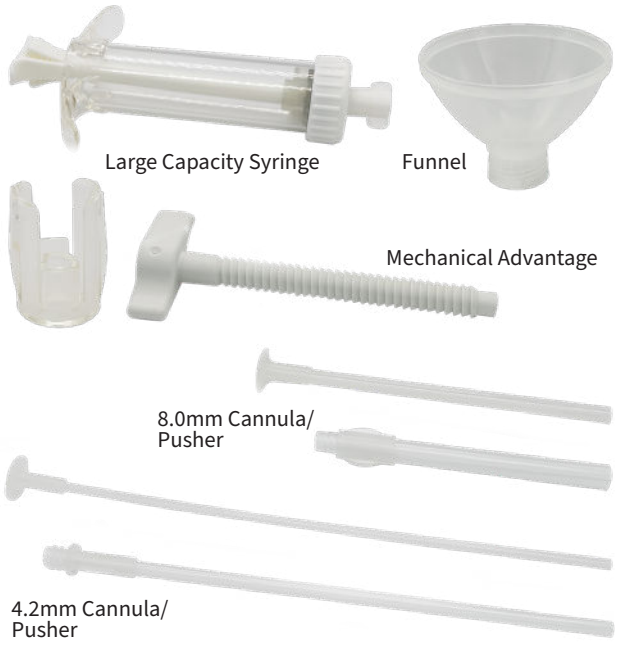
OPTIONAL DELIVERY DEVICES

This document outlines registered devices that can provide an adjunctive delivery option for surgeons desiring percutaneous targeted delivery and controlled access to bone defects, subchondral defects, lesions and cysts.

MIXING & DELIVERY SYSTEM

A delivery system that provides complete mixing of Mg OSTEOCRETE and excellent visibility for precise graft placement.

Part Number	Description
44-000-00-AUX	Mixing & Delivery System



DELIVERY CANNULA

A delivery cannula that provides complete command over placement while an ergonomic T-handle allows for easy control. The universal luer lock connector ensures an easy fit for any size delivery syringe and the radiolucency of Mg OSTEOCRETE provides excellent visibility for precise graft placement.

Part Number	Description
74174-15M	Mg OSTEOCRETE™ Bone Marrow Aspiration Needle 8 Ga
74066-01M	Mg OSTEOINJECT™ Bone Marrow Aspiration Needle 11 Ga

* Distributed by Bone Solutions

8 Ga x 150mm,
Open Tip,
End Port Delivery

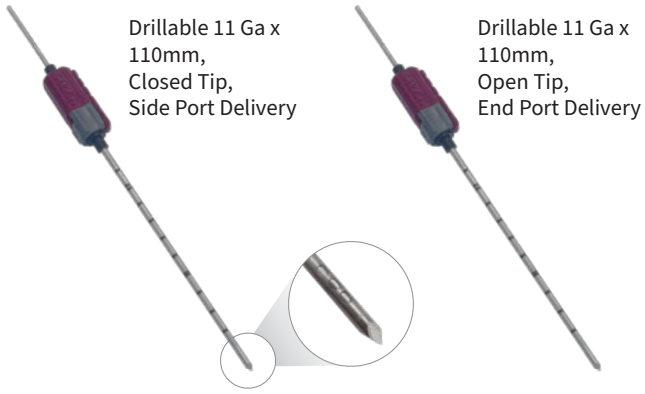
11 Ga x 110mm,
Open Tip,
End Port Delivery

DRILLABLE CANNULAS

Drillable cannulas with streamlined design for more versatile delivery options.

Part Number	Description
74358-01M	Mg OSTEOINJECT™ 11 Ga Closed Tip Drillable Delivery Cannula
74357-01M	Mg OSTEOINJECT™ 11 Ga Open Tip Drillable Delivery Cannula

* Distributed by Bone Solutions



SYRINGE PACK

Enables transport of prepared Mg OSTEOINJECT from mixing syringe to smaller injectable quantity. Consists of five 1cc syringes and two connectors that attach to the mixing syringe.

Part Number	Description
K19-00059	Mg OSTEOINJECT™ Syringe Pack

* Distributed by Bone Solutions

BEAD MAT KIT

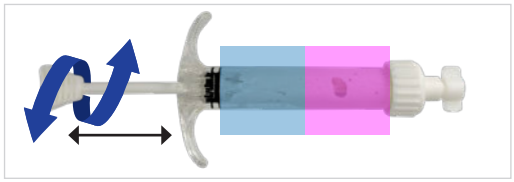
Designed for targeted of Mg OSTEOCRETE to osseous defects and for dead space management.

Part Number	Description
RM44-050	Bead Mat & Scraper

1 MIX Choose Solution: **High Viscosity** or **Medium Viscosity**

Add powder & solution to the mixing syringe Remove support rod and mix briskly with mixing rod back and forth while rotating (two cycles per second) to form a cohesive mixture.

Initially mix the material at the bottom of the syringe (toward the tip) shown in the green area above, then incorporate the remaining material in the blue area. Continue mixing the material until it is integrated into an homogenous mass.

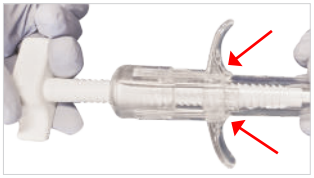


00:00-00:30

NOTE: Do not remove tip from syringe until ready to inject.

2 SPINDLE DRIVE DELIVERY

Remove support rod and snap wedge tip off from mixing stick. Attach spindle nut to base of syringe. Insert threaded spindle over mixing stick and advance spindle through nut. Remove winged cap from syringe cap and purge excess air by rotating handle clockwise.



3 REGULATE CONSISTENCY

00:30 >>> 02:00
VISCOSITY

HIGH VISCOSITY

00:30 >>> 04:00
VISCOSITY

MEDIUM VISCOSITY

NOTE: If product is not ready to be implanted or a higher viscosity is desired, a mechanical advantage will be required.

4 INJECT

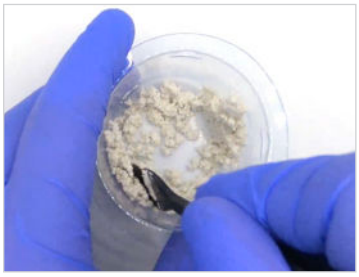
Remove tip from syringe, attach cannula and inject product into defect.

Inject +02:00

Do not touch for 2 mins to allow time for initial curing.

1 MIX

Add powder and solution to basin. Start timer. Mix briskly (two revolutions per second) to form a cohesive mixture.

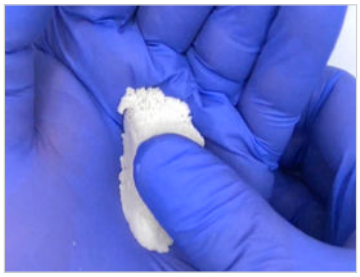


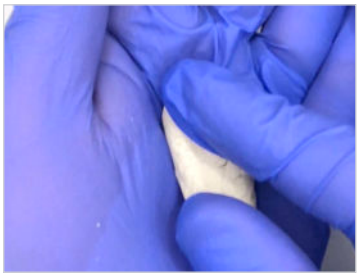
00:00-00:30

Physically work and press the material until it is integrated into a homogeneous mass.

2 REGULATE CONSISTENCY

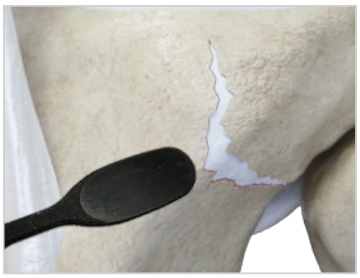
If necessary, remove product from the basin and knead by hand.





3 MOLD

Immediately place into osseous defect by hand or with spatula as desired.*



Implant +02:00

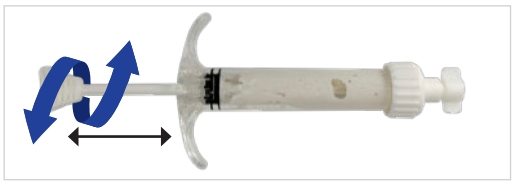
Do not touch for 2 mins to allow time for initial curing. Hardware placement and/or drilling can occur at this time.

*If immediate placement is not desired, product may be continuously manipulated and used for up to 2 minutes.

1 MIX

Add powder & solution to the mixing syringe Remove support rod and mix briskly with mixing rod back and forth while rotating (two cycles per second) to form a cohesive mixture.

Continue mixing the material until it is integrated into a homogenous mass.

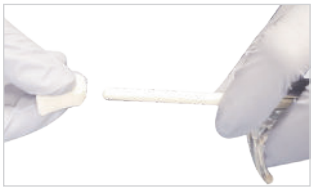


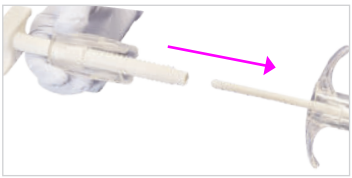
00:00-00:30

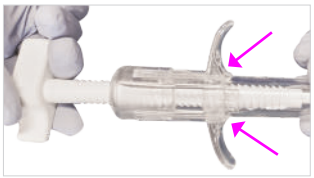
NOTE: Do not remove tip from syringe until ready to inject.

2 SPINDLE DRIVE DELIVERY

Remove support rod and snap wedge tip off from mixing stick. Attach spindle nut to base of syringe. Insert threaded spindle over mixing stick and advance spindle through nut. Remove winged cap from syringe cap and purge excess air by rotating handle clockwise.







3 REGULATE CONSISTENCY

00:30 >>> 04:00

VISCOSITY

LOW VISCOSITY

NOTE: If product is not ready to be implanted or a higher viscosity is desired, a mechanical advantage will be required.

4 INJECT

Remove tip from syringe, attach cannula and inject product into defect.

Inject +02:00

Do not touch for 2 mins to allow time for initial curing.

Mg OSTEOCRETE is fully synthetic with an ideal pH level of 7.4 ≤ pH ≥ 7.9.

Mg OSTEOCRETE Basic Kit

Contents:

- Magnesium Powder
- High Viscosity Solution (30 Second Fast-Set Putty)
- Medium Viscosity Solution
- Mixing Spatula
- Basin

Basic Kit Sizes:

- 5cc
- 10cc
- 15cc

Bead Mat Kit

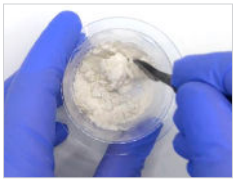
3mm Bead Mat (15cc volume per side)

Scraper

PREPARATION GUIDE

1 Mix

Add powder and High Viscosity Solution in basin. Mix briskly (two revolutions per second) to form a cohesive mixture.



Physically work and press the material until it is integrated into a homogeneous mass.

00:00-00:30

2 Transfer

Move the material from the basin onto the bead mat and use scraper to shape into beads.

Gently bend the bead mat to release the beads to be placed into contained voids.

00:30-15:00

Bone Solutions, Inc. Magnesium-Based Orthopedic Technologies

BACKGROUND

Mg OSTEO Technologies from Bone Solutions are fast-setting Magnesium-based bone substitutes that remodel into bone over time through creeping substtution. These injectable and/or moldable bone substitutes are made from a fully synthetic, pre-measured blend of magnesium, phosphates, and a proprietary solution, optimized for trauma, extremity, revision, sports medicine, intervertebral body fusions, and posterolateral spine surgery.

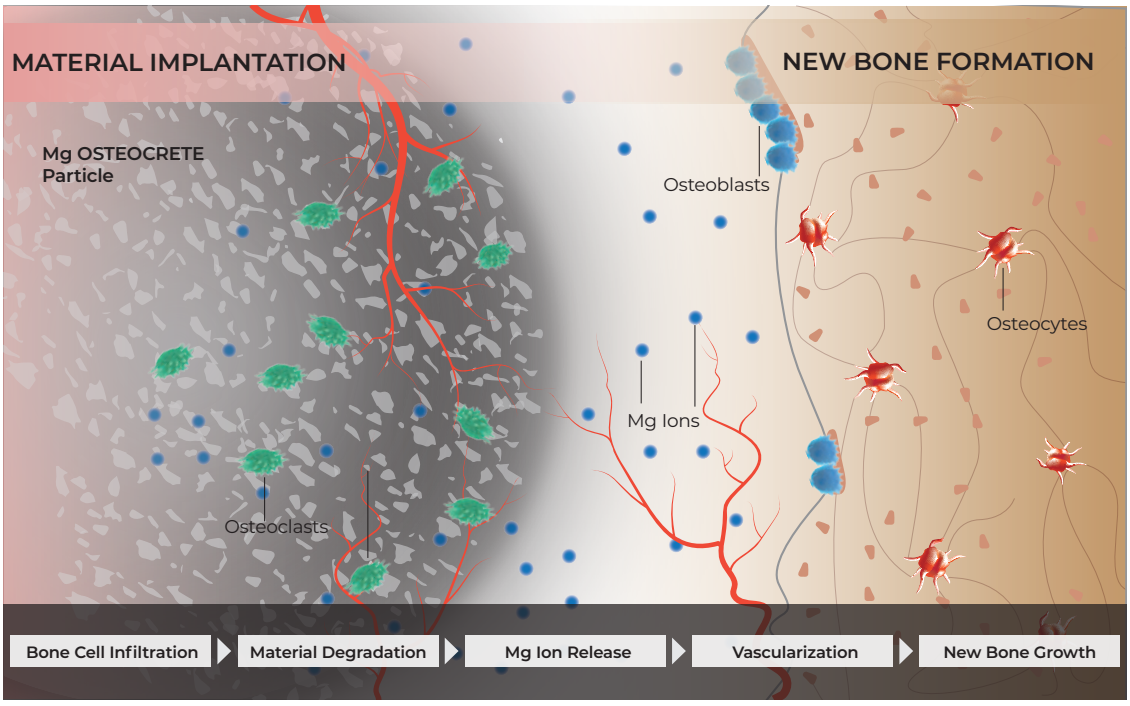
BONE REMODELING PROCESS

Mg OSTEO Technologies are bone subsitutes composed of a magnesium/potassium phosphate synthetic derived from an acid/base crystallization reaction from magnesium oxide (MgO) and blend of phosphates. The MgO component serves as a binder with adhesive/cohesive properties while the phosphates promote osteoconductivity. This union allows the Mg OSTEO Material to set/cure in situ without migration.

The material degradation process starts immediately upon the curing of the Mg OSTEO Material *in vivo* and continues through bone remodeling via the hydrolysis dissolution process. Over time, the material will become less dense with less mineral content, as the product is remodeled through bone integration via creeping substitution and resulting in optimal bone formation.[1-4]

The competitive distinction of Mg OSTEO Technologies is their inclusion of magnesium which directly impacts bone regeneration through established cellular signaling pathways.[1] The effects of which are increased proliferation of mesenchymal stem cells, promotion of osteogenic differentiation, stimulation of osteoblast activity, and advancement of mineralization. Cellular attachment and proliferation are also enhanced, elevating the rate and effectiveness of osteogenesis. Thus, the material resorbs at a higher rate, improving bone regeneration and resulting in more mineralized bone formation.[5-8] This represents a more clinically significant resorption profile as compared to competitive materials, and more closely mimics the host bone's ability to synthesize and remodel bone during healing.[9]

The chemical reaction mechanism of Mg OSTEO Technologies may be simplified and balanced to the following: KH_2PO_4 + excess MgO + $5H_2O \rightarrow MgKPO_4*6H_2O$ + MgO.



RESEARCH FINDINGS

Mg OSTEO Technologies actively partake in the process of osseous remodeling/regeneration due to magnesium ion elution. Competitive calcium phosphate cements are purely osteoconductive unless they contain DBM. Magnesium ions are directly involved with osseous signaling pathways with proven enhancement of every phase of osseous remodeling/regeneration. Mg OSTEO Technologies are the only FDA cleared resorbable cements with a unique formulation built on magnesium phosphate crystallization. Most competitive cements rely on the formation of calcium phosphate scaffolds. Every known scientific study comparing a magnesium phosphate to a calcium phosphate bone void filler has shown improved/quicker bone remodeling for the magnesium phosphate product, as described summarized in the findings below.

Increased Proliferation of bMSCs

Data from a study using tissue-engineered bone with calcium-magnesium phosphate cement (CPMC) and bone marrow stromal cells (bMSCs) in rabbits suggested that CPMC possesses moderate biodegradability and excellent osteoconductivity. The bMSCs in the magnesium-based groups proliferated more quickly than the strictly calcium-based groups, and the osteogenic differentiation of bMSCs was significantly enhanced.[6]

Improved Attachment and Growth of Osteoblasts

An in vitro study using a rabbit bone void model demonstrated enhanced attachment and proliferation of MG_{63} osteoblast-like cells on calcium magnesium phosphate cement (CPMC), in comparison with calcium phosphate cement (CPC) and magnesium phosphate cement (MPC), along with increased cellular alkaline phosphatase activity. When comparing these three formulations, CMPC resulted in increased new bone formation and mineralization compared to that with CPC and MPC, and was further enhanced with the addition of bMSCs.[8]

Stimulation of Proteins Involved in Bone Regeneration

An in vitro study found that increased $MgSO_4$ (magnesium sulfate) enhanced protein expression of collagen type X (COL10A1), vascular endothelial growth factor (VEGF), hypoxia-inducible factor (HIF)-1a, HIF-2a and peroxisome proliferator-activated receptor gamma coactivator (PGC)-1a in the human bone marrow stromal cells. COL10A1 is abundant in fractured bone at early stages of healing and VEGF is a major angiogenic signaling protein.[2]

Enhanced New Bone Formation

Histological and macroscopic findings from an in vivo rabbit study confirmed that calcium-magnesium phosphate cement (CMPC) implants exhibited high efficiency of bone regeneration and were bioactive to the host bone. It is suggested that CMPC1 presents not only good biocompatibility and biodegradability, but also faster and more effective osteogenesis at the defect area.[7]

Advanced Bone Mineralization

In a rat study comparing a polycaprolactone (PCL) scaffold with and without magnesium microparticles, particles modified with Mg significantly convinced the attachment and growth of osteoblasts as compared with the pure PCL scaffold. In addition, the hybrid scaffold was able to attract the formation of apatite layer over its surface after seven days of immersion in normal culture medium, whereas it was not observed on the pure PCL scaffold. This in vitro result indicated the enhanced bioactivity of the modified scaffold. Moreover, enhanced bone forming ability was also observed in the rat model after three months of implantation.[4]

EQUINE AND LAPINE DEFECT STUDIES

Mg OSTEO Material has demonstrated a significant increase in peak torque-to-failure of stainless-steel cortical bone screw fixation when compared with screw fixation without augmentation and screw fixation with calcium phosphate augmentation using an in vivo equine model. Additionally, Mg OSTEO Material (CPMC) resulted in an interface toughness that was significantly increased compared to that with no treatment, CPC augmentation, and polymethylmethacrylate (PMMA) augmentation. At six months after implantation, woven bone had replaced 69% of the Mg OSTEO Material at the screw interface, compared to 44% of that with CPC.

An equine study examined the effects of CPMC on bone stability and healing using a metatarsal osteotomy model; the study reported significantly improved radiographic callus formation and a greater amount of new bone formation within the fracture gap when compared to that with CPC augmentation or no augmentation. CPMC also secured the fragment significantly better than the CPC and control groups based on a decreased fracture gap over time.

Another study using a preclinical anterior cruciate ligament (ACL) reconstruction model reported that CPMC resulted in significantly better new bone formation in the tibial tunnel, a smaller amount of fibrous tissue, more cartilage formation at the tendon-bone interface, and a higher ultimate load-to-failure compared to that with standard ACL reconstruction in the contralateral limb after six weeks. CPMC and PMMA were evaluated in terms of biomechanical fixation of a stemless humeral prosthesis, with data showing that both groups have higher failure loads, failure displacements, and failure cycles when compared to those with the control, nonaugmented group.

An additional preclinical model evaluated cranial bone flap augmentation with two resorbable cements and highlighted faster cement resorption and replacement with bone, along with superior stability within the CPMC group compared to that with CPC.[18] In a preclinical bone void study conducted for obtaining FDA 510(k) clearance, CPMC resulted in 83% greater resorption than CPC after 12 weeks and 35% greater resorption at 26 weeks, with 84% of CPMC being resorbed and replaced with woven or lamellar mineralized bone of normal morphology at the 26-week time point.

These data indicate that CMPCs, such as Mg OSTEO Material, appear to have potential benefits for augmenting the healing of bone implants and bone soft tissue. These hypotheses led to another study to assess the safety and efficacy of CPMCs in anchor augmentation and tendon fixation in rotator cuff repair and bicep tenodesis procedures, respectively. This study concluded that Mg OSTEO Material had the potential for safely providing improved suture anchor and tissue fixation in patients with poor bone or tissue quality.[15]

A COMPARISON OF MG OSTEO MATERIAL TO CALCIUM PHOSPHATE AND PMMA

The data supporting the importance of magnesium and the benefit of a magnesium phosphate resorbable cement is compelling. Independent biomechanical and pre-clinical studies were performed at renowned institutions comparing Mg OSTEO Material to calcium phosphate-based resorbable cements. These studies highlight the same features previously discussed and provide further insight into additional properties that are beneficial to bone cements.

DATA SUPPORTING SUPERIOR STABILITY OF Mg OSTEO MATERIAL[11, 12, 16]		
	VS. CALCIUM PHOSPHATE	VS. PMMA
PEAK TORQUE TO FAILURE	43% INCREASE	21% INCREASE
EXTRACTION TORQUE	58% GREATER	27% GREATER
FAILURE LOAD	N/A	28% GREATER
FAILURE CYCLES	N/A	35% MORE

Stability

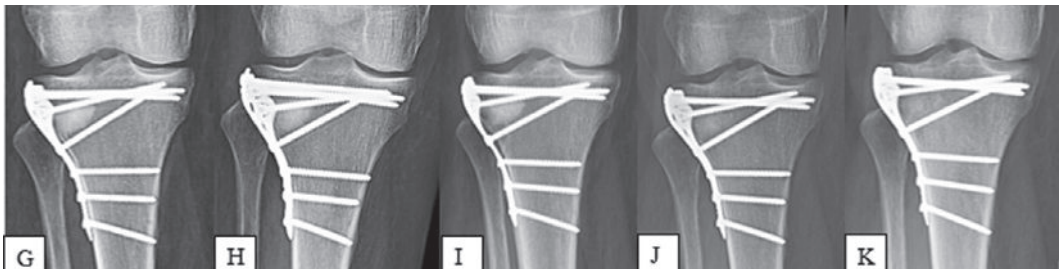
The data above from three independent studies demonstrated the stability of Mg OSTEO Material.

- Use of Mg OSTEO Material increased the peak torque to failure at bone-implant interfaces and increased interface toughness
- Mg OSTEO Material diffused into surrounding bone and provided a tight bond at the screw interface

Resorption

In a preclinical bone void study conducted for obtaining FDA 510(k) clearance, Mg OSTEO Material resulted in 83% greater resorption than calcium phosphate cement (CPC) after 12 weeks and 35% greater resorption at 26 weeks, with 84% of Mg OSTEO Material being resorbed and replaced with woven or lamellar mineralized bone of normal morphology at the 26-week time point.[15]

In a retrospective study of 42 patients, the average resorption grade of all of the patients at 1 year was nearly 4.0 (75-100% resorption) with a steady increase at each time point evaluated, indicating an optimal rate of Mg OSTEO Material resorption and corresponding bone growth.[17] Representative radiographic evaluation shown below further demonstrates these findings.



Healing

In an equine study, Mg OSTEO Material was shown to secure fragments significantly closer to parent bone compared with calcium phosphate cement. Results further demonstrated the following in Mg OSTEO Material when compared to calcium phosphate:

- 20% reduction in fracture gap distance at 7 weeks
- More than 4x more bone callus formation
- 88% increased callus area[10]

Adhesion

Additional biomechanical studies proved how the adhesive quality of Mg OSTEOCRETE will yield a statistically stronger bone over calcium phosphate when used between two adjacent osseous structures. Mg OSTEOCRETE showed significantly greater adhesive properties than calcium phosphate - 2.4x tensile load to failure.[13-14]

CONCLUSIONS

The data supporting the importance of magnesium and the benefit of a magnesium phosphate resorbable cement is compelling. Independent biomechanical and pre-clinical studies were performed at renowned institutions comparing Mg OSTEO Material to calcium phosphate-based resorbable cements. These studies highlight the same features previously discussed and provide further insight into additional properties that are beneficial to bone cements.

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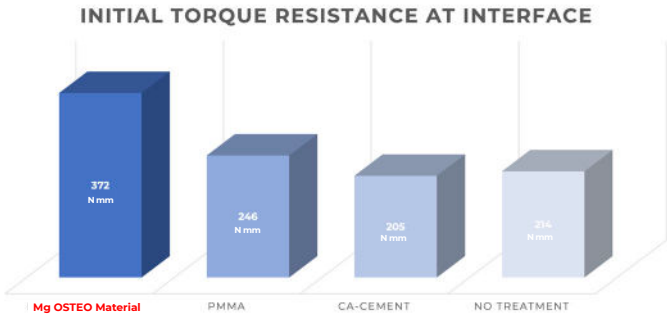
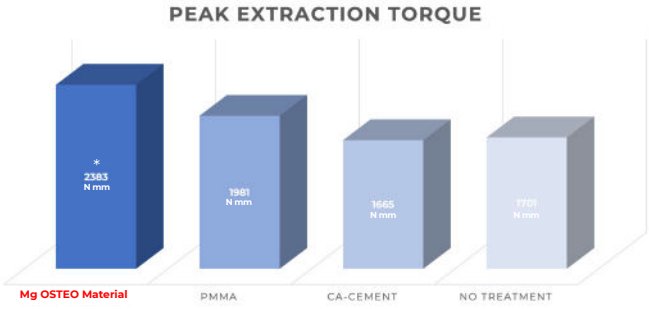
COMPARATIVE MATERIAL STUDIES

Testing data is reflective of all Magnesium-Based technologies from Bone Solutions, Inc and is referred to in this report as **Mg OSTEO Material**.

Mg OSTEO Material required **up to 81%** greater initial force to break the bone screw interface as compared to Ca-Cement, PMMA and no treatment at 5 days.[1]

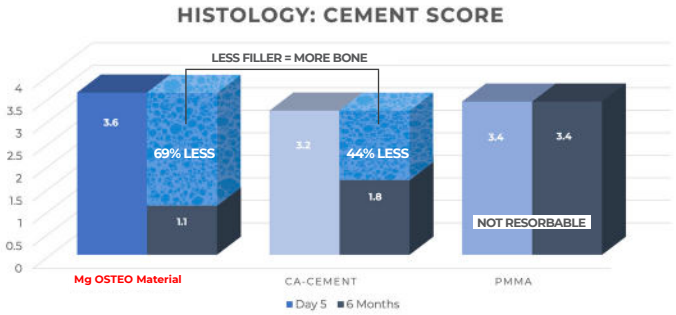


Mg OSTEO Material required **up to 43%** greater force to completely remove the bone screw as compared to Ca-Cement, PMMA and no treatment at 5 days.[1]

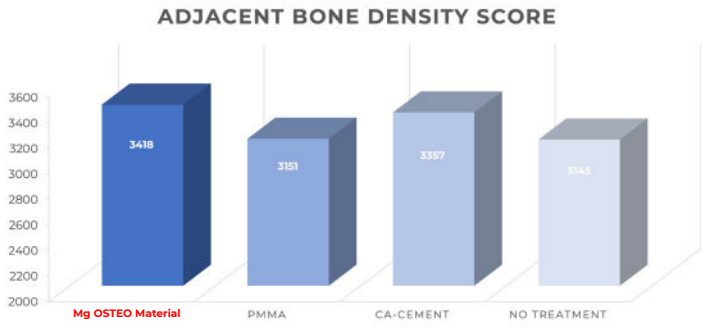


* Statistically significant

Histology results showed that **Mg OSTEO Material** was resorbed and replaced with remodeled bone; there was **69% less Mg OSTEO Material** at the bone-implant interface at 6 months vs 5 days post op, significantly less than Ca-Cement and PMMA.[1]



In the remodeled bone adjacent to the screw, **Mg OSTEO Material** increased mineral density **up to 9%** compared to Ca-Cement, PMMA and no treatment[1] at 6 months.



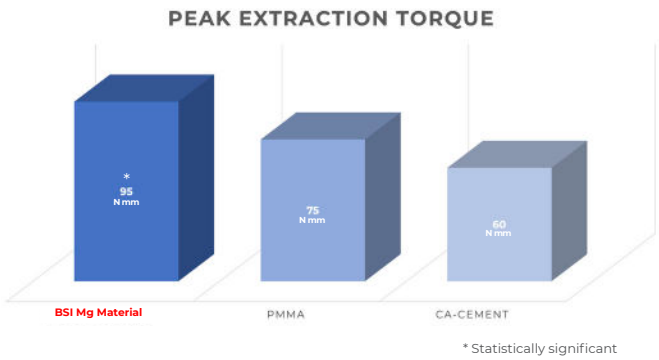
1 Influence of bone cements on bone-screw interfaces in the third metacarpal and third metatarsal bones of horses. Am J Vet Res. 2009;70(8):964-972. Hirvinen LJ, Litsky AS, Samii VF, Weisbrode SE, Bertone AL.

COMPARATIVE MATERIAL STUDIES

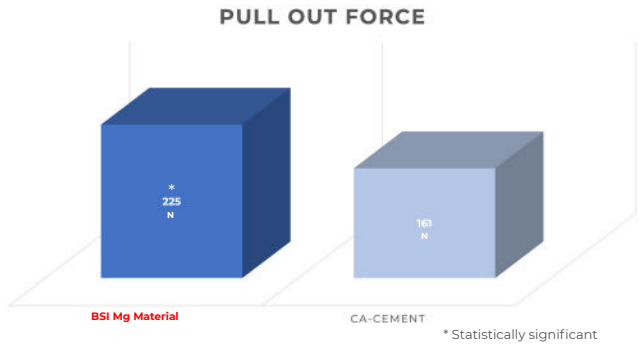
Mg OSTEO Material demonstrated superior stability, adhesion, resorbability, and healing compared to Ca-Cement and PMMA.[2]

	BSI Mg Material	PMMA	Ca-Cement
Greater Extraction Torque	✓	✓	
Diffused into Surrounding Bone	✓	✓	✓
Tight Bond at Screw Interface	✓	✓	
Resorbable	✓		✓

Mg OSTEO Material demonstrated **up to 58%** greater extraction torque at 4 days compared to Ca-Cement, PMMA and no treatment.[2]



Mg OSTEO Material improved anchoring fixation **by an average of 50%** fifteen minutes post injection, and by **99% in poor-quality bone**, compared to Ca-Cement.[3]



2 Degradable magnesium based cement adheres stainless steel screws into bone. Orthopaedic Research Society; 2006; Chicago, IL. Bertone A, DeMaria M, Johnson A, Weisbrode S, Kowaleski M.

3 Use of a Novel Magnesium-Based Resorbable Bone Cement for Augmenting Anchor and Tendon Fixation. Am J Orthop (Belle Mead NJ). 2018;47(2). Roller BL, Kuroki K, Bozynski CC, Pfeiffer FM, Cook JL.

Lapine Posterolateral Fusion Model
A Study of Remodeling Characteristics

Summary

Mg OSTEOCRETE is a combination of monopotassium phosphate, magnesium oxide, tricalcium phosphate, C/12J/22O/11 mixed with a modified saline that is osteoconductive and biodegradable. The patented, proprietary formula includes critical components to maximize the process of bone health and development.

Objectives

The objective of this study is to evaluate the performance of Mg OSTEOCRETE when combined with autograft (50:50) in a rabbit posterolateral spine fusion model. The test groups, Mg OSTEOCRETE and Mastergraft® Putty (Medtronic) were evaluated for spine fusion rate, new bone formation, graft remodeling and inflammatory response using radiographic, microCT, biomechanical and histological endpoints at 4, 8 and 12 weeks following implantation.

Methods

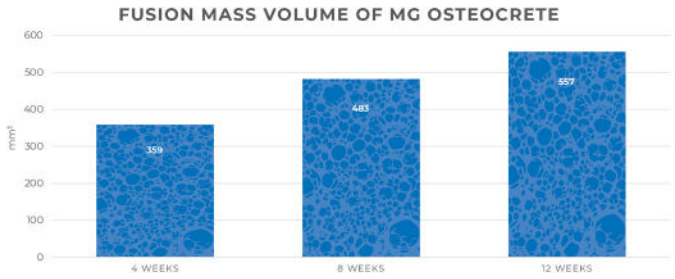
Gross examination of each grafted level demonstrated a normal tissue response to posterolateral grafting in this rabbit model.

Radiographic scoring of the fusion sites indicated a normal healing response in all test groups, with no adverse reactions and similar progressions of new bone formation observed over time.

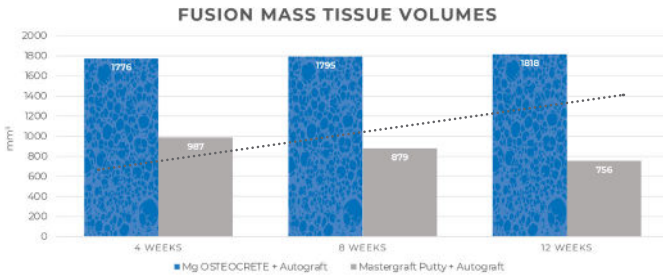
Spine fusion was assessed by manual palpation and micro-CT analysis of the treated motion segments. **Mg OSTEOCRETE demonstrated fusion in as little as 8 weeks.**

* All claims based on Lapine Posterolateral Fusion and Condyle Defect Models. It is unknown how results from the rabbit models compare with clinical results in humans.

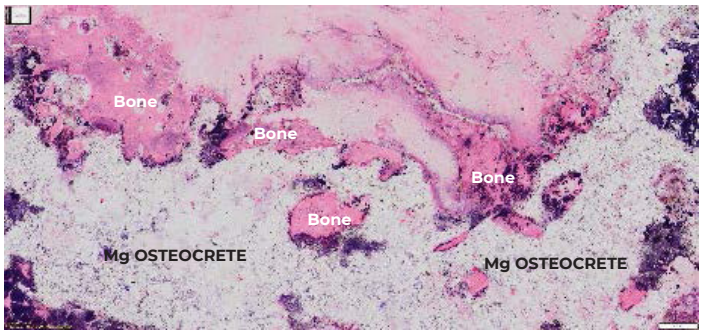
Conclusions



Mg OSTEOCRETE + Autograft fusion mass (total implant volume) maintained its size during the remodeling period whereas the fusion mass of Mastergraft + Autograft decreased over time.



Mg OSTEOCRETE continued to remodel at each time point, providing stability during the crucial healing period.



Based on histomorphometry measurements at 12 weeks, Mg OSTEOCRETE remodeled at a rate of approximately 10% after each 4-week time period. This rate corresponds to approximately 65% remodeling at 26 weeks and complete remodeling by 36-40 weeks.

Mg OSTEOCRETE™

STERILE IMPLANT KIT - Single Use Only

CAUTION: Federal (USA) LAW RESTRICTS THIS DEVICE TO SALE BY OR ON THE ORDER OF A PHYSICIAN.

IMPORTANT INFORMATION FOR PHYSICIANS, SURGEONS, AND/OR STAFF

DESCRIPTION
Mg OSTEOCRETE™ is a magnesium-based synthetic bone graft substitute that is moldable/injectable, drillable/settable, adhesive/cohesive, radiopaque, osteoconductive, remodels into bone over time through creeping substitution.

The Mg OSTEOCRETE™ Packet contains powder (Magnesium based compound) and a mixing solution (modified saline). The device is sterile, single use only.

Mg OSTEOCRETE™ is indicated as a bone graft substitute (used alone) to fill bone voids or defects of the extremities or pelvis; these defects may be traumatic or surgically created (including but not limited to: surgical excision of bony lesions, cysts, fibromas, or tumors; core decompression for avascular necrosis/osteonecrosis; excision and grafting of osteochondritis dissecans lesions).

Mg OSTEOCRETE™ is indicated as a bone graft extender used with autograft bone in the posterolateral spine and with an intervertebral body fusion device cleared by FDA for use with a bone void filler.

INDICATIONS FOR USE
Mg OSTEOCRETE™ is intended for bony voids or defects of the extremities, posterolateral spine, intervertebral disc space, and pelvis that are not intrinsic to the stability of the bony structure. These osseous defects may be the result of benign bone cysts and tumors (in adults), may be surgically created osseous defects or osseous defects created by traumatic injury to the bone.

Mg OSTEOCRETE™ can be used as an adjunct to conventional rigid hardware fixation by supporting the bone fragments during the surgical procedure only in the extremities and pelvis. Once the material has set, it acts as a temporary support medium and is not intended to provide structural support during the healing process. Mg OSTEOCRETE™ is intended to be placed into bony voids either before or after final fixation. Mg OSTEOCRETE™ is resorbed and replaced with bone during the healing process. Mg OSTEOCRETE™ must be used with morselized autograft bone at a ratio of 1:1 by volume in the posterolateral spine. When used in intervertebral body fusion procedures Mg OSTEOCRETE™ must be used with morselized autograft bone at a ratio of 1:1 by volume with an intervertebral body fusion device cleared by FDA for use with a bone void filler. Mg OSTEOCRETE™ is not intended to treat large defects that in the surgeon's opinion would fail to heal spontaneously.

CONTRAINDICATIONS
Mg OSTEOCRETE™ is not intended to provide structural support during the healing process. Mg OSTEOCRETE™ is contraindicated where the device is intended as structural support in the skeletal system. Mg OSTEOCRETE™ is contraindicated for vertebroplasty or kyphoplasty, or pedicle screw augmentation.Conditions representing relative contraindications include:

Severe neurological or vascular disease
Uncontrolled diabetes
Hypercalcemia
Pregnancy
Where stabilization of fracture is not possible
Segmental defects without supplemental fixation
Where there is significant vascular impairment proximal to the graft site
When there are systemic and/or metabolic disorders that affect the bone or wound healing
Any patient unwilling or unable to follow postoperative instructions.

WARNINGS
1. Remove any excess Mg OSTEOCRETE™ prior to closure.
2. When used for filling defects of the extremities and pelvis, do not mix the product with any other substance.
3. When used in the posterolateral spine, the product must be used with morselized autograft bone at a ratio of 1:1 by volume.
4. Highly pressurized application of the product into confined space with ready venous or arterial access is not recommended.
5. Do not use the product in infected sites.
6. Do not disturb placement site once the product begins to harden.
7. Do not overfill the defect area.
8. Do not reuse. The product is single use only.

MRI Safety Information
Mg OSTEOCRETE™ is MR Safe.

PRECAUTIONS
The long-term effects of extraosseous or intra-articular use of the product (material injected into the joint space) are unknown.
Arthritis may be a possible complication of intra-articular use of the product.
The safety and effectiveness of the product has not been established in:
- Traumatic open injuries which are predisposed to infection.
- Patients with compromised health (e.g. metabolic, vascular, or severe neurological disease, infection, immunologic deficiencies).
- Patients who are skeletally immature.
- Pregnant or nursing women.
- Patients undergoing concurrent radiotherapy or chemotherapy treatment.
- Patients with renal impairment.

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- Skin Exposure: Wash area with soap and water
- Eye Exposure: Flush thoroughly with running water

ADVERSE EVENTS
The following adverse events can occur with the use of bone void fillers:

Revisions and/or removals
Superficial wound or deep wound infection
Pain/discomfort, swelling, redness, fever, inflammation
Fluid accumulation, wound dehiscence, drainage
Debridement/irrigation
Delayed or nonunion, lack of osseointegration, impaired healing, inadequate bone formation
Material fracture, altered handling characteristics leading to failure
Protrusion, dislodgement, migration, or extravasation (leakage)
Decreased range of motion, loss of motor function, sensory deficit
Allergic/immune response
Blood pressure change
Hematoma
Cyst
Death

STERILIZATION
This device is provided sterile (gamma radiation). Contents are STERILE unless the barrier packaging is open or damaged; DO NOT USE if the package is open or damaged.

STORAGE CONDITIONS
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Mg OSTEOINJECT™

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Mg OSTEOINJECT™ is indicated as a bone graft substitute (used alone) to fill bone voids or defects of the extremities or pelvis; these defects may be the result of benign bone cysts and tumors (in adults), may be osseous defects created by traumatic injury to the bone related to weakening of the bone with resultant osseous injury as seen with insufficiency fractures, subchondral cystic changes related to osteoarthritis, or due to surgically created osseous defects (including but not limited to: surgical excision of bony lesions or cysts, core decompression for osteonecrosis, excision and grafting of unstable bone fragments).

INDICATIONS FOR USE

Mg OSTEOINJECT™ is intended for bony voids or defects of the extremities and pelvis that are not intrinsic to the stability of the bony structure. These osseous defects may be the result of benign bone cysts and tumors (in adults), may be surgically created osseous defects or osseous defects created by traumatic injury to the bone.

Mg OSTEOINJECT™ can be used as an adjunct to conventional rigid hardware fixation by supporting the bone fragments during the surgical procedure only in the extremities and pelvis. Once the material has set, it acts as a temporary support medium and is not intended to provide structural support during the healing process. Mg OSTEOINJECT™ is intended to be placed into bony voids either before or after final fixation. Mg OSTEOINJECT™ is resorbed and replaced with bone during the healing process.
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Any patient unwilling or unable to follow postoperative instructions.

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STERILE IMPLANT KIT - Single Use Only

CAUTION: Federal (USA) LAW RESTRICTS THIS DEVICE TO SALE BY OR ON THE ORDER OF A PHYSICIAN.

IMPORTANT INFORMATION FOR PHYSICIANS, SURGEONS, AND/OR STAFF

DESCRIPTION
Mg OSTEOREVIVE™ is a magnesium-based synthetic bone graft substitute that is moldable/injectable, drillable/settable, adhesive/cohesive, radiopaque, osteoconductive, remodels into bone over time through creeping substitution.

The Mg OSTEOREVIVE™ Packet contains powder (Magnesium based compound) and a mixing solution (modified saline). The device is sterile, single use only.

Mg OSTEOREVIVE™ is indicated as a bone graft substitute (used alone) to fill bone voids or defects of the extremities or pelvis; these defects may be traumatic or surgically created (including but not limited to: surgical excision of bony lesions, cysts, fibromas, or tumors; core decompression for avascular necrosis/osteonecrosis; excision and grafting of osteochondritis dissecans lesions).

Mg OSTEOREVIVE™ is indicated as a bone graft extender used with autograft bone in the posterolateral spine and with an intervertebral body fusion device cleared by FDA for use with a bone void filler.

INDICATIONS FOR USE
Mg OSTEOREVIVE™ is intended for bony voids or defects of the extremities and pelvis that are not intrinsic to the stability of the bony structure. These osseous defects may be the result of benign bone cysts and tumors (in adults), may be surgically created osseous defects or osseous defects created by traumatic injury to the bone.

Mg OSTEOREVIVE™ can be used as an adjunct to conventional rigid hardware fixation by supporting the bone fragments during the surgical procedure only in the extremities and pelvis. Once the material has set, it acts as a temporary support medium and is not intended to provide structural support during the healing process. Mg OSTEOREVIVE™ is intended to be placed into bony voids either before or after final fixation. Mg OSTEOREVIVE™ is resorbed and replaced with bone during the healing process. Mg OSTEOREVIVE™ must be used with morselized autograft bone at a ratio of 1:1 by volume in the posterolateral spine. When used in intervertebral body fusion procedures Mg OSTEOREVIVE™ must be used with morselized autograft bone at a ratio of 1:1 by volume with an intervertebral body fusion device cleared by FDA for use with a bone void filler. Mg OSTEOREVIVE™ is not intended to treat large defects that in the surgeon's opinion would fail to heal spontaneously.

CONTRAINDICATIONS
Mg OSTEOREVIVE™ is not intended to provide structural support during the healing process. Mg OSTEOREVIVE™ is contraindicated where the device is intended as structural support in the skeletal system. Mg OSTEOREVIVE™ is contraindicated for vertebroplasty or kyphoplasty, or pedicle screw augmentation.Conditions representing relative contraindications include:

Severe neurological or vascular disease
Uncontrolled diabetes
Hypercalcemia
Pregnancy
Where stabilization of fracture is not possible
Segmental defects without supplemental fixation
Where there is significant vascular impairment proximal to the graft site
When there are systemic and/or metabolic disorders that affect the bone or wound healing
Any patient unwilling or unable to follow postoperative instructions.

WARNINGS
1. Remove any excess Mg OSTEOREVIVE™ prior to closure.
2. When used for filling defects of the extremities and pelvis, do not mix the product with any other substance.
3. When used in the posterolateral spine, the product must be used with morselized autograft bone at a ratio of 1:1 by volume.
4. Highly pressurized application of the product into confined space with ready venous or arterial access is not recommended.
5. Do not use the product in infected sites.
6. Do not disturb placement site once the product begins to harden.
7. Do not overfill the defect area.
8. Do not reuse. The product is single use only.

MRI Safety Information
Mg OSTEOREVIVE™ is MR Safe.

PRECAUTIONS
The long-term effects of extraosseous or intra-articular use of the product (material injected into the joint space) are unknown.
Arthritis may be a possible complication of intra-articular use of the product.
The safety and effectiveness of the product has not been established in:
- Traumatic open injuries which are predisposed to infection.
- Patients with compromised health (e.g. metabolic, vascular, or severe neurological disease, infection, immunologic deficiencies).
- Patients who are skeletally immature.
- Pregnant or nursing women.
- Patients undergoing concurrent radiotherapy or chemotherapy treatment.
- Patients with renal impairment.

All users should become familiar with the product mixing instructions prior to use.
- The product powder and liquid should be stored at room temperature.
- The product powder and liquid should be equilibrated to 18-23°C/65-73°F prior to mixing for optional results.
- The safety and effectiveness of the product in contact with adjacent allograft, acrylic, silicone, or polymer materials has not been established.
- Do not over-pressurize the device because this may lead to extrusion of the device beyond the site of its intended application and damage to the surrounding tissue.
- Do not over-pressurize the defect site since this may lead to fat embolization or embolization of the device material into the bloodstream.
- Skin Exposure: Wash area with soap and water
- Eye Exposure: Flush thoroughly with running water

ADVERSE EVENTS
The following adverse events can occur with the use of bone void fillers:

Revisions and/or removals
Superficial wound or deep wound infection
Pain/discomfort, swelling, redness, fever, inflammation
Fluid accumulation, wound dehiscence, drainage
Debridement/irrigation
Delayed or nonunion, lack of osseointegration, impaired healing, inadequate bone formation
Material fracture, altered handling characteristics leading to failure
Protrusion, dislodgement, migration, or extravasation (leakage)
Decreased range of motion, loss of motor function, sensory deficit
Allergic/immune response
Blood pressure change
Hematoma
Cyst
Death

STERILIZATION
This device is provided sterile (gamma radiation). Contents are STERILE unless the barrier packaging is open or damaged; DO NOT USE if the package is open or damaged.

STORAGE CONDITIONS
Sterile devices must be stored in the original unopened packaging and should not be used after the expiration date.

MIXING INSTRUCTIONS
Refer to the Mixing Usage Guide for Mixing, Delivery and Setting times.

MIXING AND DELIVERY SYSTEM

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DESCRIPTION
The Mixing and Delivery System is used to mix graft material such that it can be delivered to the patient. The system is comprised of the mixing/delivery syringe and auxiliary components including a threaded spindle with nut, pusher, cannulae and bead mat which provide alternative methods of delivery for the mixed material.

MATERIALS
The Mixing and Delivery System components are manufactured from medical grade polymers including polyamide (PA), polypropylene (PP), Polybutylene terephthalate (PBT) and Medical Grade Silicone (DC QP1-250)

INDICATIONS
The Mixing and Delivery System is intended to be used for the delivery of hydrated allograft, autograft, or synthetic bone graft material to an orthopedic surgical site.

PRECAUTIONS

Surgeons are advised to review the product specific surgical technique prior to performing any surgery.

General use instructions are below.

Contact your Bone Solutions representative for an onsite demonstration.

WARNINGS

1. Prior to use, thoroughly read these instructions for use. Follow the instructions outlined in this document for successful mixing of the graft material.
2. Before use, inspect the instrument carefully for damage, wear and / or non-functioning parts.
3. Keep the instructions for use accessible to all staff.
4. Never use or process damaged or defective devices. Contact your local sales representative or Bone Solutions for a replacement.
5. DO NOT RESTERILIZE: The Mixing & Delivery System is intended for single use only.
6. DO NOT REUSE: The Mixing & Delivery System is intended to be used for mixing one time only - to only mix one mixture of materials. Repeated use could result in device failure and/or contamination of graft materials from previous use debris.
7. Only mix with the specified volumes of materials as directed by the IFU of the graft materials.
8. DO NOT OVERFILL: Do not overfill mixing syringe with materials. Overfilling syringe could result in device failure and/or ineffective mixing of the graft material.
9. If the Mixing & Delivery System does not function correctly as outlined in the instructions of this document, DO NOT USE. Discard the Mixing & Delivery System and graft materials contained in it.
10. The use of a surgical instrument for tasks other than those for which they are intended may result in damaged or broken instruments or patient injury.
11. Make sure the product is only used by qualified or trained staff.
12. Follow the general guidelines and aseptic principles when handling sterile items.

CONTRAINDICATIONS
Contraindications include, but are not limited to:

1. Blood supply limitations and previous infections, which may retard healing.
2. Any active infection or blood supply limitations.
3. Do not use for kyphoplasty or vertebroplasty procedures.

STERILIZATION
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STORAGE CONDITIONS
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MIXING & DELIVERY INSTRUCTIONS
Refer to the Mixing Usage Guide for Mixing, Delivery and Setting times.

SYMBOLS GLOSSARY

Symbol	Reference Number	Title of Symbol	Description of Symbol per Standard
	5.1.1	Manufacturer	Indicates the medical device manufacturer, as defined in EU Directives 90/385/EC, 93/42/EEC and 98/79/EC
	5.1.4	Use-by-date	Indicates the date after which the medical device is not to be used
	5.1.5	Batch code	Indicate the manufacturer's batch code so that the batch or lot can be identified
	5.1.6	Catalogue number	Indicates the manufacturer's catalogue number so that the medical device can be identified
	5.1.7	Serial number	Indicate the manufacturer's serial number so that a specific medical device can be identified
	5.2.4	Sterilized using irradiation	Indicates a medical device that has been sterilized using irradiation
	5.2.6	Do not resterilize	Indicates a medical device that is not to be sterilized.
	5.2.8	Do not use if package is damaged	Indicates a medical device thatshould not be used if the package has been damaged or opened
	5.4.2	Do not re-use	Indicates a medical device that is intended for one use, or for use on a single patient during a single procedure
	5.4.3	Consult instructions for use	Indicates the need for the user to consult the instructions for use
	5.4.4	Caution	Caution: Federal Law restricts this device to the sale by or on the order of a physician
	21 CFR 801.109 (b)(1)	Prescription only	Requires prescription in theUnitied States
	Fig. 1 ASTM F2503-23	MR Safe	An an item that poses no known hazards resulting from exposure to any MR environment
With the exception of the Rx symbol & MR, all information is from ISO 15223-1:2016, Medical Devices - Symbols to be used with medical device lable, labeling and information to be supplied - Part1: General requirements, FR recognition number 5-117.			

PRODUCT COMPLAINTS

Any healthcare professional who has any complaints or is dissatisfied with this product should notify Bone Solutions Inc, 5712 Colleyville Blvd., Colleyville, TX 76034, USA.

Telephone: 817 809-8850

Email: customerservice@bonesolutions.net

FURTHER INFORMATION

For product information, sales inquiries, customer service, or to obtain a surgical technique, please contact your sales representative or Bone Solutions Inc.

Customer Service at Email: customerservice@bonesolutions.net

DISTRIBUTOR PORTAL ACCESS

1 **Visit Bone Solutions website**
www.bonesolutions.net

2 **Select RESOURCES from the top menu**

3 **Enter (case-sensitive) password when prompted:**
BoneSolutions

REQUEST FOR PURCHASE FORMS

Requirements for Bill-Only Forms

- PO#
- Hospital Info
- Product Tracking Patient Labels
- Hospital Signature
- Bone Solutions Rep Signature

Send completed forms to:

customerservice@bonesolutions.net

or fax to Bone Solutions at

866-673-0111

Mg BONESOLUTIONS

REQUEST FOR PURCHASE ORDER
Fax RPO with PO# to: 866-673-0111 or email to:
customerservice@bonesolutions.net

Attach Institution Label Here or Necessary Information Supplied

Procedure Information		Vendor Information	
Surgeon/Physician		Assigned PO#	
Facility Name		Procedure Date	
Email / Phone Number		Account Number	
Procedure Type		Vendor Name	
Facility Staff Rep (Name/Title)		Email / Phone Number	

Product/Patient Information	Product Number	Qty	Price	Total
Attach Product Sticker Here				
	Invoice Total			

Bone Solutions Rep Signature		Hospital Signature	

5712 COLLEYVILLE BLVD., SUITE 210 COLLEYVILLE, TEXAS 76034 P: 817-809-8850 F: 866-673-0111 WWW.BONESOLUTIONS.NET
Form 10142 Rev E

Mg OSTEOCRETE™

Part Number	Description
44-050-00-BSI	Mg OSTEOCRETE – Full Kit – 5cc
44-100-00-BSI	Mg OSTEOCRETE – Full Kit – 10cc
44-150-00-BSI	Mg OSTEOCRETE – Full Kit – 15cc

Kit Contents: 5cc Mg Powder, High Viscosity Solution (30-Second Putty), Medium Viscosity Solution, Mixing Syringe, Funnel, Basin, Spatula & 4.2mm Cannula/Pusher, Mechanical Advantage

Part Number	Description
44-050-00-STR	Mg OSTEOCRETE – Basic Kit – 5cc
44-100-00-STR	Mg OSTEOCRETE – Basic Kit – 10cc
44-150-00-STR	Mg OSTEOCRETE – Basic Kit – 15cc

Kit Contents: 5cc Mg Powder, High Viscosity Solution (30-Second Putty), Medium Viscosity Solution, Basin, Spatula

Mg OSTEOINJECT™

Part Number	Description
44-050-00-INJ	Mg OSTEOINJECT – 5cc
44-100-00-INJ	Mg OSTEOINJECT – 10cc

Kit Contents: Mg Powder Pouch, Low Viscosity Solution, Mixing Syringe, Funnel, 4.2mm Cannula & Pusher, Mechanical Advantage