

mis
4BONE

Biomaterials Line





MIS's Quality System complies with international quality standards: ISO 13485: 2003 - Quality Management System for Medical Devices, ISO 9001: 2000 - Quality Management System and CE Directive for Medical Devices 93/42/EEC. 4BONE (Synthetic Bone Graft) cleared by the FDA for marketing in the USA and is CE approved. Collagen membrane is pending FDA's marketing clearance in the USA and CE approval.

MIS Warranty: MIS exercises great care and effort in maintaining the superior quality of its products. All MIS products are guaranteed to be free from defects in material and workmanship. However, should a customer find fault with any MIS product after using it according to the directions, the defective product will be replaced.

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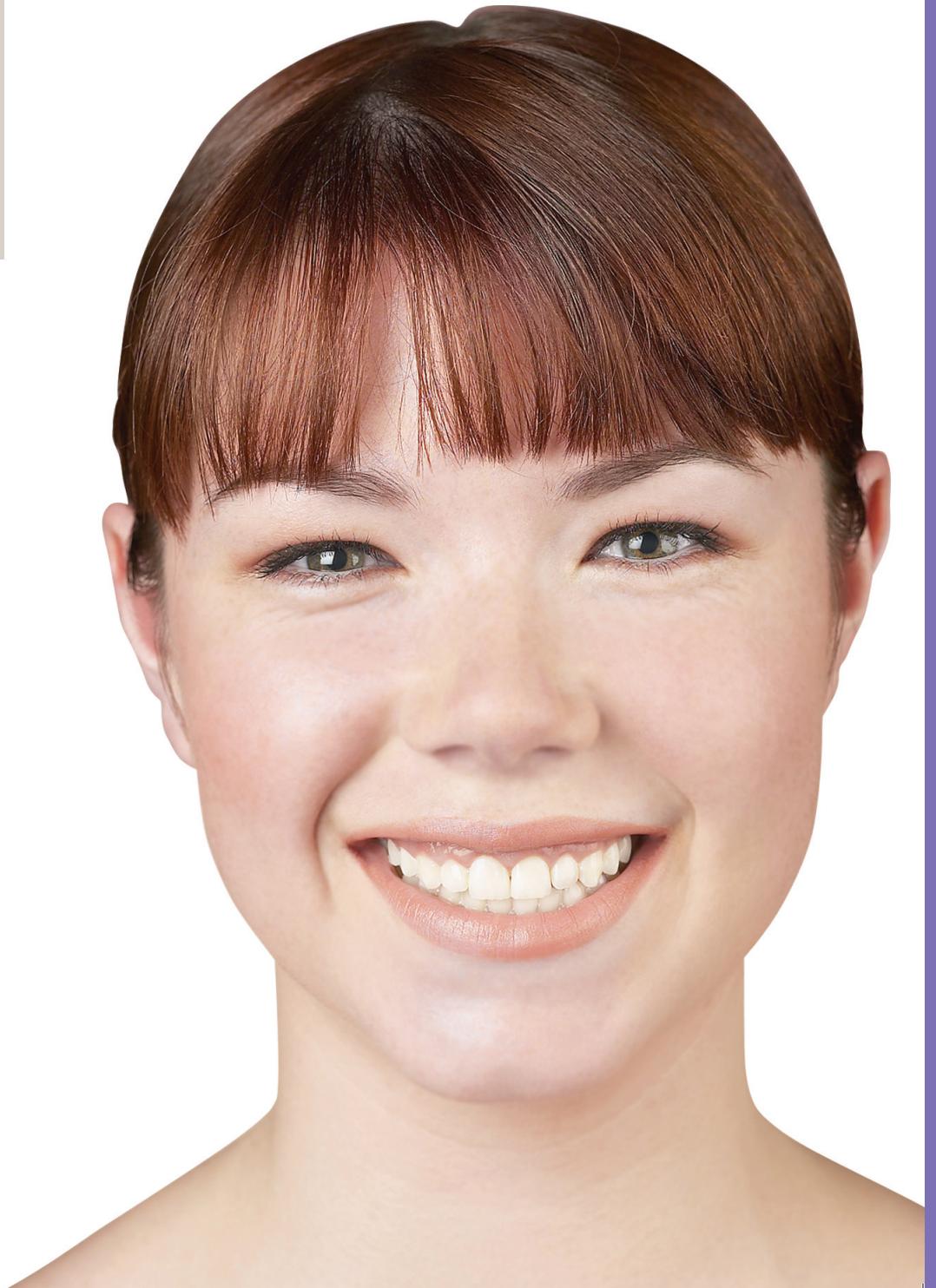
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4BONE
Synthetic Bone Graft



6.

Overview.

MIS 4BONE is a fully synthetic bone graft made of HA (60%) and β TCP(40%). A 70% interconnected Macro - and Microporosity promotes invasion of osteogenic cells by osteoconduction and allows biological fluid diffusion. 4BONE contains optimized morphology and resorption properties that achieve predictable treatment outcomes.



Product description.

Porosity: 4BONE is a fully synthetic bone graft with optimized morphology, forming an ideal habitat for architectural vital new bone to grow in. The distribution of the macro and micro porosity (70% macroporosity, 30% microporosity which are interconnected) is of great importance for the colonization of the biological fluids. 4BONE has a micro and macroporous contrary to most other ceramics, which consist of only macro porous. 4BONE global porosity is 70%, and the macro - and microporous structure is compatible with the cell size of bone generating cells. The micropores are interconnected allowing vascularization of the biological fluids into the granule. Once the biological fluids flow through the granule, the microporosity acts as a sieve that attracts the bone generating cells, allowing the formation of new bone from the inside of the granule.

Macroporosity

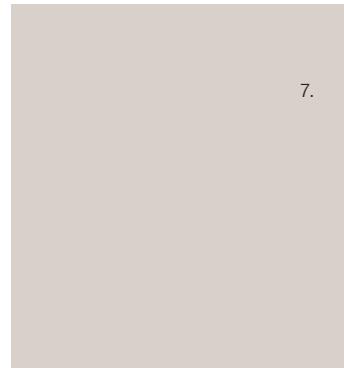
Comprising between 300 and 600 μm , similar to bone type: 2/3. promotes a deep invasion of osteogenic cells by osteoconduction.

Microporosity

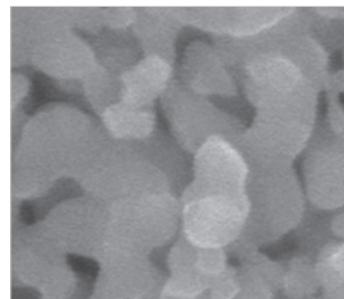
With pores inferior to 10 μm , similar to bone type: 1/3. The micropores are interconnected, allowing biological fluids diffusion distributing.

Ossteogenic Properties

By its nature, 4BONE helps to regenerate bone cell tissue. 4BONE is integrated during the natural remodeling process of the human bone and replaced by natural bony crystals similar to human bone. Chemically, the hydroxyapatite is a calcium phosphate that is as close as possible to the natural composition of the human bone mineral. The hydroxyapatite contained in 4BONE is wholly resorbable due to its small crystal size.



Macropores 400 μm , 70-80% macroporosity



Micropores <10 μm , 20-30% microporosity

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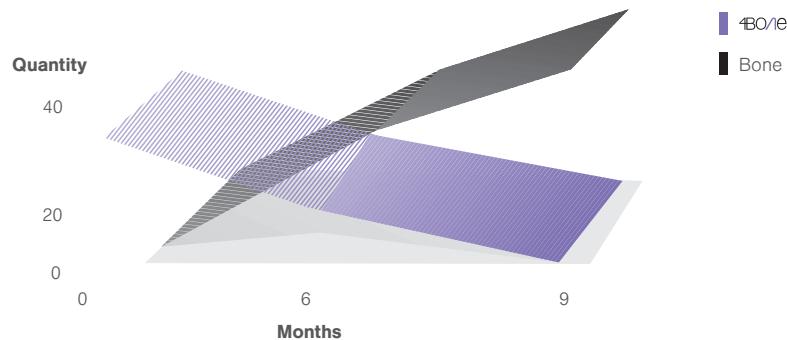
One function

Bone resorption/substitution.

Facilitates architectural bone formation by providing an osteoconductive scaffolding. Homogenous phase distribution that controls excessive resorption 4BONE serves as a scaffold for bone deposition during the bone formation process. The mechanical stability of the augmented volume is maintained as a result of the slow resorption rate of hydroxyapatite, which prevents excessive resorption. Unlike other biphasic calcium phosphates, 4BONE is not only a mixture of HA and TCP, but is chemically synthesized as a composite in order to ensure homogenous distribution of the two phases. 4BONE is integrated during the natural remodeling process of the human bone and is replaced by natural bony crystals similar to human bone. 4BONE's effective bone regeneration, safety and biocompatibility have been clinically and scientifically proven for more than 20 years in all scopes of surgery. 4BONE benefits from the largest scientific and clinical literature on the market since 1986 (500 publications).

Recommendations based on experience with 4BONE:

Sinus-healing - 6 to 8 months ■ Alveolus filing - 5 to 6 months ■ Healing time can be reduced when 4BONE is mixed with autologous bone.



Comparison Bone graft types.

Among the available materials used for pre-implant bone reconstruction, autologous bone is currently the gold standard, since it does not need any resorption/substitution process. To overcome the autograft limits, many substitution biomaterials were proposed. However, sometimes there have been supply problems with materials of human and animal origins, increasing the risk of cross-contamination. Consequently, products of synthetic origins were developed, among them biphasic calcium phosphate, an association of hydroxyapatite (HA) and beta-tricalcium phosphate (β -TCP). 4BONE offers great potential for bone reconstruction since it has a chemical composition close to biologic bone apatites. 4BONE has already proven its efficiency as a bone substitution material in different human clinical applications.

Type of bone graft	Autograft	Allograft (cadaver) Xenograft	Hydroxyapatite TCP	4BO/1E Synthetic Bone Graft
Origin	Patient bone	Human origin Animal origin	Calcium phosphate	Biocompatible calcium phosphate hydroxyapatite
Quantity	Limited	Unlimited	Ships/blocs	Granules
Benefits	Best & fastest results autograft takes 4 to 6 months to mature in the sinus	- Available in large quantities - Mechanical properties	100% Synthetic Biocompatible	100% Synthetic Biocompatible
Disadvantages	- Considerable volume needed (5cc-10cc per side) for typical sinus augmentation - Harvested from intra- oral donor sites - Requires additional invasive surgery	- Dead bone provides limited - Very slow resorption - Contamination risks - Limited storage	Slow resorption	No initial mechanical properties

10.

Advantages.

4BONE Synthetic Bone Graft offers many advantages as a result of great efforts that have been made to find an effective substitute material.



Safety

100% Synthetic. No human or animal origin. Twenty years of clinical studies have demonstrated the efficiency, biocompatibility and safety of 4BONE bioceramic.



Efficiency

Bioactive. 4BONE allows cell attachment, proliferation and cell expression.



Architectural bone remodeling

Specific microstructure and macrostructure represent a dynamic process, including physico-chemical processes, crystal/protein interactions, cell and tissue colonization, and bone remodeling.



Easy

Easy to handle. The granules of the 4BONE bone replacement substance easily absorb the patient's blood or physiological solution in a syringe, which is easily applied to the implant site.

0.5cc Indication.

4BONE is intended for use as a bone void filler or augmentation material for use in oral, periodontal or maxillofacial defects. These defects may be surgically created osseous defects or osseous defects created from traumatic injury to the bone. It may be used as a bone graft extender. 4BONE is intended only for bony voids or gaps that are not intrinsic to the stability of the bony structure. When packed into a bony site, 4BONE gradually resorbs and is replaced with bone during the healing process.

Typical uses include:

Periodontal/intrabony defects ■ Ridge augmentation ■ Extraction sites (implant preparation/placement) ■ Sinus lifts ■ Cystic cavities
 ■ 4BONE is also very efficient in immediate implanting and may be used as a bone graft extender.



Easy procedure for mixing with saline water and/or patient's blood.



Injection of the fully absorbed 4BONE substance into the implantation site.



Important roles

- 1-Bone granules should be wetted with saline solution.
- 2-Do not compact or jam 4BONE granules when delivery is attempted.

4BONE comes in an easy-to-use syringe:

Quantity: 0.5cc(0.36g)
Granule size: 0.5-1mm

1cc/ 2cc/ 6cc Indication.

For large volumes, particles need greater spaces around them in order to be colonized by cells. Using larger particles of 4BONE leads to greater surface contact for cell attachment and bone ingrowth spaces.

4BONE Synthetic Bone Graft injections of 2-6cc are indicated for large augmentations where long resorption time is crucial for the success of the procedure.



4BONE is supplied in tubes and is available in three quantities:

1cc (0.6gr) granules size: 1-2mm
2cc (1.2gr) granules size: 1-2mm
6cc (3.6gr) granules size: 1-2mm

Packaging.

4BONE granules are supplied in sterile vials or syringes. The unique packaging of 4BONE in a syringe lets the clinician mix the substance with saline water and/or the patient's blood. After the blood and/or saline water is fully absorbed in the 4BONE, placing the substance in the patient's mouth is simple to perform with the syringe.





4BO/e RCM

Resorbable Collagen Membrane

Overview.

4BONE RCM is a line of products of resorbable collagen membranes that are used in guided tissue regeneration and guided bone regeneration. 4BONE RCM is indicated for use in oral surgery procedures to assist in wound healing.

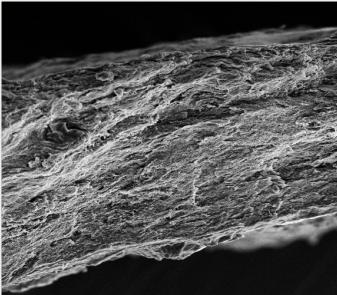


Product description.

4BONE RCM is a resorbable porcine skin-sourced collagen dental membrane for guided bone regeneration (GBR) and guided tissue regeneration (GTR), and is manufactured using unique cross linkage technology that provides the membrane with its ability to maintain as a barrier 4-6 months. 4BONE RCM is derived from porcine collagen which, has been successfully used in a variety of medical and dental applications for many years due to its high degree of biocompatibility. Porcine tissue is viewed as the material of choice in many medical xenograft procedures. In the literature it has been demonstrated that the immunogenicity of porcine collagen is very low (lower than seen with bovine collagen). Porcine collagen also avoids many of the issues related to bovine spongiform encephalopathy (BSE).

Purified collagen

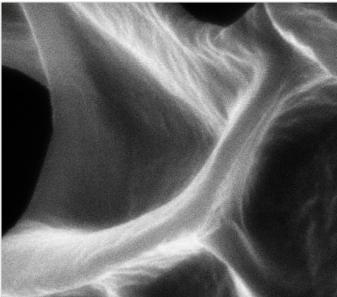
Purified collagen from skin ■ Collagen types I and III ■ Conservation of the fibrous structure (mechanical strength)



Macropores 100 μ m

Crosslinkage

A bath in the crosslinking reagent ■ Chemical bounds between the molecules ■ Enhancement of the resorption time ■ Neutralization: elimination of the residual crosslinker ■ Chemical analysis of residual reagent



Micropores <5 μ m

Resorption Control

Unique cross-linkage technology.

The controlled process of collagen cross-linking allowing sufficient time for osseous defects to achieve optimum bone regeneration. We can directly control the level of collagen cross-links to affect the longevity and degradation profile of the material. 4BONE RCM permits the diffusion of fluids through microporosity and nutrients related to soft tissue health. Cross-linking technology differs from one membrane to the next, and these differences influence considerably the degradation of the membrane over time. 4BONE RCM degradation has been tested in animal models.



Cross-linkage

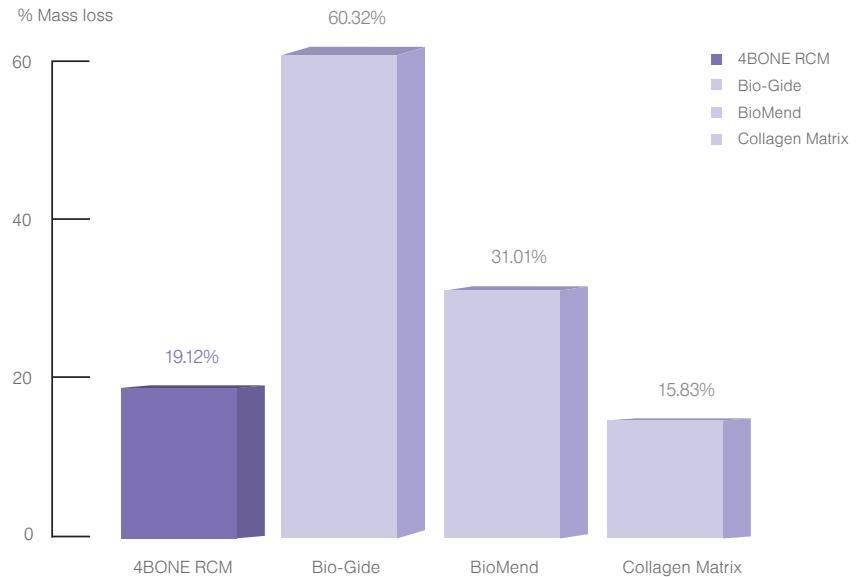


Collagen structure

In vitro resorption control results.

Results demonstrate the percentage of loss of mass in membranes, calculated during 48 hours of in vitro degradation.

Averages loss of mass



Results

Results demonstrate membranes percentage of loss of mass calculated during 48 hours of in vitro degradation.

Advantages.

The advantages of 4BONE RCM result from extensive research in finding a functional product that will act as a barrier and stay intact for a desired period of time.

Safety

The porcine source results in improved sanitary safety. Complete and validated traceability. Limited exposure of the membrane will not affect the success of the procedure.



Efficiency

Barrier functionality guarantees that the 4BONE RCM can be successfully used in a number of medical applications. Ability to allow sufficient time for osseous defects to achieve optimum bone regeneration.



Architectural bone remodeling

Specific microstructure and macrostructure represent a dynamic process, including physico-chemical processes, crystal/protein interactions, cell and tissue colonization, and bone remodeling.



Easy

Easy to handle, cut to size, shape and apply. Easy to place, with no need for sutures or pins. Flexible and adaptable to varying bone topographies.



4BONE RCM Indications.

4BONE RCM is a bioabsorbable membrane. It is intended for use in periodontal/dental surgery procedures as a material for placement in the area of a periodontal defect, dental implant, bone defect or ridge reconstruction to aid in wound healing post surgery. Considering 4BONE RCM indications and resorption time, it is recommended to combine the membrane with bone graft to new bone healing by osteoconduction and osteoinduction.

4BONE RCM is available three sizes:

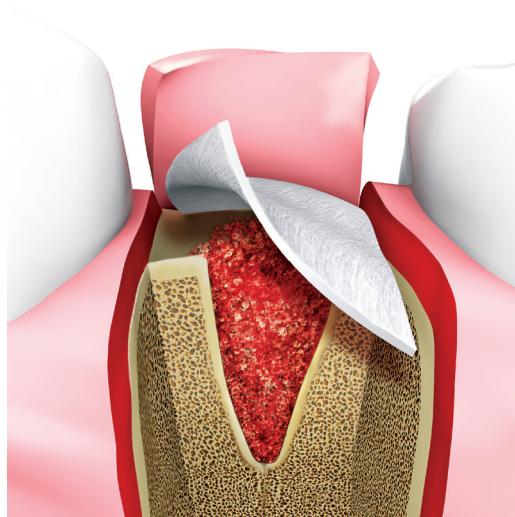
BR-C1525 - 15x25x0.3mm

BR-C2030 - 20x30x0.3mm

BR-C3040 - 30x40x0.3mm

“

As much tissue as possible should be preserved to allow for primary closure of the wound and correct positioning of the flaps.



Packaging.

4BONE RCM is packaged in a double sterile pouch. The outer pouch should be opened carefully and the inner pouch placed onto a sterile field. The membrane should be removed from the inner pouch with sterile gloves or instruments.



4BONE product line.

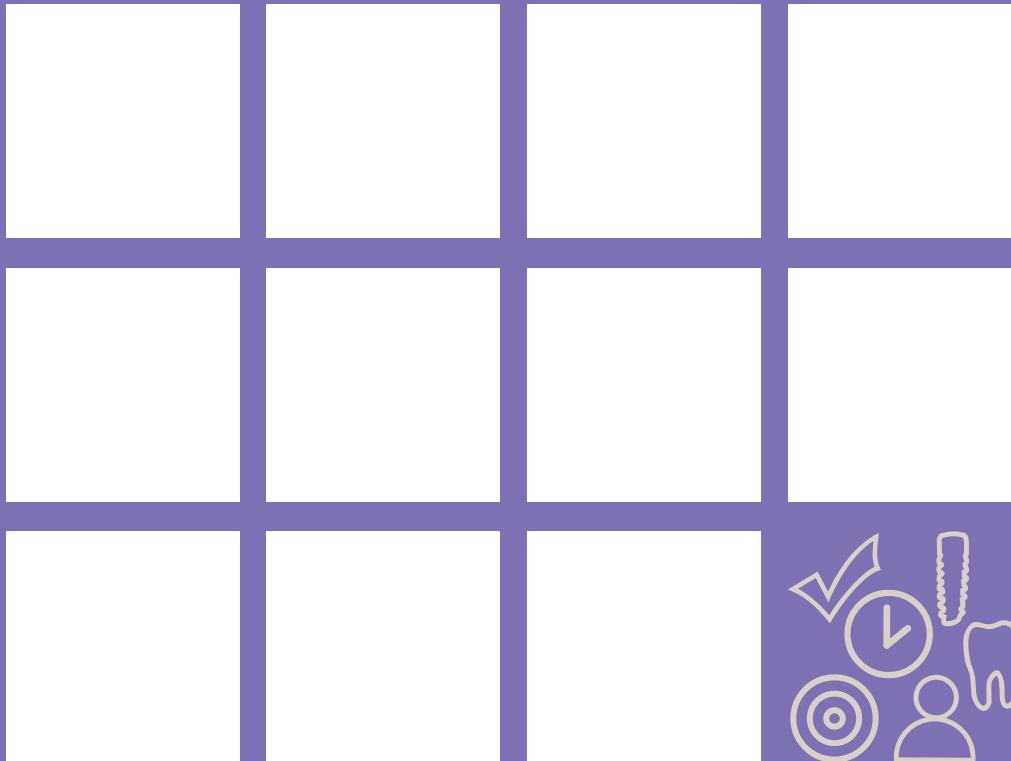


4BONE Synthetic Bone Graft



4BONE Regeneration
Collagen Membrane

Description	4BONE Synthetic Bone Graft				4BONE Regeneration Collagen Membrane		
Product Catalog Number	BS-4BS01	BS-4BS10	BS-4BS20	BS-4BS60	BR-C1525	BR-C2030	BR-C3040
Particle Size	0.5-1mm	1-2mm	1-2mm	5-6mm	15×25×0.3mm	20×30×0.3mm	30×40×0.3mm
Volume/Weight	0.5cc / 0.37g	1cc / 0.6g	2cc / 1.2g	6cc / 3.6g	-	-	-
Volume/Weight	0.5cc / 0.37g	1cc / 0.6g	2cc / 1.2g	6cc / 3.6g	-	-	-



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