# UBGEN®
# RE-BONE® BOVINE BONE SUBSTITUTE


UBGEN

## RE-BONE®

A specific line of bone substitutes of bovine origin treated at low temperature to promote the regeneration of hard tissues in bone reconstruction surgery.

# RE-BONE®
# WHY CHOOSE IT?

## Because it works.

- Fully resorbable
- Processed at low temperatures thanks to the Thermagen production process
- Produced by an entirely Italian supply chain
- CE marked as a product compliant with Directive 93/42 EEC (CE 0373)

UBGEN® is the only certified Italian company that processes bovine material at low temperatures.
Most of the commercially available biomaterials do not use raw material of bovine origin, or exploit bovine bone treated at high temperatures.
This means that the resorption index is significantly lower and that the bone graft remains in the oral cavity even after many years.

At UBGEN® we exploit the winning characteristics of the bone substitute of bovine origin, treated at low temperature through our unique Thermagen production process. The bone substitute thus produced has been shown to facilitate in situ volumetric stability, thanks to the superficial cracking of the granules technology. Moreover, this low temperature cleaning process prevents ceramization, while keeping the bovine bone matrix perfectly resorbable and biocompatible.

RE-BONE® is completely reabsorbed in 6-8 months.

Its safety is ensured by the choice of raw material in compliance with the standards required in the reference protocol.

## 1. CHARACTERISTICS

### BIOCOMPATIBILITY

Tests performed in compliance with ISO 10993-5:2009 guidelines have demonstrated that RE-BONE® has proven biocompatibility properties and is entirely free of exogenous or cytotoxic elements.

### STERILITY

It is a single-use device, gamma-ray sterilized, with a shelf life of 5 years.

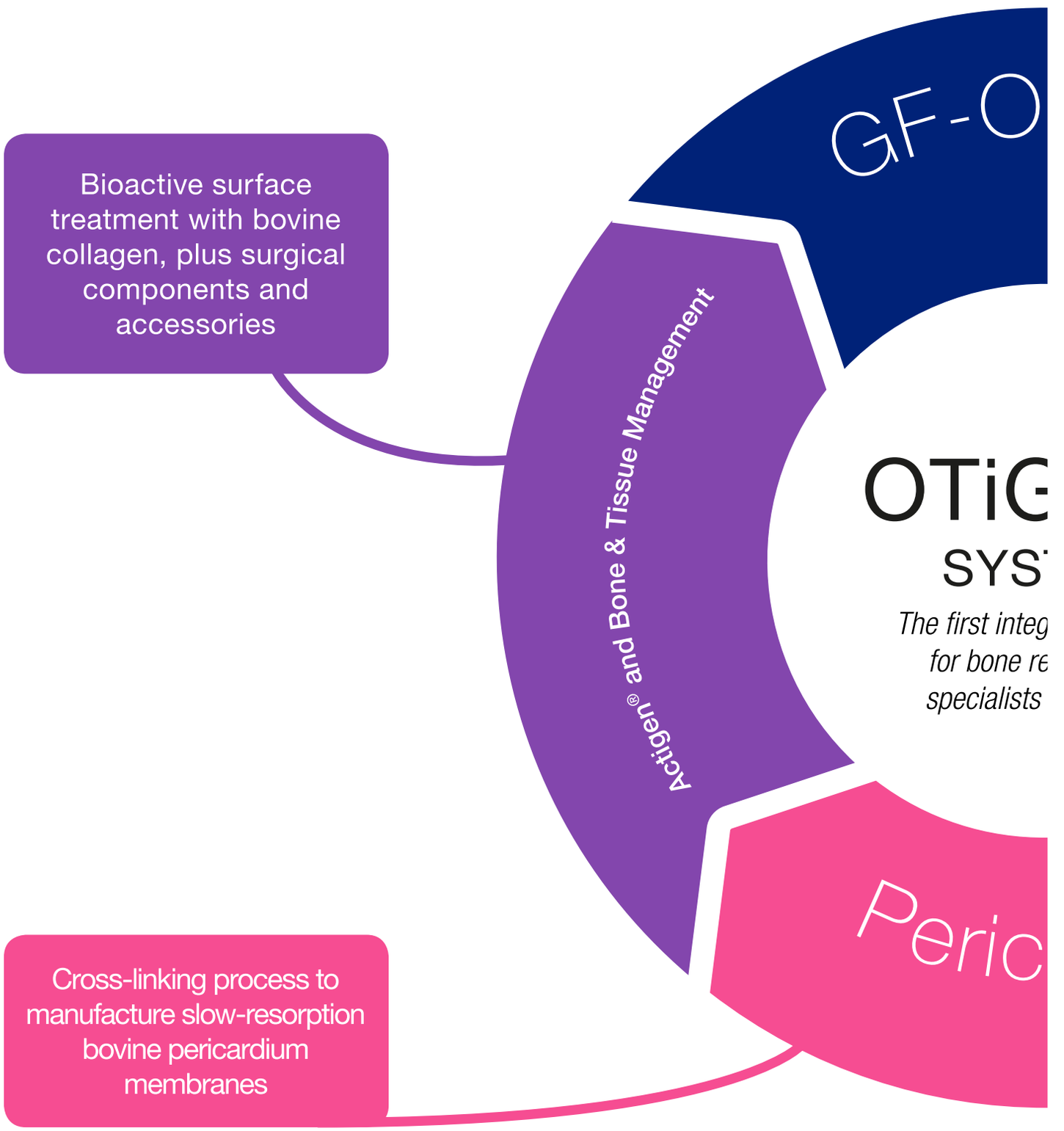
### RESORPTION AND REMODELLING

The complete replacement of RE-BONE® with newly formed bone tissue depends on anatomical variables (ratio between vital bone surface and volume of the grafted site) and on individual patient factors. Resorption: between 6-8 months. | Remodelling: biological times of bone remodelling.

## 2. BENEFITS

- Biocompatible
- Volumetrically stable
- Shortened resorption time
- Rough surface

# UBGEN PRESENTS OTiGEN SYSTEM



Ubgen the specialists of bone surgery in dentistry created OTiGEN SYSTEM: the first complete system of products and services specifically designed to meet the needs of those who work in tissue engineering, with a specific focus in the dental field.


Certified IIa technology for the production of blood concentrates

Production process that ensure deproteinization of bovine bone at low-temperature

# RE-BONE® BONE SUBSTITUTE

RE-BONE® is the bone substitute of bovine origin treated at low temperature through the innovative Thermagen® production process, CE certified and produced by an entirely Italian supply chain.

While the other producers supply bone substitutes of bovine origin treated at high temperature or do not use raw material of bovine origin (porcine, equine or synthetic), we enhance the winning characteristics of the bovine bone substitute with the innovative low temperature production process Thermagen®, guaranteeing high biocompatibility, greater porosity of the granules and the absence of ceramization with relative total reabsorption of the raw material.

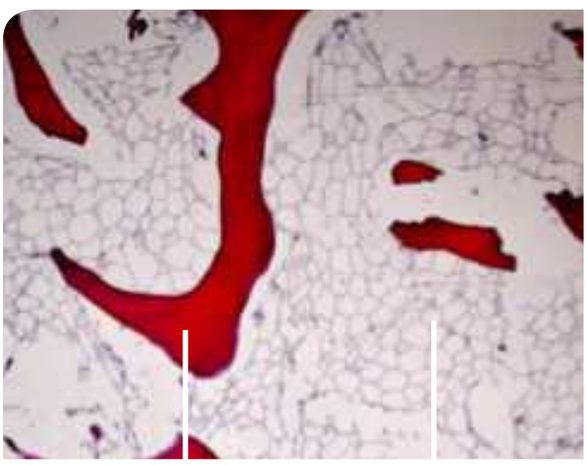
This technology for the decellularization of the raw material was developed by our team of bioengineers and subsequently confirmed by tests performed by the Department of Biology of the University of Padua.

In addition to Thermagen®, our secret lies in the choice of the raw material. In UBGEN we know each step of the production chain: from the quality of the land used for grazing, to the natural cultivation used for the production of forage, to the healthiness of the rooms that welcome the animals themselves.

If animals live and grow well, in a healthy environment, that is respected in its territorial characteristics, the derived products intrinsically meet the health and safety requirements.

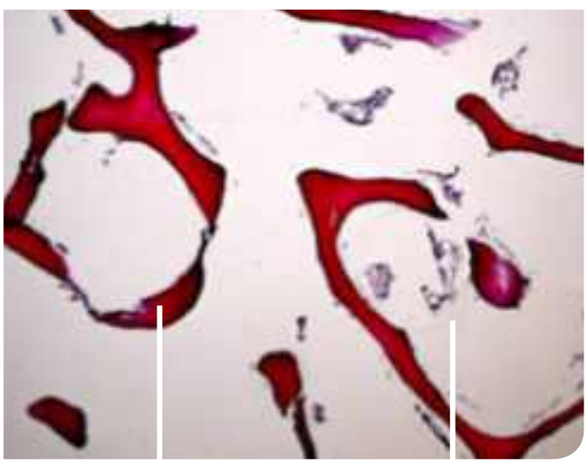
*RE-BONE® is a bone substitute that is very similar to human bone tissue. Therefore, it allows the creation of a favourable environment to chemotaxis, osteoblast proliferation and neoangiogenesis thanks to the maintenance of extracellular matrix proteins.*[7]

Hematoxylin/eosin stain.
Histological section of untreated bovine bone (20x)



Bone Tissue Adipose Tissue

Hematoxylin/eosin stain.
Histological section of RE-BONE®



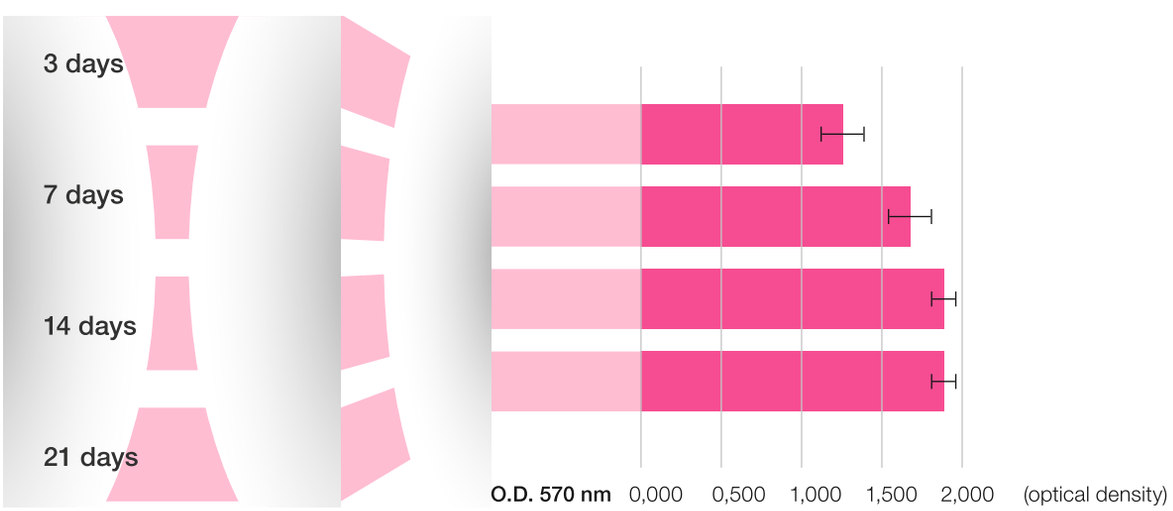
Bone Tissue Adipose Tissue

## Biocompatibility of RE-BONE

Laboratory and literature studies have shown the regenerative efficacy of UBGEN decellularization process.

### Tab.1 - ADSC Proliferation

Proliferation ADSC (Adipose Derived Stem Cells) in culture on RE-BONE bone substitute evaluated at different time intervals (MTT test).

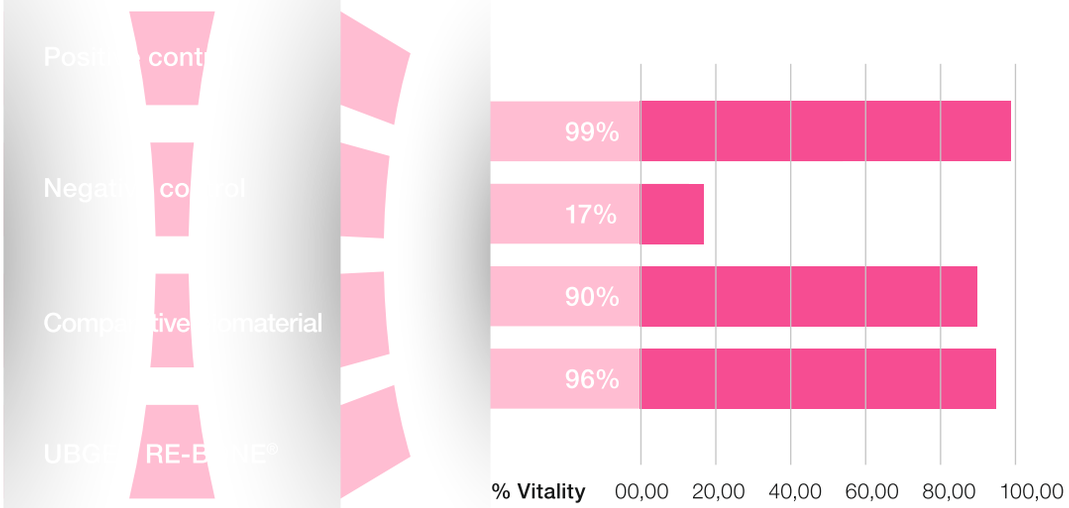



By growing adipose-derived mesenchymal stem cells with RE-BONE®, cell proliferation increased up to 35% after more than 14 days of culture.

7. Miller A. Collagen: The organic matrix of bone. Philosophical Transaction of the Royal Society B: Biological Sciences. 1984, 304-455.

## Tab.2 - Viability test

Cellular viability test of the osteoblasts.




aring the c ability of th osteoblasts in contact with RE-BONE with other commercially
e bovine deri materials, a higher cell survival can be seen, from 90% (comparison sample)
o (RE-BONE sa

## Osteoconductive capacity

Osteoconductivity is the ability of the graft to ensure adhesion, survival and proliferation of osteogenic cells, providing an interconnected structure through which new cells can migrate and new vessels can be formed.[5]

*Studies on humans[11] and animals in the sinus lift procedure, have shown that RE-BONE® can induce an excellent guided bone regeneration (GBR).*

## Histological analysis

In a study on animals (ovine)[13], 15 days after sinus grafting with RE-BONE granules, we note the presence of some vessels around the bone substitute; this is a fundamental requirement for the formation of new bone tissue as it guarantees:

_ nourishment and elimination of residual substances;
_ migration of osteoprogenitor cells into the graft;
_ differentiation of osteoprogenitor cells induced by the biomaterial;
_ movement of osteoblasts already differentiated by the deposition of a new matrix.

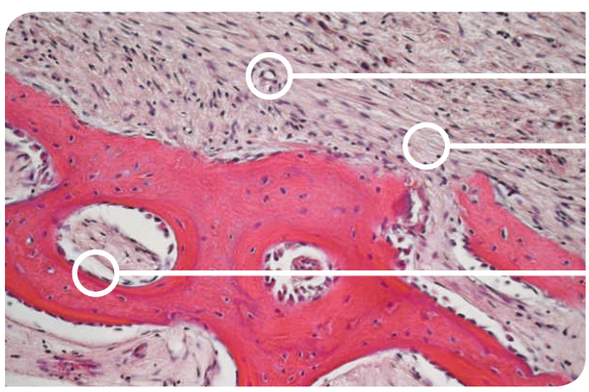
5. Flnkemeier CG. Bone-grafting and bone-graft substitutes. Journal of Bone & Joint Surgery. 2002, 84:454-464.
11. Maxillary sinus augmentation with decellularized bovine compact particles: a radiological, clinical and histologic report of 4 cases. Antonio Scarano. BioMed Research International 2017
13. Data on file with RE-BONE/UBGEN.

It is also possible to notice the approach of the osteoblasts towards the contact surface of the biomaterial/host tissue and their insertion in the structure of the biomaterial with the deposition of collagen fibers.
**30-days bone grafts histological analyses demonstrate marked presence of osteoblasts that penetrated into the pores of the biomaterial, depositing new collagen matrix.**

Collagen deposition by osteoblasts contributes to the formation of woven bone, a very dense collagen structure that at a later stage, will be mineralized and transformed into mature bone.

*The correct bone regeneration that can be noticed from these images is made possible by the presence of numerous vessels near the biomaterial helping the migration of osteoprogenitor cells and the supply of nutrients as well as the elimination of residual substances.*[9]

**BIOMATERIAL**



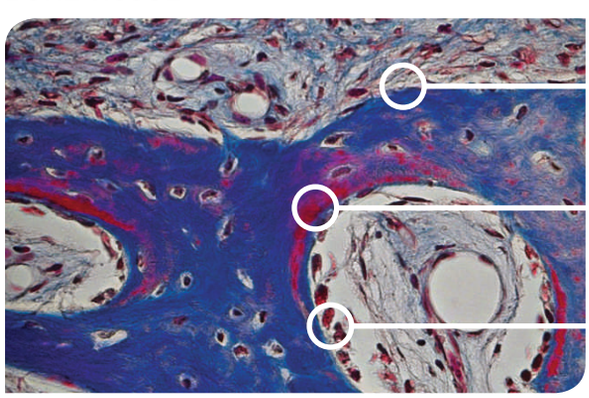
Vessel.

Collagen fibers deposited by sheep fibroblasts.

Osteoblasts in contact with the biomaterial.

Hematoxylin/eosin coloring (20x).

**BONE TISSUE**



Collagen fibers deposited by sheep fibroblasts.

Beginning of the mineralization of the matrix process.

Osteoblast adhesion to decellularized bovine bone.

Masson's Trichrome coloring (20x).

9. Clarke B. Normal Bone Anatomy and Physiology. Clinical Journal of the American Society of Nephrology. 2008, 3 (Suppl. 3): S131-S139.

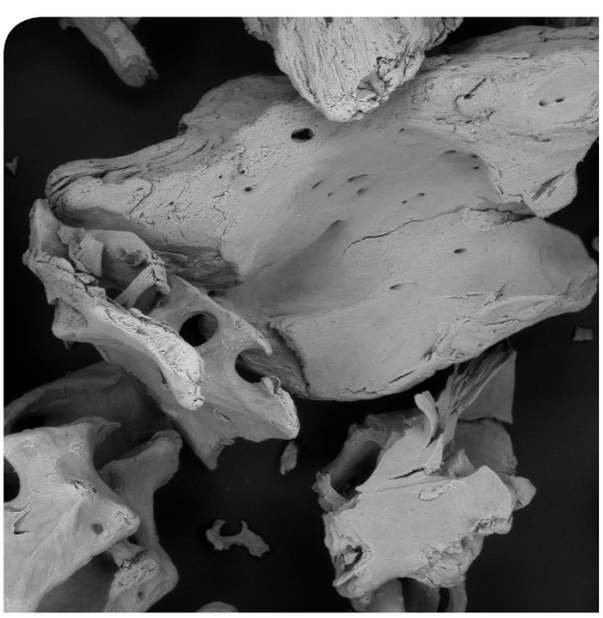
## Microporosity of the mineral structure

In literature it is widely documented that the microporosity of biomaterials is an important factor for tissue regeneration. By increasing the contact surface of the graft with the cells of the surrounding tissue, the possibility for the biomaterials to be colonized by bone progenitor cells is increased. Nanostructured biomaterials, in fact, mimic the extracellular matrix of the natural bone, creating a micro-environment that promotes cell adhesion, proliferation and differentiation.[6]

Scanning electron microscope (SEM) was then performed to qualitatively evaluate the microporosity of the bone substitute RE-BONE.

*From the images shown, it can be seen that the micro-roughness of the material meaning the opening, cracking and non-continuity of the surface is present both at the macroscopic and the microscopic level (at the cellular level).*

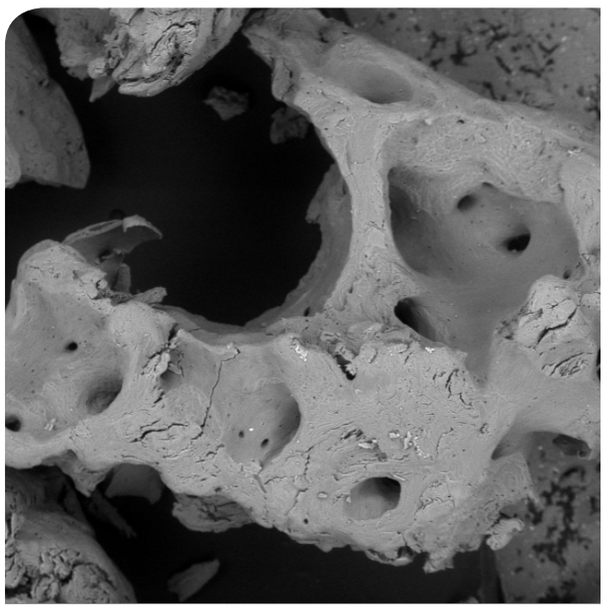
*It is also obvious that the presence of internal cracks in the granule will allow cells and vessels to colonize the graft in depth, shortening the time of resorption of the bone substitute.*



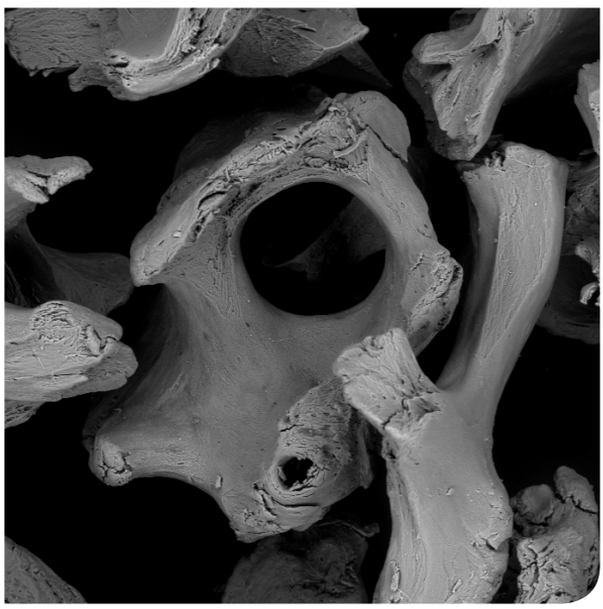
RE-BONE 100x granules

RE-BONE 100x granules

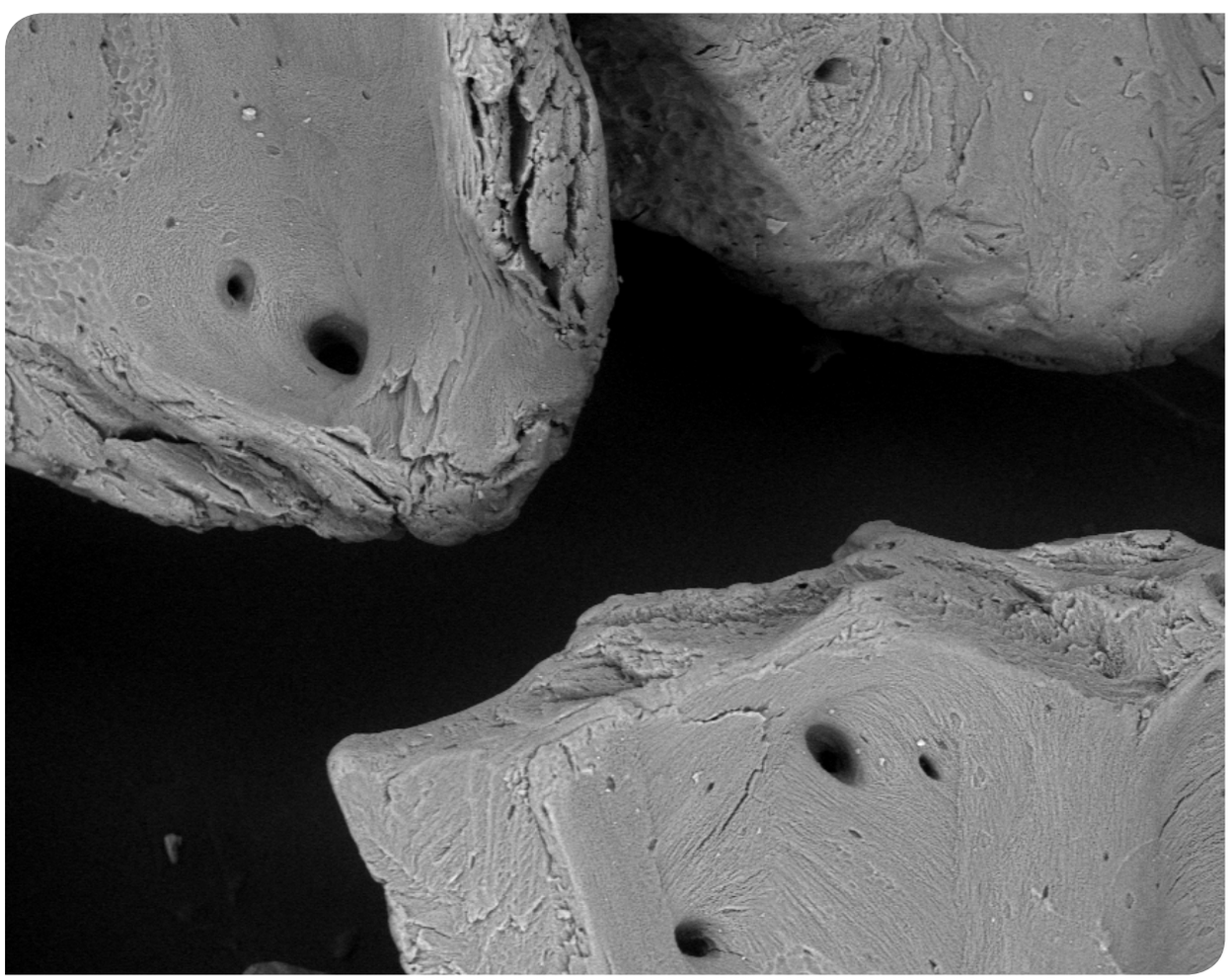
6. Gardin C, Ferroni L, Favero L, Stellini E, Stomaci D, Sivolella S, Bressan E, Zavan B. Nanostructured Biomaterials for Tissue Engineered Bone Tissue Reconstruction. International Journal of Molecular. Science. 2012, 13: 737-757.



RE-BONE 150x granules



RE-BONE 195x granules



RE-BONE 300x granules

| PRODUCT | PACKAGING | CODE |
|---|---|---|
| RE-BONE® Granules | Cortico-cancellous granules 0.25g - 0.25-1 mm | BM01A (pack of 1) \| BM01A6 (pack of 6) |
| | Cortico-cancellous granules 0.5g - 0.25-1 mm | BM01B (pack of 1) \| BM01B6 (pack of 6) |
| | Cortico-cancellous granules 1g - 0.25-1 mm | BM01C (pack of 1) \| BM01C6 (pack of 6) |
| | Cortico-cancellous granules 2g - 0.25-1 mm | BM01D (pack of 1) \| BM01D6 (pack of 6) |
| | Cortico-cancellous granules 0.5g - 1-2 mm | BM01E (pack of 1) \| BM01E6 (pack of 6) |
| | Cortico-cancellous granules 1g - 1-2 mm | BM01F (pack of 1) \| BM01F6 (pack of 6) |
| | Cortico-cancellous granules 2g - 1-2 mm | BM01G (pack of 1) \| BM01G6 (pack of 6) |
| | Cortico-cancellous granules 5g - 1-2 mm | BM01H (pack of 1) \| BM01H6 (pack of 6) |
| | Cancellous granules 0.25g - 0.25-1 mm | BM01I (pack of 1) \| BM01I6 (pack of 6) |
| | Cancellous granules 0.5g - 0.25-1 mm | BM01J (pack of 1) \| BM01J6 (pack of 6) |
| | Cancellous granules 1g - 0.25-1 mm | BM01K (pack of 1) \| BM01K6 (pack of 6) |
| | Cancellous granules 2g - 0.25-1 mm | BM01L (pack of 1) \| BM01L6 (pack of 6) |
| | Cancellous granules 0.5g - 1-2 mm | BM01M (pack of 1) \| BM01M6 (pack of 6) |
| | Cancellous granules 1g - 1-2 mm | BM01N (pack of 1) \| BM01N6 (pack of 6) |
| | Cancellous granules 2g - 1-2 mm | BM01O (pack of 1) \| BM01O6 (pack of 6) |
| | Cancellous granules 5g - 1-2 mm | BM01P (pack of 1) \| BM01P6 (pack of 6) |

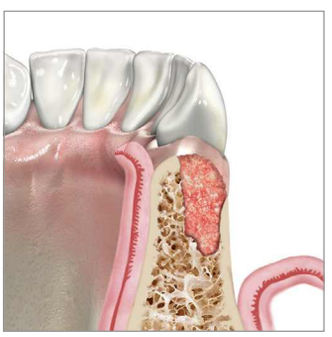
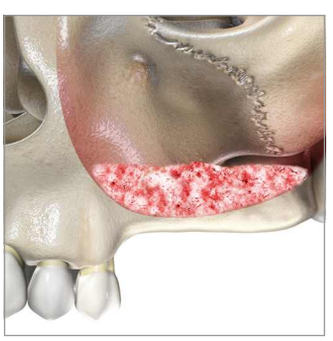
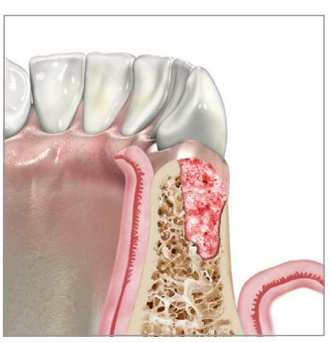
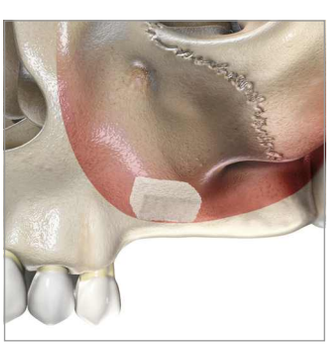
| PRODUCT | PACKAGING | CODE |
|---|---|---|
| RE-BONE® Block | Block of 10x10x10 mm | BM02A (pack of 1) |
| | Block of 10x10x20 mm | BM02B (pack of 1) |

| PRODUCT | PACKAGING | CODE |
|---|---|---|
| RE-BONE® Syringe | Syringe of 0.25g for granules of 0.25-1mm | BM03A |
| | Syringe of 0.5g for granules of 0.25-1mm | BM03B |
| | Syringe of 0.5g for granules of 1-2mm | BM03C |
| | Syringe of 1g for granules of 0.25-1mm | BM03BA |
| | Syringe of 1.5g for granules of 0.25-1mm | BM03BB |
| | Syringe of 2g for granules of 0.25-1mm | BM03BC |
| | Syringe of 1g for granules of 1-2mm | BM03CA |
| | Syringe of 1.5g for granules of 1-2mm | BM03CB |
| | Syringe of 2g for granules of 1-2mm | BM03CC |

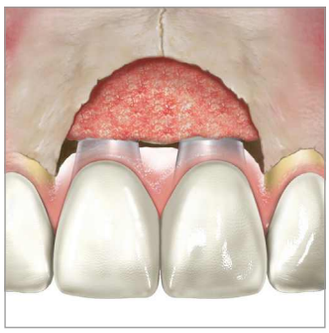
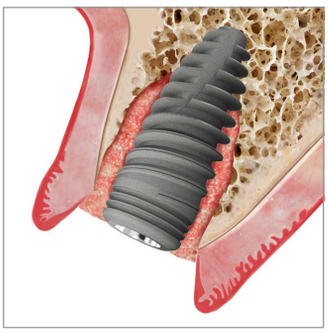
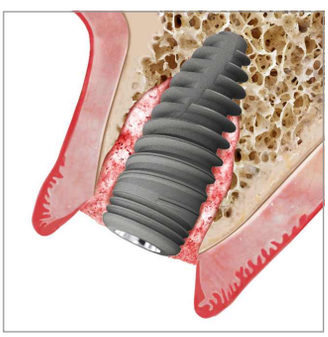
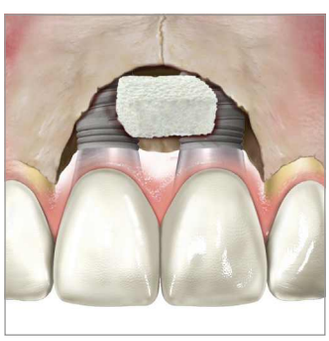
# 3. CLINICAL APPLICATIONS

- Maintenance of the socket and bone crest
- Maxillary sinus lift surgery
- Horizontal and vertical augmentation in 2-wall defects
- Dehiscences and fenestrations in peri-implant lesions
- Periodontal regeneration in infrabony defects and 2-3 wall furcation defects

## RE-BONE® clinical applications

| | Support of the alveolus and bone crest. | Sinus lift surgery. | Horizontal increase in 2-wall defects. |
|---|---|---|---|
| Granules  |  |  |  |
| Syringe  |  |  |  |
| Block  |  |  |  |

# RE-BONE® clinical applications

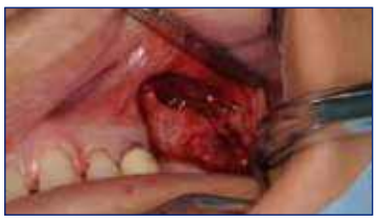
| | Vertical increase in 2-wall defects. | Dehiscences and fenestrations in peri-implant lesions. | Periodontal regeneration in intra-osseous defects and 2-or 3-wall furcation defects. |
|---|---|---|---|
| Granules |  |  |  |
| Syringe |  |  |  |
| Block |  | | |



## 1st Case Report: Prof. Ugo Covani

Camaiore (LU), Italy

*Maxillary sinus lift procedure with lateral approach.*



*Opened window on the lateral wall of the sinus.*

*Preparation of RE-BONE® biomaterial mixed with PRF.*

*RE-BONE® biomaterial and PRF positioning.*

*Use of PRF membrane to protect Schneider's membrane.*

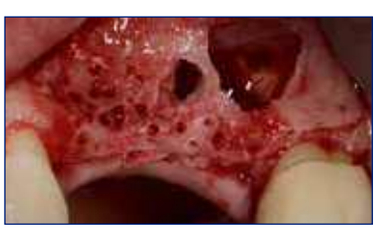
*Site closure; sutures removal after 2 weeks.*

## 2nd Case Report: Dott. Filippo De Paolis

Rome, Italy

*Vertical and Horizontal Maxillary Bone Defects.*

*Maxillary sinus lift and lateral osteotomy.*



*Maxillary sinus lift with GBR lateral and contextual osteotomy.*

*RE-BONE® biomaterial in situ and SHELTER® resorbable pericardium membrane.*

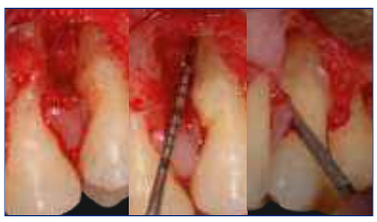
*SHELTER® resorbable pericardium membrane to cover the graft and retention pins.*

*Site closure; removal of sutures after two weeks.*

## 3rd Case Report: Dott. Walter Stablum

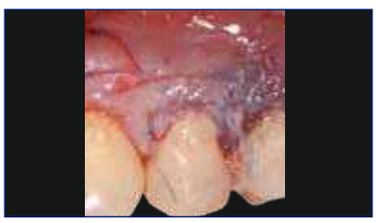
Borgo Valsugana (TN), Italy

*Regenerative therapy of an intrabony defect, 1-2 walls with single flap approach technique: initial clinical and radiographic situation.*

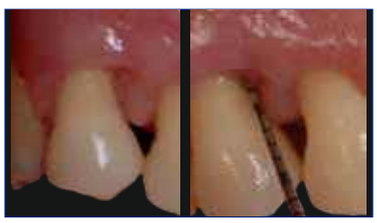


*1. Incision and flap detachment with single flap approach technique*
*2. Intra-operative measurement of intrabony defect 9 mm*
*3. Scaling and root planning with curette and rotary instruments*

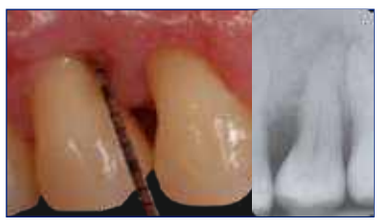
*1. Root surface conditioning with EDTA*
*2. RE-BONE® graft mixed with amelogenin*



*Internal mattress suture and use of cyanoacrylate.*



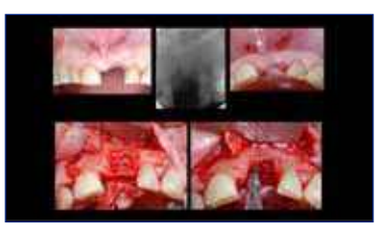
*1. One-month follow-up*
*2. Six-month follow up*



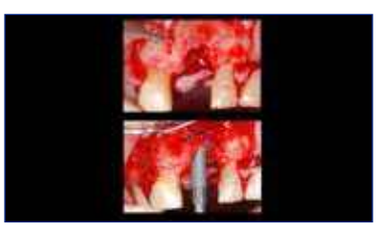
*Final clinical and radiographic situation.*

## 4th Case Report: Dott. Stefano Parma Benfenati

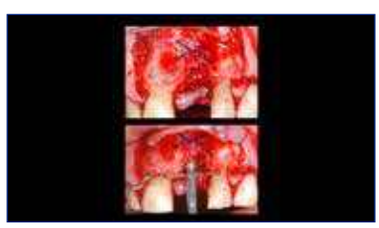
Ferrara, Italy



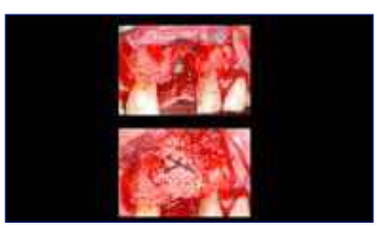
*X-ray of the defect - flap detachment.*



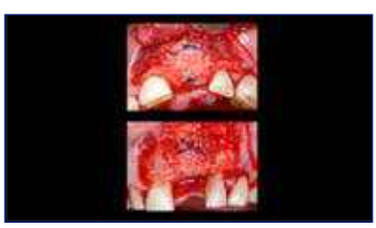
*Defect uncovering and implant insertion.*



*Evaluation of correct implant placement.*



*RE-BONE® Biomaterial positioned to fill the defect.*



*Occlusal and vestibular images of RE-BONE® Biomaterial at the end of defect filling.*

*Positioning of SHELTER® resorbable pericardium membrane to cover the graft, and site closure with PTFE sutures. After 9 months the surgical phase will be performed.*

**Mobil: 0733 10 9393 / 0722 750 218**
**E-mail: info@ardsimplant.ro Web: www.ardsimplant.ro**