The Earth: a grain of sand in a vast cosmic arena. To date, the only known world capable of supporting life. Everyone we love and every human being has lived their existence here. This is where we are. This is our home. This is who we are. This is why we have decided to dedicate our professional lives to improving the lives of other people. To achieve this, we have undertaken difficult and risky paths. Indeed, considered by many to be impossible. With the awareness that failures would be greater in number than successes. But life is only worth living if we realize our uniqueness by kindly caring for each other. Within this type of approach, each of us has one primary mission, and only one: to fulfil their potential in harmony with their surroundings.

UBGEN


UBGEN
A complete range of **solutions**
for **tissue** regeneration that meet
multiple **needs** in bone regenerative
surgery.

UBGEN®
SPECIALISTS IN BONE SURGERY IN DENTISTRY

WE TAKE CARE OF PEOPLE
FOR A NEW ETHIC OF WELLBEING

By carefully listening to dentists in their daily clinical practice, we convey our commitment to offering innovative solutions that protect patient's health and shorten healing times.

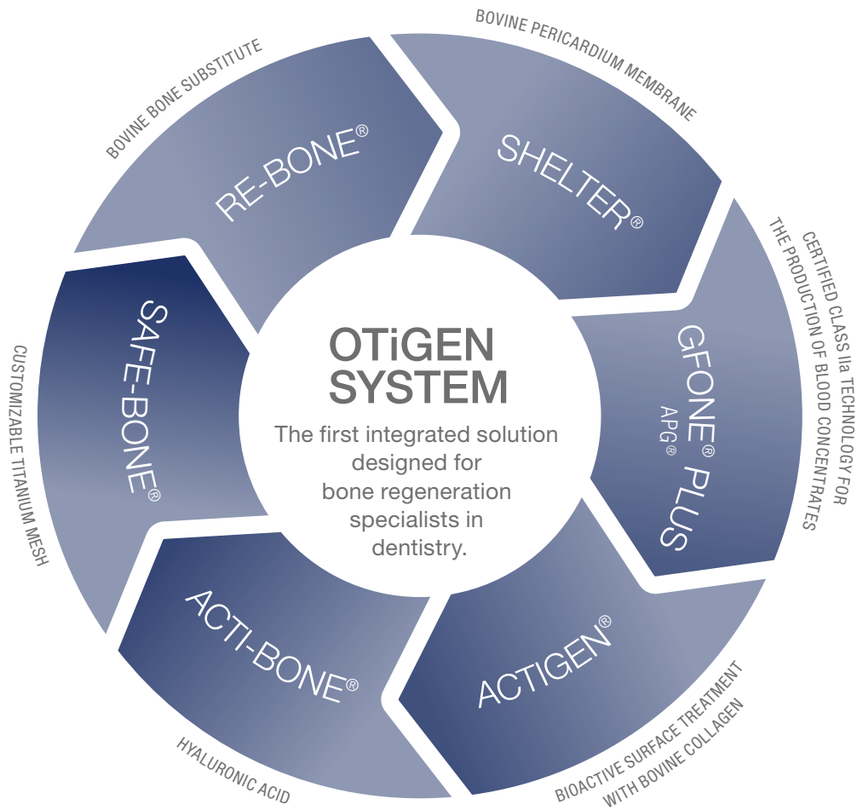
CONTENTS

UBGEN®
PRESENTS
THE OTiGEN SYSTEM

The panorama of companies operating in the biomedical sector in Europe is made up of different firms that offer Users a wide range of choices in terms of the most suitable partner for their needs.

At UBGEN® we strongly believe in technological innovation, to the point that every investment is an essential step to anticipate the future.
This enables us to adapt to a constantly changing market.

Our corporate responsibility focuses on bone surgery in dentistry and is aimed towards creating solutions that put the health and well-being of patients first.



This is why at UBGEN® we have created the **OTiGEN SYSTEM**: the first system of products and services designed to work in synergy with the requests of clinicians in the dental field.

OTiGEN SYSTEM is the link that allows clinicians to have a single commercial partner able to respond to all their needs across all phases, from choosing the graft, up to healing of the tissues.

For our partners, this means having the first and only integrated system where each component has been designed to interact with the others, thus ensuring full compatibility and predictability of results.

UBGEN®
RE-BONE® BOVINE BONE SUBSTITUTE

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

UBGEN

RE-BONE®

The bone substitute of bovine origin treated at low temperature through the innovative Thermagen production process, produced by an entirely Italian supply chain.

Compared to the presence on the market of bone substitutes of bovine origin treated at high temperatures or produced with raw materials from other sources (porcine, equine, synthetic), at UBGEN® we enhance the winning characteristics of the bovine bone substitute with the Thermagen innovative production process at low temperatures. Thanks to this protocol, we are able to avoid the so-called "ceramization" of the bone substitute, thus ensuring its total resorption and giving it high biocompatibility as well as adequate macro/microporosity.

The decellularization process of the Thermagen raw material was developed by a team of internal and external bioengineering experts and subsequently proven by tests performed by authoritative University Departments.

Together with the Thermagen production process, it is the choice of the raw material that makes the difference. At UBGEN® we are aware of the details of each step of the production chain: from the wholesomeness of the land used for grazing, to the natural cultivation used for the production of forage, to the healthful state of the facilities 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 is able to create an environment favourable to chemotaxis, osteoblast proliferation and neoangiogenesis thanks to the maintenance of the native three-dimensional structure of the extracellular matrix.[1]

1. Gardin C, Ricci S, Ferroni L, Guazzo R, Sbricoli L, DeBenedictis G, Finotti L, Isola M, Bressan E, Zavan B. Decellularization and Delipidation Protocols of Bovine Bone and Pericardium for Bone Grafting and Guided Bone Regeneration Procedure PLOSONE|DOI:10.1371/July20,2015

FIG. 1 - Hematoxylin/eosin stain.
Histological section of untreated bovine bone (20x)

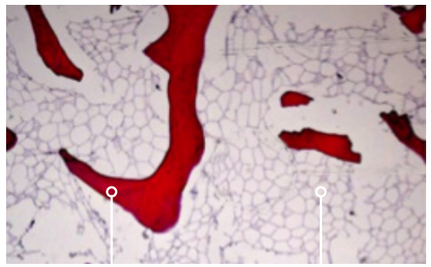
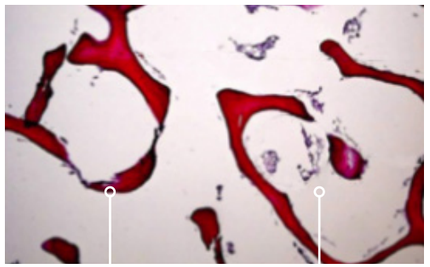


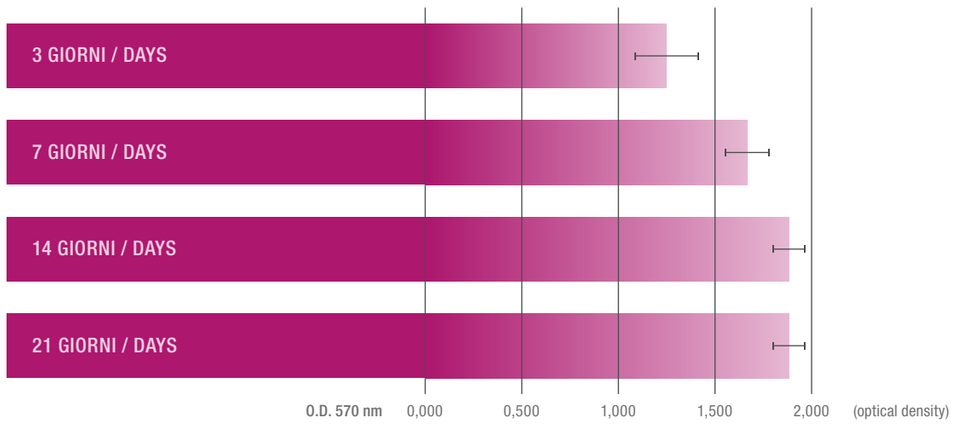
FIG. 2 - Hematoxylin/eosin stain.
Histological section of RE-BONE®.



Biocompatibility of RE-BONE® bone substitute

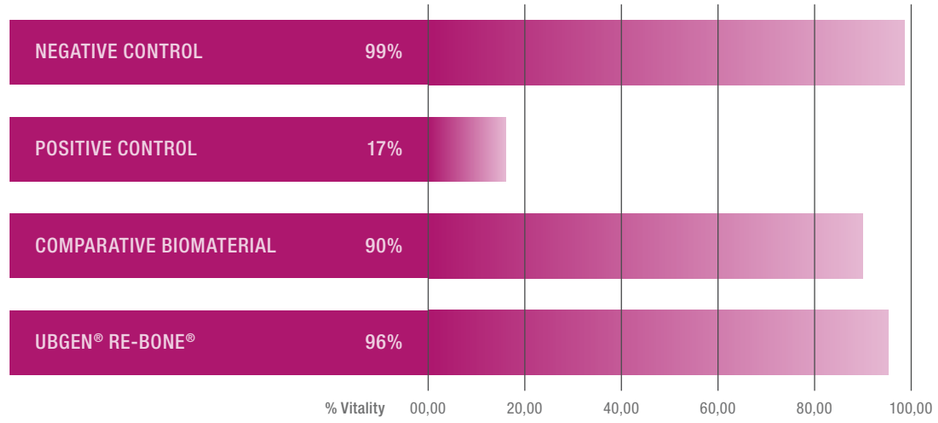
Laboratory studies and scientific literature have demonstrated the regenerative efficacy of RE-BONE® bone substitute produced by UBGEN®.

FIG. 3 - Proliferation ADSC (Adipose Derived Stem Cells) in culture on RE-BONE® bone substitute evaluated at different time intervals (MTT test).



By cultivating adipose-derived mesenchymal stem cells with RE-BONE® bone substitute, an increase in cell proliferation was documented, **until reaching 35% more cells than the starting cell population after a 14-day cell culture.**

FIG. 4 - Cellular viability test of osteoblasts.



Cell viability tests of osteoblasts cultured with RE-BONE® bone substitute or with other commercially available bovine-derived biomaterials have shown increased cell survival: 90% (comparison sample) versus 96% (RE-BONE® sample).

Osteoconductive capability

Osteoconductivity is the ability of the graft to ensure adhesion, survival and proliferation of the osteogenic cells, providing an interconnected structure through which the new cells can migrate and the new vessels can form.[2]

Studies conducted on animal models and humans in the maxillary sinus lift procedure have shown that the RE-BONE® bone substitute is capable of inducing excellent guided bone regeneration (GBR - Guided Bone Regeneration).[3]

2. Flnkemeier CG. Bone-grafting and bone-graft substitutes. Journal of Bone & Joint Surgery. 2002, 84:454-464.
3. Maxillary sinus augmentation with decellularized bovine compact particles: a radiological, clinical and histologic report of 4 cases. Antonio Scarano. BioMed Research International 2017.

Microporosity of the mineral structure

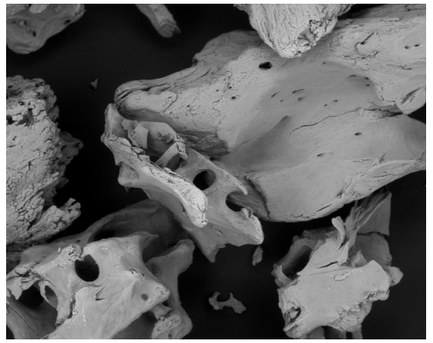
In literature it is widely documented that the microporosity of biomaterials is an important factor for tissue regeneration.
By increasing the contact surface of the graft with the cells of the surrounding tissue, the possibility for the biomaterials to be colonized by bone progenitor cells is increased.
Nanostructured biomaterials, in fact, mimic the extracellular matrix of the natural bone, creating a micro-environment that promotes cell adhesion, proliferation and differentiation.[4]

Scanning electron microscope (SEM) analyses were therefore conducted to qualitatively evaluate the microporosity of the RE-BONE® bone substitute.

The SEM analyses to qualitatively evaluate the microporosity of the RE-BONE® bone substitute demonstrate how the micro-roughness of the material, in terms of opening, cracking and non-continuity of the surface, is also present at a microscopic level (compatible with the cellular dimensions of the osteoblasts).

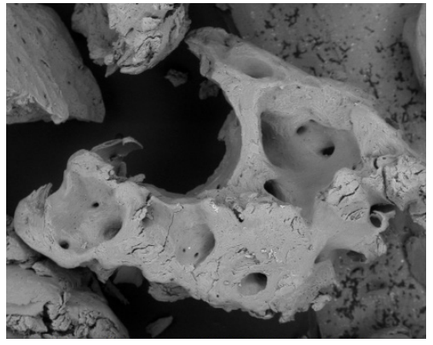
The presence of cracks inside the granule is also evident, which will allow the cells and blood vessels to colonize the graft in depth, shortening the resorption time of the bone substitute itself.

RE-BONE® Granules 100x

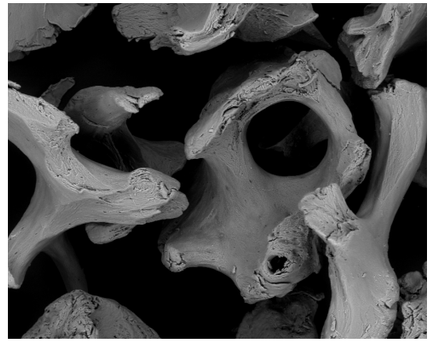


RE-BONE® Granules 100x

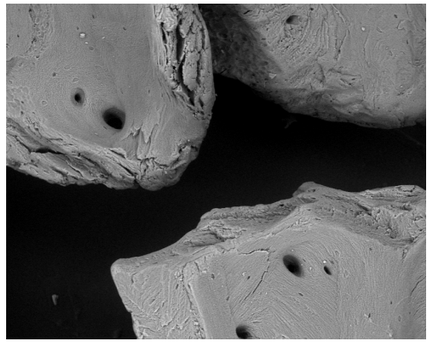
RE-BONE® Granules 150x



RE-BONE® Granules 195x



RE-BONE® Granules 300x



4. 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.

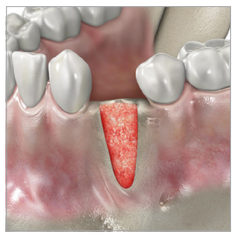
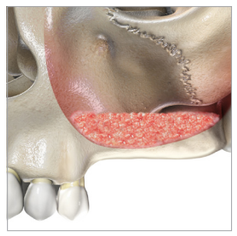
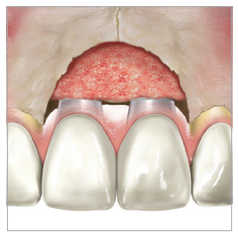
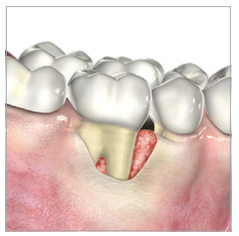
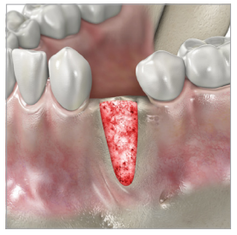
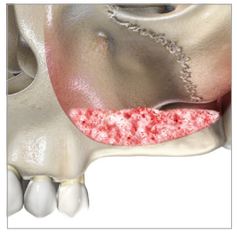
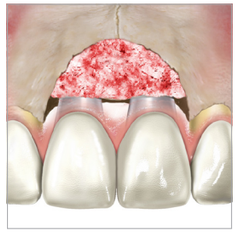
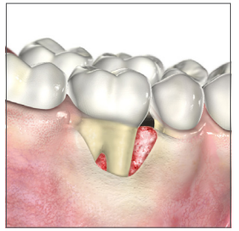
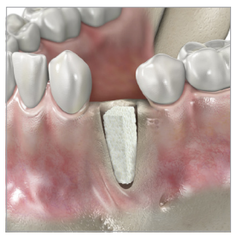
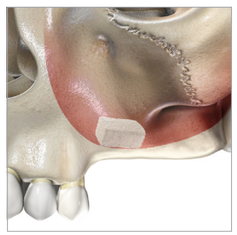
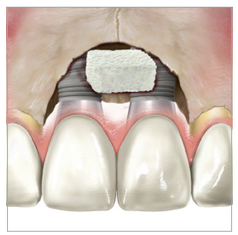
RE-BONE®
CLINICAL APPLICATIONS

Maintenance of socket and bone crest, maxillary sinus lift surgery, horizontal augmentation in two-walled defects, vertical augmentation in two-walled defects, dehiscences and fenestrations in peri-implant lesions, periodontal regeneration in infrabony defects and 2-3 wall furcation defects.

UBGEN

RE-BONE®

Clinical applications.

	Maintenance of alveolus and bone crest.	Maxillary sinus lift surgery.	Horizontal augmentation in 2-wall defects.	Vertical augmentation in 2-wall defects.	Dehiscences and fenestrations in peri-implant lesions.	Periodontal regeneration in intra-osseous defects and 2-3 wall furcation defects.[5]
Granules						
Syringe						
Block						

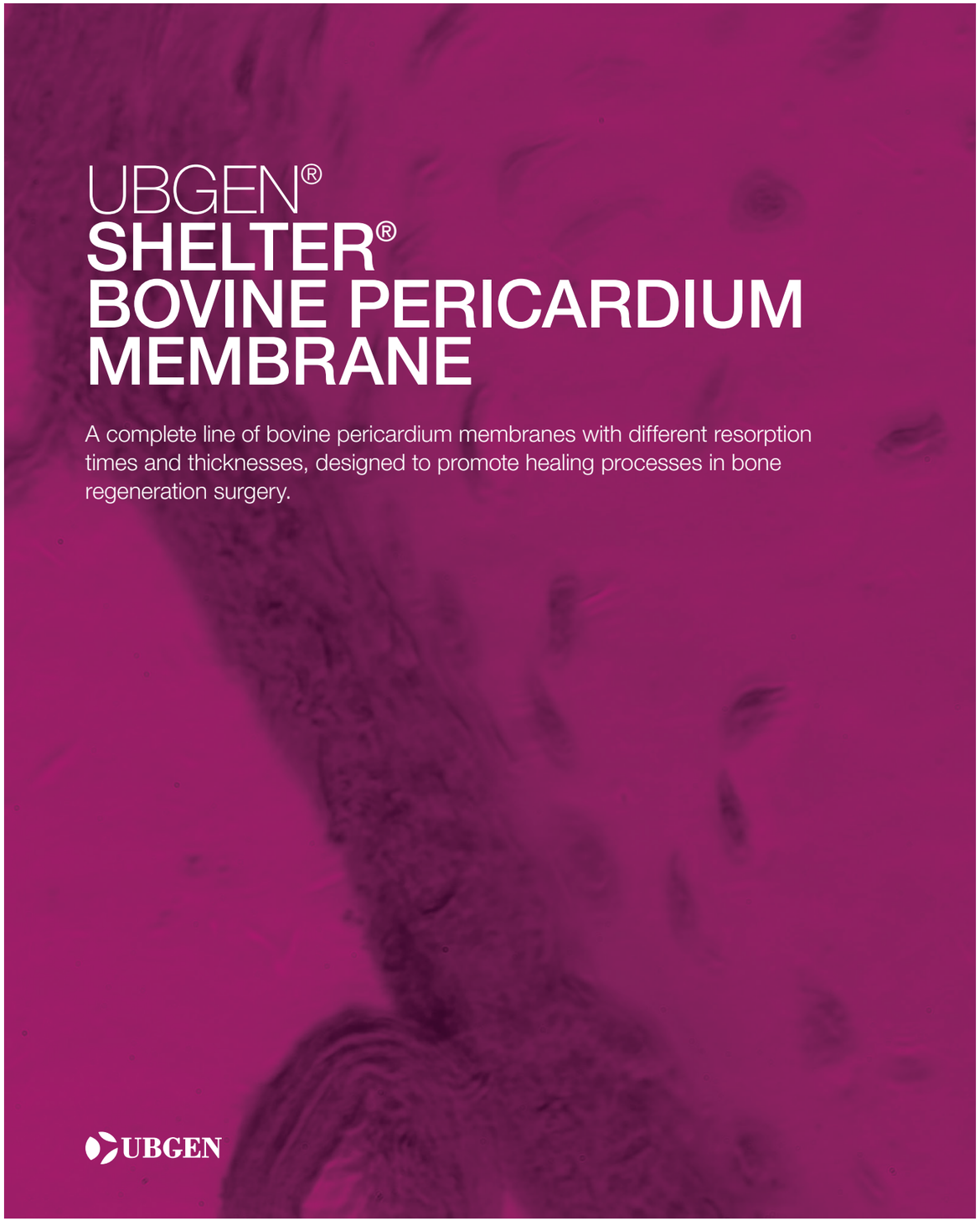
5. Bressan E, Favero V, Gardin C, Ferroni L, Iacobellis L, Favero L, Vindigni V, Berengo M, Sivolella S, Zavan B. Biopolymers for Hard and Soft Engineered Tissue: Application in Odontoiatric and Plastic Surgery Field. Polymers 2011, 3:509-526.

PRODUCT	PACKAGING	CODE
RE-BONE®	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)

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

PRODUCT	PACKAGING	CODE
RE-BONE®	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



UBGEN®
SHELTER® BOVINE PERICARDIUM MEMBRANE

A complete line of bovine pericardium membranes with different resorption times and thicknesses, designed to promote healing processes in bone regeneration surgery.

UBGEN

SHELTER®

The resorbable bovine pericardium membrane specifically designed for bone surgery in dentistry and produced by an entirely Italian supply chain.

At UBGEN® we have developed two types of membranes capable of using the beneficial effects of bovine pericardium which acts as a natural protective barrier:

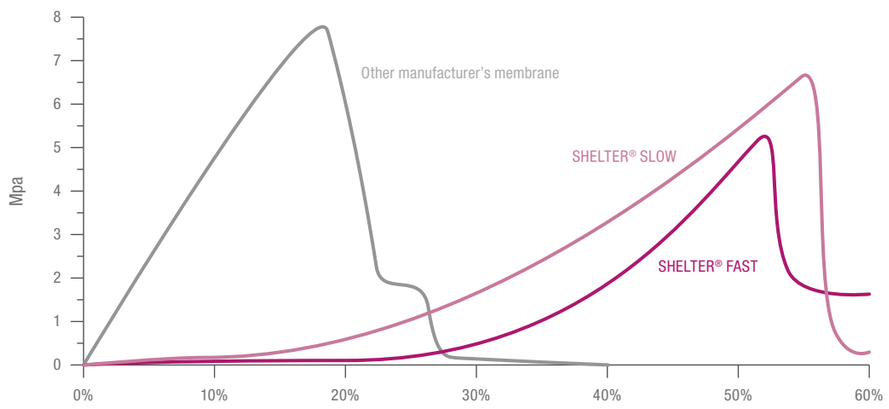
- **SHELTER® FAST**
  Membrane with natural resorption of 4-5 weeks and excellent traction resilience, thanks to the intertwined structure of the collagen fibres.
- **SHELTER® SLOW**
  Slow resorption membrane (4-6 months) thanks to the reinforced bonds of the collagen fibres, made more resistant by the ***Pericross*** cross-linking process capable of making the membrane resorbable in the long-term compared to the SHELTER® FAST version.
  In the thicker version, it can replace non-resorbable solutions in some types of surgery with the benefit of being completely reabsorbed and allowing to avoid the second removal surgery.

SHELTER® FAST and SHELTER® SLOW are occlusive to the passage of cells. They are designed to promote osteoblastic and periodontal ligament cells proliferation, protecting the site from soft tissue colonization; stable and resistant to traction, they are easy and manageable during placement.

Mechanical properties

SHELTER® membranes have been tested through mechanical traction tests from which it has been possible to obtain stress/strain curves (FIG. 5) with a characteristic trend of collagen materials as proof of the fact that the UBGEN®, production processes, and Pericross in particular, keep the structure of the collagen fibres and other components, such as elastin, intact.

FIG. 5 - Stress/strain curve for pericardium membrane



Zone 1: alignment of the fibres with very low elastic modulus. It indicates the need for a very low force to stretch the membrane.

Zone 2: the collagen fibrils are realigned with the direction of the effort and begin to oppose a certain resistance due to the inter and intra-molecular bonds.

Zone 3: inter-fibrillar bonds break and plastic deformation occurs until the sample breaks.

Based on the results obtained, it can be asserted that, even in hydrated conditions, SHELTER® FAST and SHELTER® SLOW have the typical natural structure of the pericardium:

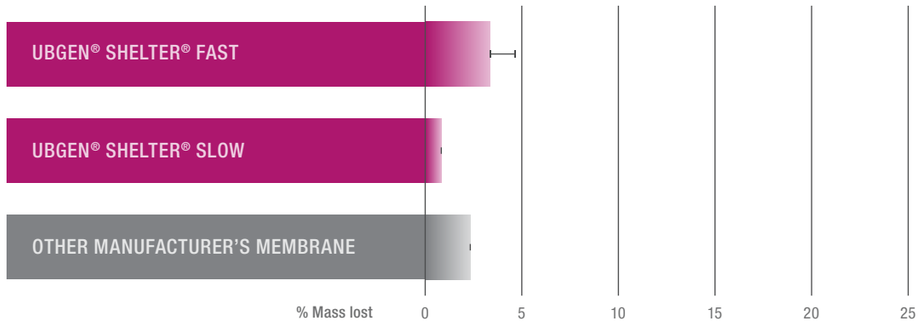
- a first region of fibrillar alignment
- an area of resistance to stress
- a third phase of gradual breaking with fibres that continue to hold the membrane together and in situ.

The graph clearly shows that the SHELTER® SLOW membrane requires higher tractive stress to reach the breaking point, indicating greater resistance to degradation.

Resorption properties

The SHELTER® FAST and SHELTER® SLOW membranes have also been subjected to *in vitro* degradation tests.

FIG. 6 - In vitro degradation tests conducted on SHELTER® FAST and SHELTER® SLOW compared to another manufacturer's membrane.

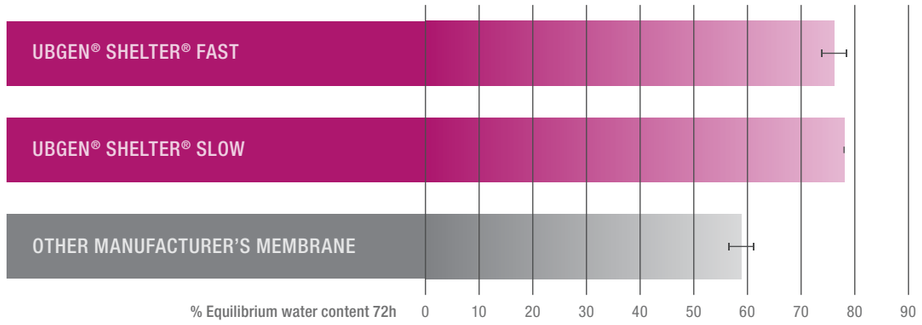


The cross-linking process of the SHELTER® SLOW membrane allows the latter to be reabsorbed in a longer period of time (4-6 months).
This is due to the greater number of intramolecular bonds between the collagen fibrils.
The SHELTER® FAST membrane, on the other hand, has a certified degradation time of 4-5 weeks.

Properties of hydration

The SHELTER® production process allows the membrane to maintain the reticular structure of the collagen matrix conferring a certain porosity after dehydration (FIG. 7).

FIG. 7 - Dehydration tests conducted on SHELTER® FAST and SHELTER® SLOW compared to another manufacturer's membrane.



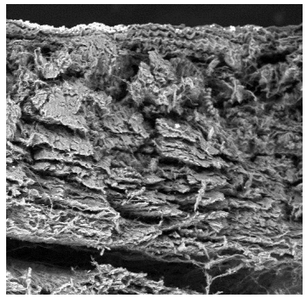
In vitro studies have shown that the SHELTER® membrane is highly hydrophilic, as it is capable of rapidly absorbing the solution it comes into contact with, while maintaining its three-dimensional structure (without collapsing).
Following hydration, SHELTER® acquires high adhesive properties and adaptation to surfaces: this is extremely important for applications in which the membrane must be used and must conform even to very irregular surfaces.

From this it can be seen that SHELTER® FAST and SHELTER® SLOW membranes are suitable for applications in the regeneration of alveolar bone tissue using the GBR and GTR techniques.

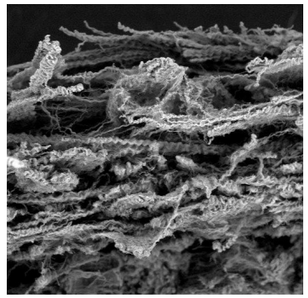
Their ability to hydrate makes them easy to handle, able to adhere to irregular surfaces even in difficult to reach positions.

UBGEN

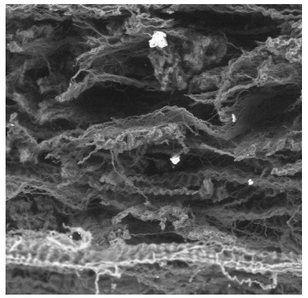
Images under scanning electron microscope (SEM)



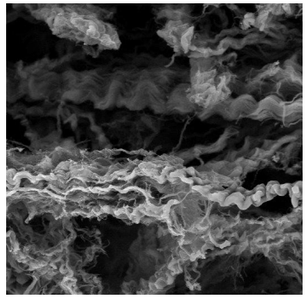
SHELTER® FAST,
cross-section, 100 µm



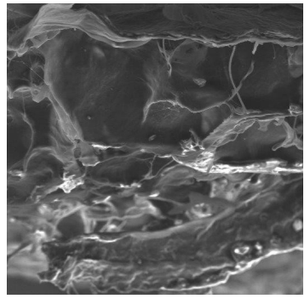
SHELTER® FAST,
cross-section, 100 µm



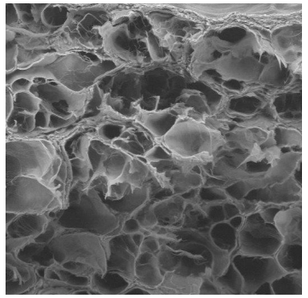
SHELTER® FAST,
cross-section, 100 µm



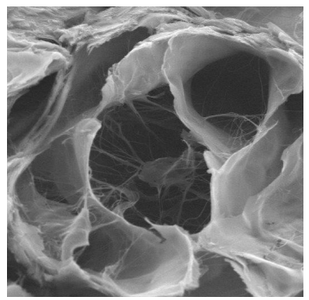
SHELTER® FAST,
cross-section, 10 µm



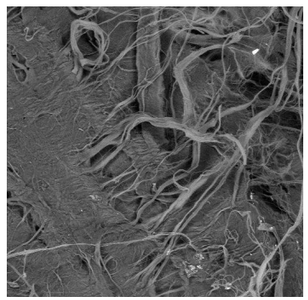
SHELTER® SLOW,
cross-section, 100 µm



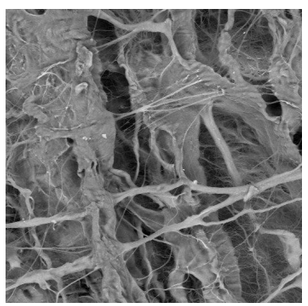
SHELTER® SLOW,
cross-section, 100 µm



SHELTER® SLOW,
cross-section, 20 µm



SHELTER® SLOW,
plane, 100 µm



SHELTER® SLOW,
plane, 10 µm

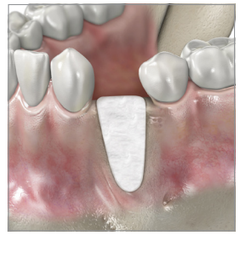
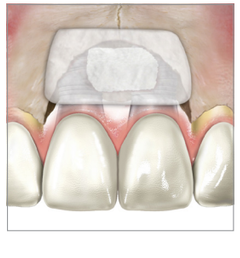
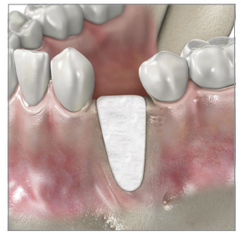
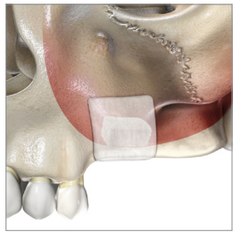
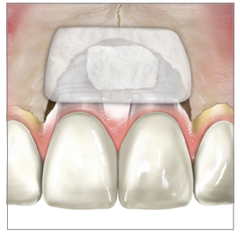
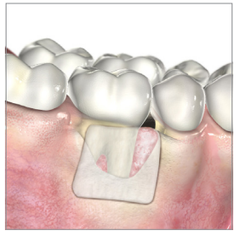
SHELTER®
CLINICAL APPLICATIONS

Maintenance of socket and bone crest, maxillary sinus lift surgery, horizontal augmentation in two-walled defects, vertical augmentation in two-walled defects, dehiscences and fenestrations in peri-implant lesions, periodontal regeneration in infrabony defects and 2-3 wall furcation defects.

UBGEN

SHELTER®

Clinical applications.

	Maintenance of alveolus and bone crest.	Maxillary sinus lift surgery.	Horizontal augmentation in 2-wall defects.	Vertical augmentation in 2-wall defects.	Dehiscences and fenestrations in peri-implant lesions.	Periodontal regeneration in intra-osseous defects and 2-3 wall furcation defects.[5]
FAST membrane 						
SLOW membrane 						

5. Bressan E, Favero V, Gardin C, Ferroni L, Iacobellis L, Favero L, Vindigni V, Berengo M, Sivolella S, Zavan B. Biopolymers for Hard and Soft Engineered Tissue: Application in Odontoiatric and Plastic Surgery Field. Polymers 2011, 3:509-526.

PRODUCT	PACKAGING	CODE
SHELTER® F	Pericardium membrane 15x20x0.2 mm	BMF04A
	Pericardium membrane 30x25x0.2 mm	BMF04B
	Pericardium membrane 50x30x0.2 mm	BMF04C
	Pericardium membrane 15x20x0.4 mm	BMF04D
	Pericardium membrane 30x25x0.4 mm	BMF04E
	Pericardium membrane 50x30x0.4 mm	BMF04F
	Pericardium membrane 15x20x0.8 mm	BMF04G
	Pericardium membrane 30x25x0.8 mm	BMF04H
	Pericardium membrane 50x30x0.8 mm	BMF04I
	Pericardium membrane 15x20x1 mm	BMF04J
	Pericardium membrane 30x25x1 mm	BMF04K
	Pericardium membrane 50x30x1 mm	BMF04L
SHELTER® S	Pericardium membrane 15x20x0.2 mm	BMS05A
	Pericardium membrane 30x25x0.2 mm	BMS05B
	Pericardium membrane 50x30x0.2 mm	BMS05C
	Pericardium membrane 15x20x0.4 mm	BMS05D
	Pericardium membrane 30x25x0.4 mm	BMS05E
	Pericardium membrane 50x30x0.4 mm	BMS05F
	Pericardium membrane 15x20x0.8 mm	BMS05G
	Pericardium membrane 30x25x0.8 mm	BMS05H
	Pericardium membrane 50x30x0.8 mm	BMS05I
	Pericardium membrane 15x20x1 mm	BMF05J
	Pericardium membrane 30x25x1 mm	BMF05K
	Pericardium membrane 50x30x1 mm	BMF05L

Bibliography

1. Finkermeier CG.
   Bone grafting and bone-graft substitutes.
   Journal of Bone & Joint Surgery 2002, 84: 454-464.
2. Robey PG.
   Vertebrate mineralized matrix proteins: structure and function.
   Connective Tissue Research 1996, 35: 131-136.
3. Mc Namara LM, et al.
   Attachment of osteocyte cell processes to the bone matrix.
   The anatomical record: advances in integrative anatomy and evolutionary biology (Hoboken) 2009, 292: 355-363.
4. Rodan GA, et al.
   Gene expression in osteoblastic cells.
   Critical Reviews in Eukaryotic Gene Expression 1991, 1(2): 85-98.
5. FInkemeier CG.
   Bone-grafting and bone-graft substitutes.
   Journal of Bone & Joint Surgery 2002, 84:454-464.
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.
7. Miller A.
   Collagen: The organic matrix of bone.
   Philosophical Transaction of the Royal Society B: Biological Sciences 1984, 304-455.
8. Roach HI.
   Why Does Bone-Matrix COntain Noncollagenous Proteins-the Possible Roles of Osteocalcin, Osteonectin, Osteopontin and Bone Sialoprotein in Bone Mineralization and Resorption. Cell Biology International 1994, 18:617-628.
9. Clarke B.
   Normal Bone Anatomy and Physiology.
   Clinical Journal of the American Society of Nephrology 2008, 3 (Suppl. 3): S131-S139.
10. Bressan E, Favero V, Gardin C, Ferroni L, Iacobellis L, Favero L, Vindigni V, Berengo M, Sivolella S, Zavan B.
    Biopolymers for Hard and Soft Engineered Tissue: Application in Odontoiatric and Plastic Surgery Field.
    Polymers 2011, 3:509-526.
11. Scarano A.
    Maxillary sinus augmentation with decellularized bovine compact particles: a radiological, clinical and histologic report of 4 cases.
    BioMed Research International 2017:2594670.
12. Scarano A, Inchingolo F, Murmura G, Traini T, Piattelli A, Lorusso F.
    Three-Dimensional Architecture and Mechanical Properties of Bovine Bone Mixed with Autologous Platelet Liquid, Blood, or Physiological Water: An In Vitro Study.
    Int J Mol Sci 2018;19(4).

Data on file with RE-BONE®/UBGEN®.

UBGEN®
ACTI-BONE® HYALURONIC ACID

Takes advantage of the regenerative properties of high molecular weight hyaluronic acid, widely documented in oral surgery.

UBGEN

ACTI-BONE®

Hyaluronic acid is one of the main components of connective tissues together with collagen and elastin fibres.
It is a polysaccharide naturally produced by the body in order to protect the tissues and keep them hydrated.

It is possible to apply ACTI-BONE® directly on the surgical site, or use it in combination with RE-BONE® bone substitute to obtain the so-called "sticky bone" or with SHELTER® FAST or SHELTER® SLOW pericardium membranes to enhance their chemotactic capacity.

ACTI-BONE®, why use it in oral surgery?

Hyaluronic acid is characterized by the ability to retain a very high amount of water.[1]

Anti-inflammatory properties

Numerous studies report that hyaluronic acid is effective in minimizing the inflammation in the surgical site, thus facilitating bone regeneration.[2]

Osteogenic and immunomodulatory properties

In case of trauma at a local level, hyaluronic acid is naturally produced by the body in order to promote the regeneration of soft tissues.[3]

Angiogenic properties

The ability of hyaluronic acid to interact with specific membrane receptors makes it a stimulating factor for the migration and proliferation of endothelial cells.[4]

Fibroblast proliferation

High molecular weight hyaluronic acid is recognized for its chemotactic and stimulatory properties toward fibroblasts, involved in the synthesis of new collagen.[5]

Bacteriostatic effect

Scientific studies have shown that the clinical application of hyaluronic acid in surgical therapy reduces bacterial contamination of the surgery site and the risk of post-operative infections.[6]

ACTI-BONE® finds its specific application in implant, periodontal, and extraction surgery, and in the treatment of peri-implantitis as a powerful adjuvant capable of regenerating bone tissue and protecting the implant and the implant site.

Bibliography

1. Sudha PN, Rose MH.
   Beneficial effects of hyaluronic acid.
   Adv Food Nutr Res. 2014;72:137-176. doi: 10.1016/B978-0-12-800269-8.00009-9. PMID: 25081082.

2. Casale M, Moffa A, Vella P, Sabatino L, Capuano F, Salvinelli B, Lopez MA, Carinci F, Salvinelli F.
   Hyaluronic acid: Perspectives in dentistry. A systematic review.
   Int J Immunopathol Pharmacol. 2016 Dec;29(4):572-582. doi: 10.1177/0394632016652906. Epub 2016 Jun 8. PMID: 27280412; PMCID: PMC5806851.

3. Xing, Fei, Zhou, Changchun, Hui, Didi, Du, Colin, Wu, Lina, Wang, Linnan, Wang, Wenzhao, Pu, Xiaobing, Gu, Linxia, Liu, Lei, Xiang, Zhou and Zhang, Xingdong.
   Hyaluronic acid as a bioactive component for bone tissue regeneration: Fabrication, modification, properties, and biological functions.
   Nanotechnology Reviews, vol. 9, no. 1, 2020, pp. 1059-1079. https://doi.org/10.1515/ntrev-2020-0084

4. Luo Y, Liang F, Wan X, Liu S, Fu L, Mo J, Meng X, Mo Z.
   Hyaluronic Acid Facilitates Angiogenesis of Endothelial Colony Forming Cell Combining With Mesenchymal Stem Cell via CD44/ MicroRNA-139-5p Pathway.
   Front Bioeng Biotechnol. 2022 Mar 8;10:794037. doi: 10.3389/fbioe.2022.794037. PMID: 35350177; PMCID: PMC8957954.

5. Kawano Y, Patrulea V, Sublet E, Borchard G, Iyoda T, Kageyama R, Morita A, Seino S, Yoshida H, Jordan O, Hanawa T.
   Wound Healing Promotion by Hyaluronic Acid: Effect of Molecular Weight on Gene Expression and In Vivo Wound Closure.
   Pharmaceuticals (Basel). 2021 Mar 28;14(4):301. doi: 10.3390/ph14040301. PMID: 33800588; PMCID: PMC8065935.

6. Pirnazar P, Wolinsky L, Nachnani S, Haake S, Pilloni A, Bernard GW.
   Bacteriostatic effects of hyaluronic acid.
   J Periodontol. 1999 Apr;70(4):370-4. doi: 10.1902/jop.1999.70.4.370. PMID: 10328647.

7. Lopez MA, Manzulli N, D'Angelo A, Candotto V, Casale M, Lauritano D.
   The use of hyaluronic acid as an adjuvant in the management of mucositis.
   J Biol Regul Homeost Agents. 2017 Dec 27;31(4 Suppl 2):115-118. PMID: 29202570.

8. Lopez MA, Manzulli N, D'Angelo A, Lauritano D, Casale M, Candotto V.
   The use of hyaluronic acid as an adjuvant in the management of periodontitis.
   J Biol Regul Homeost Agents. 2017 Dec 27;31(4 Suppl 2):119-122. PMID: 29202571.

9. Lopez MA, Manzulli N, D'Angelo A, Lauritano D, Papalia R, Candotto V.
   The use of hyaluronic acid as an adjuvant in the management of peri-implantitis.
   J Biol Regul Homeost Agents. 2017 Dec 27;31(4 Suppl 2):123-127. PMID: 29202572.

10. Fujioka-Kobayashi M, Müller HD, Mueller A, Lussi A, Sculean A, Schmidlin PR, Miron RJ.
    In vitro effects of hyaluronic acid on human periodontal ligament cells.
    BMC Oral Health. 2017 Jan 16;17(1):44. doi: 10.1186/s12903-017-0341-1. PMID: 28093072; PMCID: PMC5240222.

11. Zhao N, Wang X, Qin L, Zhai M, Yuan J, Chen J, Li D.
    Effect of hyaluronic acid in bone formation and its applications in dentistry.
    J Biomed Mater Res A. 2016 Jun;104(6):1560-9. doi: 10.1002/jbm.a.35681. Epub 2016 Apr 9. PMID: 27007721.

12. Salwowska NM, Bebenek KA, Żądło DA, Wcisło-Dziadecka DL.
    Physiochemical properties and application of hyaluronic acid: a systematic review.
    J Cosmet Dermatol. 2016 Dec;15(4):520-526. doi: 10.1111/jocd.12237. Epub 2016 Jun 21. PMID: 27324942.

13. Yazan M, Kocyigit ID, Atil F, Tekin U, Gonen ZB, Onder ME.
    Effect of hyaluronic acid on the osseointegration of dental implants.
    Br J Oral Maxillofac Surg. 2019 Jan;57(1):53-57. doi: 10.1016/j.bjoms.2018.08.014. Epub 2018 Dec 14. PMID: 30558816.

14. Cervino G, Meto A, Fiorillo L, Odorici A, Meto A, D'Amico C, Oteri G, Cicciù M.
    Surface Treatment of the Dental Implant with Hyaluronic Acid: An Overview of Recent Data.
    Int J Environ Res Public Health. 2021 Apr 27;18(9):4670. doi: 10.3390/ijerph18094670. PMID: 33925742; PMCID: PMC8125310.

UBGEN®
SAFE-BONE® TITANIUM MESH

Made-to-measure titanium membrane for the regeneration of large bone defects and designed for the specific needs of each patient.

Each reticular structure is customized to obtain a precise product, which accurately reflects the specific anatomical data of the patient.

UBGEN

SAFE-BONE®

HOW IS IT MADE?

SAFE-BONE® is produced through a selective laser melting process (SLM) using specific grade 5 titanium powders, historically recognized as inert and biocompatible.[1-2]

Each individual titanium mesh is designed to adapt to the patient's anatomical details, based on images created with CAD/CAM and an intra-oral scan provided by the clinician.

1. Sidambe AT. Biocompatibility of Advanced Manufactured Titanium Implants-A Review.Materials (Basel). 2014 Dec 19;7(12):8168-818 doi: 10.3390/ma7128168. PMID: 28788296; PMCID: PMC5456424.
2. Degidi M, Scarano A, Piattelli A. Regeneration of the alveolar crest using titanium micromesh with autologous bone and a resorbable membrane. J Oral Implantol. 2003;29(2):86-90. doi: 10.1563/1548-1336(2003)029<0086:ROTACU>2.3.CO;2. PMID: 12760452.

WHY USE TITANIUM MESH?

SAFE-BONE® is the most suitable solution in horizontal and vertical bone defects, in combination with a bone substitute.[3-4]

While any early exposure of a non-resorbable membrane almost always leads to an infection capable of compromising the result of the surgical technique, indeed, several studies show that in case of exposure of the mesh the success of the regeneration is not affected and the regenerated bone volume is maintained.[6-7]

SAFE-BONE® can be used alone or in combination with SHELTER® FAST or SHELTER® SLOW resorbable membranes.

Compared to pre-shaped titanium meshes, SAFE-BONE® offers many advantages, including speed and ease of application, requiring no further modelling or shaping adjustments.

UBGEN® offers the clinician the opportunity to fully customize the SAFE-BONE® structure, allowing for defining the thickness of the mesh, shape and size of the texture, as well as 3D planning of the placement of openings useful for future allocation of the implants.

Bibliography

1. Sidambe AT.
   Biocompatibility of Advanced Manufactured Titanium Implants-A Review.
   Materials (Basel). 2014 Dec 19;7(12):8168-8188. doi: 10.3390/ma7128168. PMID: 28788296; PMCID: PMC5456424.
2. Degidi M, Scarano A, Piattelli A.
   Regeneration of the alveolar crest using titanium micromesh with autologous bone and a resorbable membrane.
   J Oral Implantol. 2003;29(2):86-90. doi: 10.1563/1548-1336(2003)029<0086:ROTACU>2.3.CO;2. PMID: 12760452.
3. Xie Y, Li S, Zhang T, Wang C, Cai X.
   Titanium mesh for bone augmentation in oral implantology: current application and progress.
   Int J Oral Sci. 2020 Dec 30;12(1):37. doi: 10.1038/s41368-020-00107-z. PMID: 33380722; PMCID: PMC7773733.
4. Roccuzzo M, Ramieri G, Bunino M, Berrone S.
   Autogenous bone graft alone or associated with titanium mesh for vertical alveolar ridge augmentation: a controlled clinical trial.
   Clin Oral Implants Res. 2007 Jun;18(3):286-94. doi: 10.1111/j.1600-0501.2006.01301.x. Epub 2007 Feb 13. PMID: 17298495.
5. Scipioni A, Bruschi GB, Calesini G.
   The edentulous ridge expansion technique: a five-year study.
   Int J Periodontics Restorative Dent 1994; 14(5): 451-459. Clinical Oral Implants Research 2007; 18: 620–629.
6. Her S, Kang T, Fien MJ.
   Titanium mesh as an alternative to a membrane for ridge augmentation.
   J Oral Maxillofac Surg 2012;70:803-10.
7. Von Arx T, Kurt B.
   Implant placement and simultaneous perimplant bone grafting using a microtitanium mesh for graft stabilization.
   Int J Perio Rest Dent 1998;18:117-27.
8. Boyne P.
   Restoration of osseous defects in maxillofacial casualities.
   J Am Dent Assoc 1969;78:767-76.
9. Boyne JP, Cole MD, Stringer D, et al.
   A technique for osseous restoration of deficient edentulous maxillary ridges.
   J Oral Maxillofac Sur 1985;43:87-91.
10. Malchiodi L, Scarano A, Quaranta M, et al.
    Rigid fixation by means of titanium mesh in edentulous ridge expansion for horizontal ridge augmentation in the maxilla.
    Int J Oral Maxillofac Implants 1998;13:701-5.
11. Poli PP, Beretta M, Cicciu M, et al.
    Alveolar ridge augmentation with titanium mesh.
    A retrospective clinical study. Open Dent J 2014; 8: 148-158.
12. Rasia dal Polo M, Poli PP, Rancitelli D, et al.
    Alveolar ridge reconstruction with titanium meshes: a systematic review of the literature.
    Med Oral Patol Oral Cir Bucal 2014;19:e639-46.
13. Assenza B, Piattelli M, Scarano A, et al.
    Localized ridge augmentation using titanium micromesh.
    J Oral Implantology 2001;27:287-92.
14. Rakhmatia YD, Ayukawa Y, Furuhashi A, et al.
    Current barrier membranes: titanium mesh and other membranes for guided bone regeneration in dental applications.
    J Prosthodont Res 2013;57:3-14.
15. Leghissa GC, Zaffe D, Assenza B, et al.
    Guided bone regeneration using titanium grids: report of 10 cases.
    Clin Oral Implants Res 1999;10:62-8.
16. Corinaldesi G, Pieri F, Sapigni L, et al.
    Evaluation of survival and success rates of dental implants placed at the time of or after alveolar ridge augmentation with an autogenous mandibular bone graft and titanium mesh: a 3- to 8-year retrospective study.
    Int J Oral Maxillofac Implants 2009;24:1119-28.

Look deeply into nature to understand change

UBGEN® is the first integrated system for the preparation of platelet concentrates specifically designed for bone surgery in dentistry.

This technology and its applications provide a unique and complete solution in order to simplify the procedure used and certification of the method, allowing the clinician to achieve exclusive benefits in terms of predictability of results.

The role of platelets

Platelets play a key role in controlling the first phase of haemostasis. In recent years, the identification of some special molecules inside them - known as Platelet Growth Factors - has revealed new perspectives and possible applications in the medical and surgical field.

Numerous studies in the sector have highlighted the ability of platelets to metabolically stimulate various cell lines. These, in fact, can be induced to release growth factors which immediately intervene to stimulate the regeneration of injured tissues and significantly accelerate healing.

Each of these identified factors targets a specific cell line (skin, muscle, ligaments and tendons, bone, blood vessels), acting on the metabolism of the treated tissue with a synergistic, anti-inflammatory and reparative action.

Functions of platelet growth factors

Growth factors are locally and constantly released through continuous platelet degranulation.

Growth factors main properties are listed below:

- *they act proactively toward angiogenic processes;*
- *they are chemotactic towards the cells involved in the regenerative processes;*
- *they are mitogenic toward the cells they come into contact with, triggering a multiplier effect;*
- *they significantly increase cell membrane receptor expression.*

GROWTH FACTORS	EXPECTED EFFECT
PDGF Platelet Derived Growth Factor	Chemotactic for fibroblasts and macrophages, mitogen for fibroblasts, smooth muscle cells, endothelial cells.
TGF-1/2 Transforming Growth Factor	Angiogenesis mediator, chemotactic for fibroblasts, keratinocytes and macrophages.
VEGF Vascular Endothelial Growth Factor	Chemotactic and mitogen for endothelial cells, and a mediator of angiogenesis.
EGF Epidermal Growth Factor	Fibroblast mitogens, endothelial cells, keratinocytes, and an angiogenesis mediator.
FGF Fibroblast Growth Factor	Tissue organisation and regeneration mediator.

Treatment with platelet growth factors is widely used in many branches of medicine (orthopaedics, trichology, ophthalmology...) due to the proven properties of accelerating healing times and for providing significant improvements in the presence of trauma, wounds or injuries.

The APG® technique

The APG® (Autologous Platelets Gel) technique is the most advanced autologous system for obtaining a Platelets Concentrate.

This technology is based on the activation of platelets deriving from the patient's own blood. These are concentrated through centrifugation of a small sample of autologous blood (7-10 ml) and used to stimulate and accelerate tissue regeneration.

The one developed by UBGEN® is a procedure that offers truly extraordinary results in numerous pathologies, without side effects and which significantly reduces the recovery time in case of surgical procedures.

Patient benefits

Applying APG® to the area to be treated allows for a faster and better-quality healing process.
It involves an autograft, as the patient’s own platelets are reused on the same patient to generate and accelerate the reparative processes and tissue regeneration.

Benefits include:

- *reduction of pain and risk of infection*
- *improved healing time and quality of hard and soft tissue, thus accelerating osteogenetic processes*
- *possibility of combining it with medicinal products and/or other biomaterials such as grafts, and implants*

Research and analysis

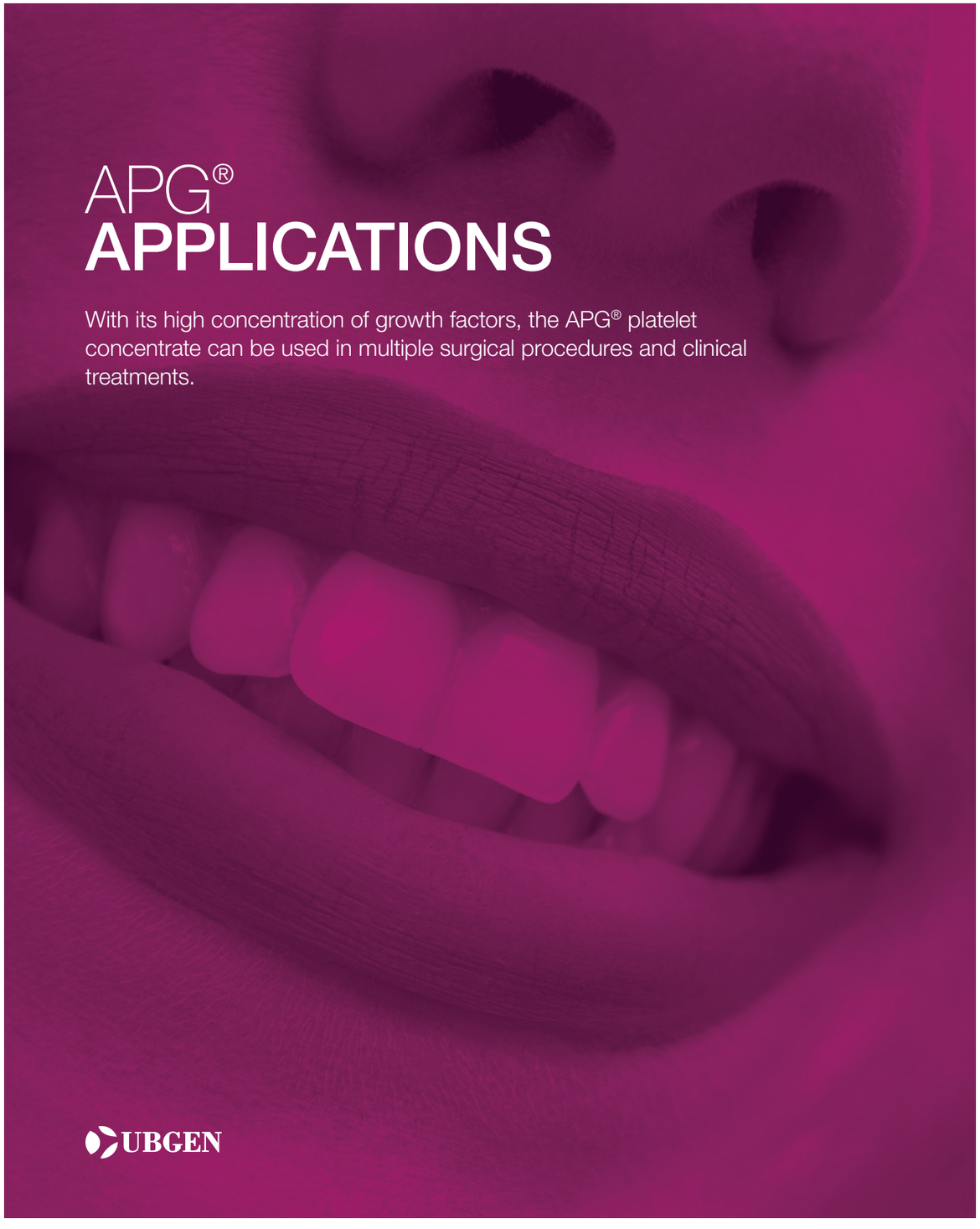
Several studies, also including tests conducted *in vivo* on animal models, suggest that numerous stimulatory molecules deriving from platelets, such as growth factors, can be used to accelerate the healing process of bone and soft tissues.[6-7]

In particular, a recent *in vitro* study conducted at the University of Chieti has demonstrated that the use of platelet concentrates combined with RE-BONE® allows for obtaining a single material defined as *sticky bone*.
This graft increases the mechanical resistance, creating an actual three-dimensional *scaffold* with high regenerative properties.[8]

The *sticky bone* technique allows to easily fill the bone defect, with reduced dispersion of the granules and a high level of stability. These characteristics allow it to be easily placed in bone defects of various sizes and shapes.

An additional benefit of using the *sticky bone* technique is the slow release of growth factors which lead to better wound healing.

6. Soft Tissue Augmentation with Autologous Platelet Gel and ß-TCP: A Histologic and Histometric Study in Mice. Antonio Scarano, Maurizio Ceccarelli, Massimiliano Marchetti, Adriano Piattelli, and Carmen Mortellaro. Biomed Res Int. 2016; 2016: 2078104. Published online 2016 Jul 12. doi: 10.1155/2016/2078104.
7. Soft Tissue Augmentation of the Face With Autologous Platelet-Derived Growth Factors and Tricalcium Phosphate. Microtomography Evaluation of Mice. Scarano, Antonio DDS, MD; Valbonetti, Luca DVM; Marchetti, Massimiliano MD; Lorusso, Felice DDS; Ceccarelli, Maurizio MD, PhD. Journal of Craniofacial Surgery: July 2016 - Volume 27 - Issue 5 - p 1212-1214 doi: 10.1097/.
8. Scarano A, Inchingolo F, Murmura G, Traini T, Piattelli A, Lorusso F. Three-Dimensional Architecture and Mechanical Properties of Bovine Bone Mixed with Autologous Platelet Liquid, Blood, or Physiological Water: An In Vitro Study. Int J Mol Sci. 2018;19(4). SCS.0000000000002712.



APG®
APPLICATIONS

With its high concentration of growth factors, the APG® platelet concentrate can be used in multiple surgical procedures and clinical treatments.

UBGEN

The APG® concentrate in dentistry

Numerous studies indicate that the use of platelet concentrate improves the final result and significantly increases the patient's well-being and healing speed, both alone and in combination with other surgical techniques, or even as a support for implant devices.

In dentistry, the APG® method is used for:

- accelerating healing of surgical wounds;
- decreasing post-operative inflammation and discomfort;
- surgical treatment of post-extraction sockets in bone regeneration combined with biomaterials;
- maxillary sinus surgery;
- periodontal and mucogingival surgery;
- surgical treatment of patients with bisphosphonate-induced osteonecrosis.

In all these treatments, the adhesive nature of APG® facilitates handling of implant material, in addition to improving haemostasis and wound closure compared to traditional techniques.[9]

Recent studies have also demonstrated that the use of platelet concentrates in the early stages of healing increases microvascular proliferation, followed by improved osteoblastic activity.

9. Parikh B, Navin S, Vaishali P. A comparative evaluation of healing with a computed tomography scan of bilateral periapical lesions treated with and without the use of platelet-rich plasma.Indian J Dent Res 2011;22:497-498.

APG® concentrate in cosmetic surgery

Since APG® concentrate contains a number of growth factors that regulate skin regeneration, it can induce the synthesis of collagen and other components of the skin by stimulating and activating fibroblasts, thereby encouraging skin cells to rejuvenate.

It has been shown that in aesthetic laser treatments the use of APG® concentrate increases skin elasticity, inducing a greater collagen synthesis by fibroblasts with consequent aesthetic improvement and rapid healing of skin wounds.[10]

The APG® method is used for:

- treating forehead wrinkles, wrinkles around the eyes, nasolabial folds, wrinkles on the neck and on the neckline
- treating acne scars
- toning and reduction of skin relaxation
- treating stretch marks
- treating and re-epithelialising skin wounds and ulcers[11]

10. Franco Forni, Massimo Marzagalli, Patrizia Tesei, Alessandra Grassi Platelet gel: applications in dental regenerative surgery Hospital Dentistry Service, Foundation I.R.C.C.S, San Matteo Hospital, Pavia, Italy.
11. Platelet-Rich Plasma (PRP) for Acute Muscle Injury: A Systematic Review Mohamad Shariff A. Hamid1*, Ashril Yusof2, Mohamed Razif Mohamed Ali3.

UBGEN®
GFONE® PLUS BLOOD PHASE SEPARATOR

The certified UBGEN®-branded separator dedicated to dentistry.

GFONE® PLUS blood phase separator

Class IIA medical device specifically designed for the separation of blood components, it is intuitive and easy to use, with the possibility of customizing the programs.

GFONE® PLUS KIT

Single-use kit for preparation and application of Platelet Gel in the dental field containing:

- 4 blue vials with anticoagulant of 9 ml
- 4 white vials for fractionation of 9 ml
- 2 red vials with serum activator of 9 ml
- 1 syringe of 2.5 ml
- 1 syringe for activator of 1 ml
- 1 21G needle with a safety device for withdrawal
- 1 20G needle

Bibliography

1. Arshdeep, Kumaran M S.
   Platelet-rich plasma in dermatology: Boon or a bane?
   Indian J Dermatol Venereol Leprol 2014;80:5-14.

2. Ning Zhang, Yong-Ping Wu, Sheng-Jun Qian, Chong Teng, Shuai Chen, and Hang Li.
   Research Progress in the Mechanism of Effect of PRP in Bone Deficiency Healing.
   Hindawi Publishing Corporation The Scientific World Journal Volume 2013, Article ID 134582, 7 pages http://dx.doi.org/10.1155/2013/134582.

3. Department of Orthopaedics and Rehabilitation, University of Iowa http://uiortho.com/index.php/ prp.html

4. Albanese et al.
   Immunity & Ageing 2013, 10:23.
   Platelet-rich plasma (PRP) in dental and oral surgery: from the wound healing to bone regeneration. http://www.immunityageing.com/content/10/1/23.

5. Parikh B, Navin S, Vaishali P.
   A comparative evaluation of healing with a computed tomography scan of bilateral periapical lesions treated with and without the use of platelet-rich plasma.
   Indian J Dent Res 2011;22:497-498.

6. Franco Forni, Massimo Marzagalli, Patrizia Tesei, Alessandra Grassi.
   Platelet gel: applications in dental regenerative surgery Hospital Dentistry Service, Foundation I.R.C.C.S, San Matteo Hospital, Pavia, Italy.

7. Platelet-Rich Plasma (PRP) for Acute Muscle Injury: A Systematic Review Mohamad Shariff A. Hamid1*, Ashril Yusof2, Mohamed Razif Mohamed Ali3.

8. Muscles Ligaments Tendons J.
   2013 Jul-Sep; 3(3): 139-149. PMCID: PMC3838322 Published online Aug 11, 2013.
   Augmenting tendon and ligament repair with platelet-rich plasma (PRP) Ting Yuan,1,2 Chang-Qing Zhang, 2 and James H-C. Wang1.

9. Comparison of short-term results of intraarticular platelet-rich plasma (PRP) and hyaluronic acid treatments in early-stage gonarthrosis patients.
   Guler O., Mutlu S., Isyar M, Seker A., Kayaalp ME, Mahirogullari M.; Eur J ORthop Surg Traumatol 2014 Aug 2.

10. Dae Hun Kim, M.D., Young Jin Je, M.S., Chang Deok Kim, Ph.D., Young Ho Lee, M.D.1, Young Joon Seo, M.D., Jeung Hoon Lee, M.D., Young Lee, M.D.
    Can Platelet-rich Plasma Be Used for Skin Rejuvenation?
    Evaluation of Effects of Platelet-rich Plasma on Human Dermal Fibroblast Departments of Dermatology and 1Anatomy, College of Medicine, Chungnam National University, Daejeon, Korea.

11. Platelet growth factors in treating wounds Use of platelet growth factors in treating wounds and soft-tissue injuries P. Ro'man and Z. Bolta.

12. Shin MK1, Lee JH, Lee SJ, Kim NI.
    Platelet-rich plasma combined with fractional laser therapy for skin rejuvenation.
    Dermatol Surg. 2012 Apr;38(4):623-30. doi: 10.1111/j.1524-4725.2011.02280.x. Epub 2012 Jan 30.

13. Application of platelet-rich plasma in plastic surgery: clinical and in vitro evaluation.
    Tissue Eng Part C Methods. 2009 Dec;15(4):625-34. doi: 10.1089/ten.TEC.2008.0518.
    Cervelli V, Gentile P, Scioli MG, Grimaldi M, Casciani CU, Spagnoli LG, Orlandi A.

14. Cervelli,1 S. Garcovich,2 A. Bielli,3 G. Cervelli,4 B. C. Curcio,1 M. G. Scioli,3 A. Orlandi,3 and P. Gentile.
    The Effect of Autologous Activated PlateletRich Plasma (AA-PRP) Injection on Pattern Hair Loss: Clinical and Histomorphometric.
    Hindawi Publishing Corporation BioMed Research InternationalVolume 2014, Article ID 760709, 9 pages http://dx.doi.org/10.1155/2014/760709 Evaluation V.
    1,51 Plastic and Reconstructive Surgery Department, University of Rome Tor Vergata.

15. Antonio Scarano, Maurizio Ceccarelli, Massimiliano Marchetti, Adriano Piattelli, and Carmen Mortellaro.
    Soft Tissue Augmentation with Autologous Platelet Gel and ß-TCP: A Histologic and Histometric Study in Mice.
    Biomed Res Int. 2016; 2016: 2078104. Published online 2016 Jul 12. doi: 10.1155/2016/2078104

16. Scarano, Antonio DDS, MD; Valbonetti, Luca DVM; Marchetti, Massimiliano MD; Lorusso, Felice DDS; Ceccarelli, Maurizio MD, PhD.
    Soft Tissue Augmentation of the Face With Autologous Platelet-Derived Growth Factors and Tricalcium Phosphate. Microtomography Evaluation of Mice.
    Journal of Craniofacial Surgery: July 2016 - Volume 27 - Issue 5 - p 1212-1214 doi:10.1097/SCS.0000000000002712

17. Scarano A, Inchingolo F, Murmura G, Traini T, Piattelli A, Lorusso F.
    Three-Dimensional Architecture and Mechanical Properties of Bovine Bone Mixed with Autologous Platelet Liquid, Blood, or Physiological Water: An In Vitro Study.
    Int J Mol Sci. 2018;19(4).

18. De Pascale MR, Sommese L, Casamassimi A, Napoli C. Platelet derivatives in regenerative medicine: an update.
    Transfus Med Rev. 2015 Jan;29(1):52-61. doi: 10.1016/j.tmrv.2014.11.001.
    Epub 2014 Nov 18. PMID: 25544600.

19. Marchetti E, Mancini L, Bernardi S, Bianchi S Cristiano L, Torge D, Marzo G, Macchiarelli G.
    Evaluation of Different Autologous Platelet Concentrate Biomaterials: Morphological and Biological Comparisons and Considerations.
    Materials MDPI, May 2020.

20. Scarano A., Inchingolo F., Rapone B., Lucchina AG., Qorri E., Lorusso F.
    Role of Autologous Platelet Gel (APG) in Bone Healing: A Rabbit Study Appl.
    Sci. 2021, 11, 395. https://doi.org/10.3390/app11010395

21. Scarano A, Bugea C, Leo L, De Oliveira PS, Lorusso F.
    Autologous Platelet Gel (APG): A Preliminary Evaluation of the Mechanical Properties after Activation with Autologous Thrombin and Calcium Chloride.
    Materials 2021, 14, 3941. https://doi.org/10.3390/ma14143941

UBGEN®
ACTIGEN®
TREATMENT OF IMPLANT SURFACE

The new and exclusive implant surface coating made with bovine collagen.
A biological surface that facilitates and accelerates the osteointegration process of the implant.

UBGEN

The strength of compatibility

ACTIGEN® is the exclusive surface treatment in bovine collagen type I which significantly promotes the osseointegration of dental implants.
Dental implants with this surface treatment are class III medical devices available only from a few selected, certified implant manufacturers.

UBGEN® has developed the only bioactive surface treatment, with osteoinductive effect, with the ability to:

- stimulate platelet activity
- predispose the surface of the implants to be rapidly colonized by the bone[6-7]
- increase the bone/implant contact area (Bone Implant Contact - BIC)
- shorten recovery times

For our users, this means being able to make a safe choice, with predictable results even in patients defined as high-risk.

6. Morra M eta al. Surface analysis and effects on interfacial bone microhardness of collagen-coated titanium implants: a rabbit model. Int J Oral Maxillofac Implants. 2005 Jan-Feb;20(1):23-30.
7. Morra M et al. Collagen I-coated titanium surfaces: mesenchymal cell adhesion and in vivo evaluation in trabecular bone implants. J Biomed Mater Res A. 2006 Sep 1;78(3):449-58.

Analysis and research of the UBGEN® process

Starting from today's implant coating technologies, UBGEN® has invested in research for a biological surface able to accelerate and increase the osseointegration process of implant fixtures.

The topography and the chemical composition of the surface are used as a tool to address cellular behaviour and therefore the process of bone regeneration. For some time, we have been talking about the possibility of activating implant surfaces through their functionalization with different biologically active molecules for bone formation: from peptide synthesis, to growth factors and many others.[3-4]

In order to make the most performing and bioactive product available, UBGEN® has worked on the development of ACTIGEN®, the exclusive implant surface coating.

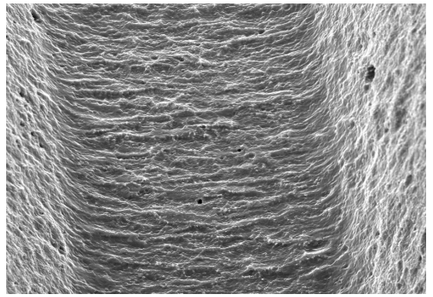
3. Morra M. Biochemical modification fo titanium surfaces: peptides and ECM proteins. Eur Cell Mater. 2006 Jul 24;12:1-15.
4. De Jonge LT et al. Organic-inorganic surface modifications for titanium implant surfaces. Pharm Res. 2008 Oct;25(10):2357-69. doi: 10.1007/s11095-008-9617-0. Epub 2008 May 29.

ACTIGEN®: the evolution of the implant coating

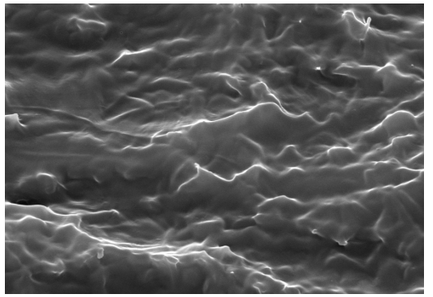
The significant result in terms of osseointegration was obtained by immobilizing type I collagen, extracted from bovine dermis, on etched surfaces. This type of collagen is the main component of the organic portion of the bone, where it acts as a support for vital processes.[5-7]

In the regenerative processes, in fact, the osteoblastic cells initially deposit a collagen matrix which is then mineralized. This collagen matrix exerts a series of positive biological effects. This in fact promotes the adhesion of osteoblasts and osteoclasts and acts as a cofactor for numerous growth factors.[5-16]

The use of collagen was a decisive choice for UBGEN® in order to create a biological solution that anticipates future needs in the world of dentistry.



IMPLANT COLLAGEN LOOP DETAIL - 100 µm



COLLAGEN SURFACE DETAIL - 10 µm

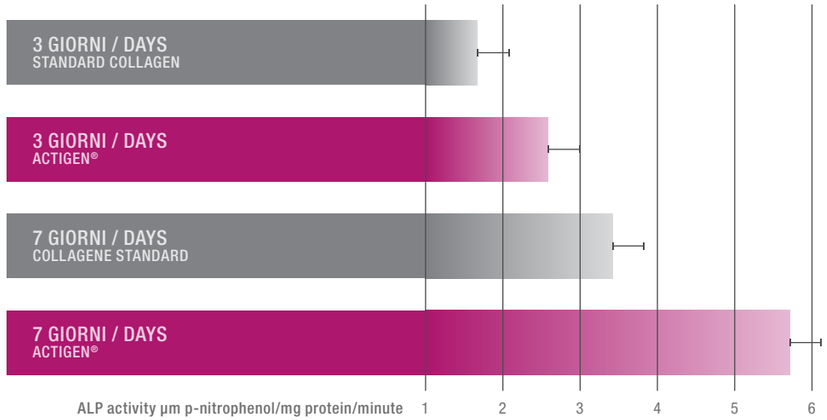
5. Morra M et al. Surface engineering of titanium by collagen immobilization. Surface characterization and in vitro and in vivo studies. Biomaterials. 2003 Nov;24(25):4639-54.
7. Morra M et al. Collagen I-coated titanium surfaces: mesenchymal cell adhesion and in vivo evaluation in trabecular bone implants. J Biomed Mater Res A. 2006 Sep 1;78(3):449-58.
16. Regazzoni C. et al. Type I collagen induces expression of bone morphogenetic protein receptor type II Biochem. Biophys. Res. Commun. 2001; 4 ; 283(2): 316-322.

The presence of ACTIGEN® on the implant surface anticipates the first stage of the new bone formation process, presenting a matrix ready for mineralization by the designated cells (osteoblasts) and subsequent bone growth, at the same time, providing biochemical stimulation to osseointegration events.

In vitro *test*

To confirm the cell adhesion properties and stimulation of cell differentiation of collagen, some *in vitro* tests on implants coated with the ACTIGEN® treatment have been published

Alkaline Phosphatase (ALP) Enzyme Production Test



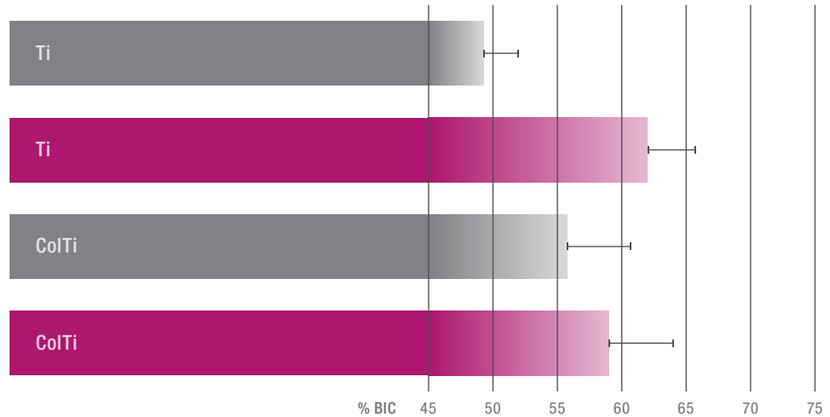
Test on the production of the enzyme alkaline phosphatase (ALP) by osteoblasts cultured on titanium bars and titanium bars coated with collagen. The results after 3 and 7 days of culture show that the collagen-coated titanium produced more ALP, the main marker of osteoblastic activity, confirming the role of collagen inducing pro-osteogenic activity.

The collagen coating was applied to titanium screws which were then inserted into rabbit femurs for an in vivo assessment after four weeks.
The trabecular bone showed improvements of the bone-implant contact surface compared to the control (non-treated titanium implant) which corresponds to faster regeneration of the bone surrounding the implant site.

A second set of implants was inserted into rabbit femurs and histomorphometric analyses were performed at two and four weeks (Fig. 12).

After two weeks, these analyses showed a significant increase in bone-implant contact surface, whereas at four weeks bone healing was complete on both implant surfaces.
These data support the hypothesis that collagen induces faster bone production at the interface with the implant in accordance with the biological role of collagen.

Histomorphometric evaluation of Ti and ColTi implants.



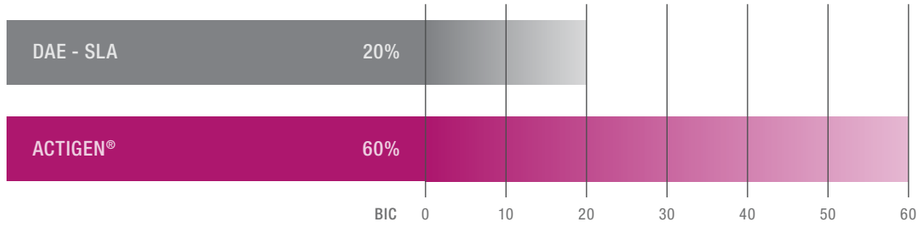
Case report

In a series of case reports made on animals in 2016, 160 implants with ACTIGEN® coating were inserted following a strict surgical and clinical follow-up protocol, in order to demonstrate the effectiveness of the coating with the following guidelines:

- placement in native bone D4
- uncovering after 10 weeks
- ASA 1 patient

Upon uncovering, two tests were performed to demonstrate the achievement of implant stability: the percussion test and the torque removal test at 20 N·cm.
All surgical steps were documented with x-rays and photographs.
After one year, all the implants are correctly osseointegrated and stable, as verified when the implant was uncovered after ten weeks.

Implant stability test.



ACTIGEN® the difference lies in the result

Data analysis from histomorphometric studies on implants treated with ACTIGEN® coating indicate that the localization of collagen molecules on the interface has increased both the percentage of bone-implant contact and bone growth within the loops in a statistically significant manner.

The results, therefore, demonstrate that ACTIGEN® surface treatment allows for an increase of up to 3 times the BIC (Bone Interface Contact) compared to the traditional surface in just two weeks.[6]

Why collagen?

- stimulates angiogenesis
- promotes cell adhesion
- promotes osteoblastic behaviour
- facilitates remodelling and mineralization

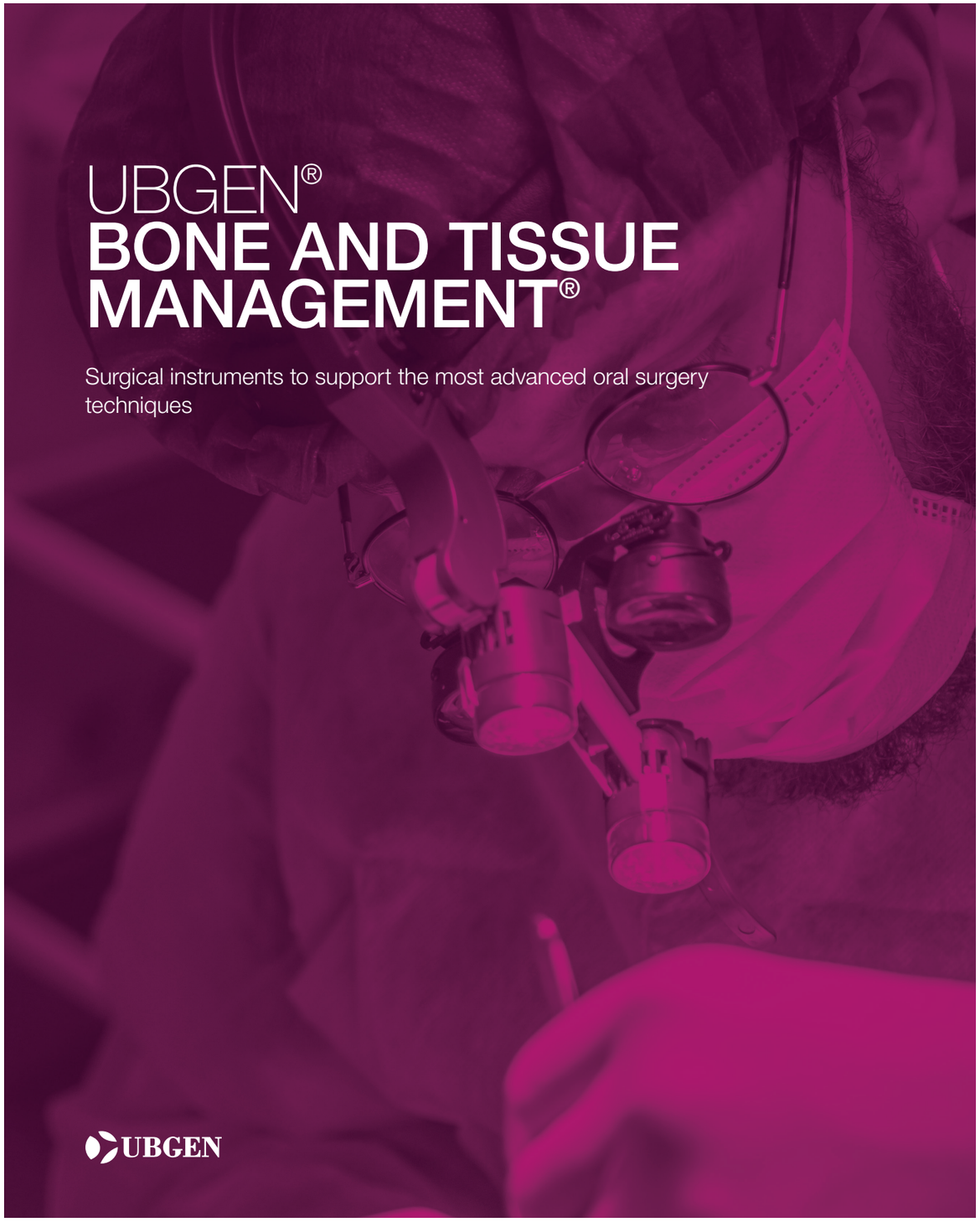
What benefits does it involve?

- predisposes the surface of the implants to be rapidly colonized by the bone
- increases BIC
- allows for faster regeneration of the bone, with better results, also in terms of quality
- stimulates platelet activity
- protection and safety of the patient (the class III certification provides a far more rigorous protocol compared to other classes)

6. Morra M eta al. Surface analysis and effects on interfacial bone microhardness of collagen-coated titanium implants: a rabbit model. Int J Oral Maxillofac Implants. 2005 Jan-Feb;20(1):23-30.

ACTIGEN® Bibliography

1. Boyan BD et al.
   Titanium surface roughness alters responsiveness of MG63 osteoblast-like cells to 1 alpha, 25-(OH)2D3.
   J Biomed Mater Res. 1998 Jan;39(1):77-85.
2. Lincks J et al.
   Response of MG63 osteoblast-like cells to titanium and titanium alloy is dependent on surface roughness and composition.
   Biomaterials 1998; 19(23): 2219.2232.
3. Morra M.
   Biochemical modification for titanium surfaces: peptides and ECM proteins.
   Eur Cell Mater. 2006 Jul 24;12:1-15.
4. De Jonge LT et al.
   Organic-inorganic surface modifications for titanium implant surfaces.
   Pharm Res. 2008 Oct;25(10):2357-69. doi: 10.1007/s11095-008-9617-0. Epub 2008 May 29.
5. Morra M et al.
   Surface engineering of titanium by collagen immobilization. Surface characterization and in vitro and in vivo studies.
   Biomaterials. 2003 Nov;24(25):4639-54.
6. Morra M eta al.
   Surface analysis and effects on interfacial bone microhardness of collagen-coated titanium implants: a rabbit model.
   Int J Oral Maxillofac Implants. 2005 Jan-Feb;20(1):23-30.
7. Morra M et al.
   Collagen I-coated titanium surfaces: mesenchymal cell adhesion and in vivo evaluation in trabecular bone implants.
   J Biomed Mater Res A. 2006 Sep 1;78(3):449-58.
8. Baslé MF et al.
   Type I collagen in xenogenic bone materials regulates attachement and spreading of osteoblasts over the beta 1 integrin subunit.
   Orthopade 1998; 27(2): 136-142.
9. Paralkar VM et al.
   Interaction of osteogenin, a heparin binding bone morphogenetic protein, with type IV collagen.
   J Biol Chem. 1990 Oct 5;265(28):17281-4.
10. Toroian D et al.
    The size exclusion characteristics of type I collagen: implication for the role of noncollagenous bone constituents in mineralization.
    J. Biol. Chem. 1990; 5; 265(28): 17281-17284.
11. Sampath T.K. Dissociative extraction and recostruction of extracellular matrix components.
12. Green J et al.
    Cell-matrix interaction in bone: type I collagen modulates signal transduction in osteoblast like cells.
    Am. J. Physiol. 1995; 268(5 Pt 1): C1090-1103.
13. Liu G. et al.
    Effect of type I collagen on the adhesion, proliferation and osteoblastic gene expression of bone marrow-derived mesenchymal stem cells.
    Chin J. Traumatol. 2004; 7(6): 358-362.
14. Mizuno M. et al.
    Type I collagen-induced osteoblastic differentiation of bone-marrow cells mediated by collagen-alpha2beta1 integrin interaction.
    J. Cell Physiol. 2000; 184(2): 207-213.
15. Gungormus M. et al.
    The effect of osteogenesis of type I collagen applied to experimental bone defects.
    Dent. Traumatol. 2004; 7(6).
16. Regazzoni C. et al.
    Type I collagen induces expression of bone morphogenetic protein receptor type II.
    Biochem. Biophys. Res. Commun. 2001; 4 ; 283(2): 316-322.
17. Morra M, Cassinelli C, Cascardo G, Bollati D, Baena RR.
    Gene expression of markers of osteogenic differentiation of human mesenchymal cells on collagen I-modified microrough titanium surfaces.
    J Biomed Mater Res A 2011; 96(2):449-55.

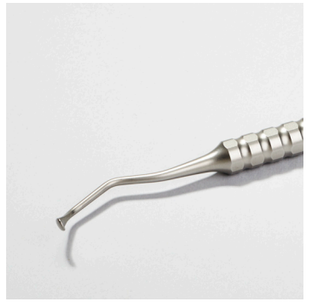


BONE AND TISSUE MANAGEMENT®

To complete the solutions available for clinicians, UBGEN® offers a range of surgical instruments to support the most advanced oral surgery techniques.

SURGICAL INSTRUMENTS

UBGEN® provides clinicians with a set of surgical instruments designed for the most complex oral and pre-implant regenerative surgery operations: from an innovative tray for periodontal microsurgery, a kit for osteosynthesis and screws for fixing membranes, to a set of expanders for the split crest surgical technique.



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