



UBGEN®

Специалисты костной хирургии в стоматологии

# UBGEN PRESENTS OTiGEN SYSTEM

Биоактивная поверхность лечение крупного рогатого скота коллаген, плюс хирургические компоненты и аксессуары

Процесс перекрестных ссылок на производство перикарда крупного рогатого скота с медленной резорбцией мембраны

Actigen® and Bone & Tissue Management

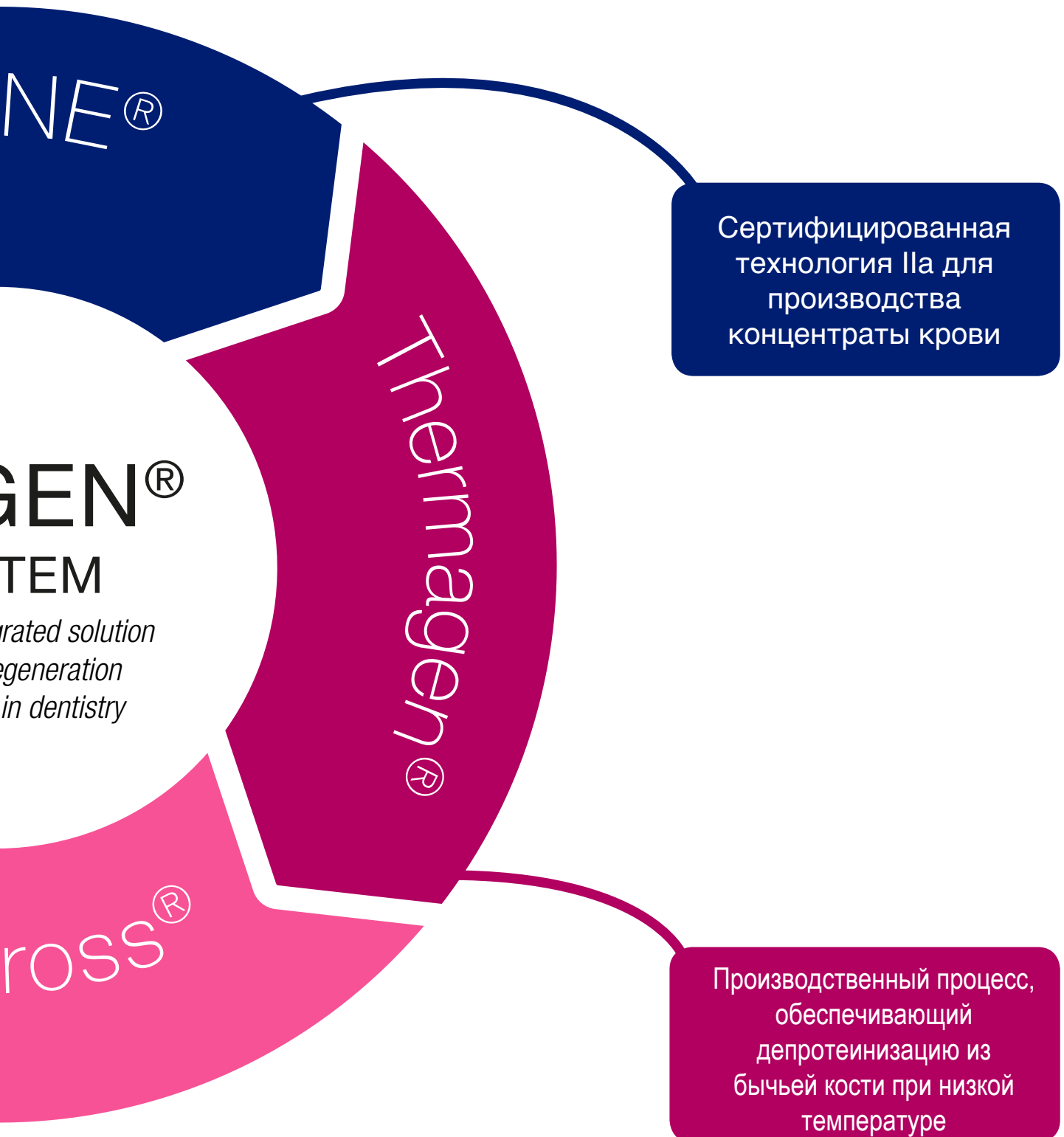
GF-O

## OTiGEN SYSTEM

*The first integrated system for bone repair specialists*

Pericard

Специалисты по костной хирургии в стоматологии Ubgen создали OTiGEN SYSTEM: первую полную систему продуктов и услуг, специально разработанную для удовлетворения потребностей тех, кто работает в тканевой инженерии, с особым упором на стоматологию.



Панорама компаний, работающих в области биомедицины в Европе, а следовательно, и в Италии, состоит из двух совершенно разных бизнес-реалий.

С одной стороны, есть транснациональные компании, которые, безусловно, внимательно относятся к технологическим инновациям, но часто из-за медленных и расслоенных процессов принятия решений не очень реагируют на преобразование этих инноваций в рыночные продукты.

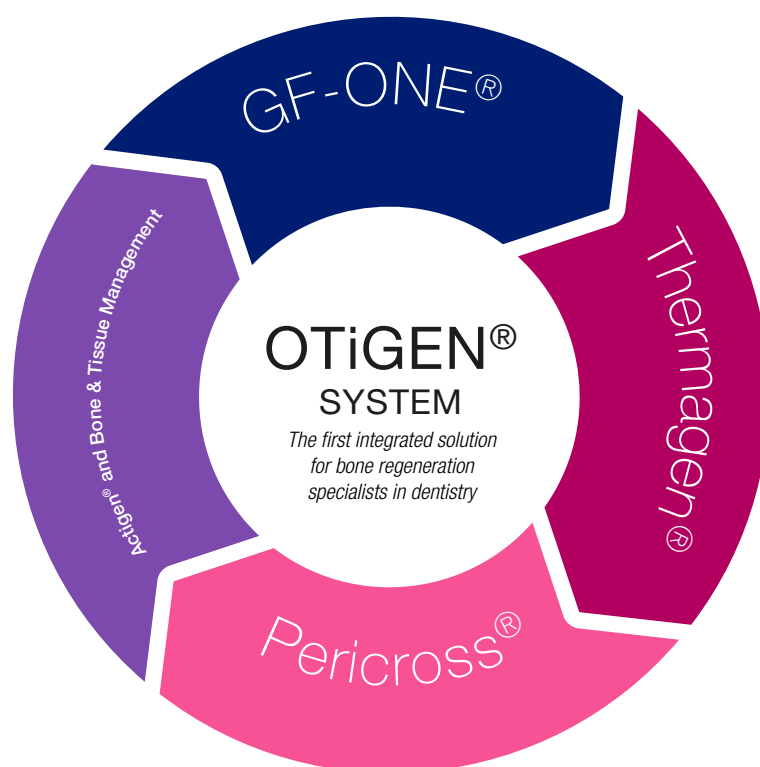
С другой стороны, существует множество малых предприятий, обычно менее склонных к инновациям, часто из-за недальновидного управленческого отношения, которое рассматривает экономические риски как непосредственный риск, а не как конкурентное преимущество в будущем.

У нас в UBGEN совершенно иное видение, мы твердо верим в технологические инновации и считаем вложения в них фундаментальным элементом для предвидения будущего. Поэтому мы разработали бережливую структуру, которая способна адаптироваться к меняющимся условиям рынка.

Из анализа, который мы провели внутри компании, мы поняли, что решения, предлагаемые в области биомедицины другими коммерческими организациями, являются неполными, универсальными и недифференцированными.

По этой причине клиницисту необходимо обратиться к разным поставщикам, чтобы получить все, что ему нужно для работы в области костной хирургии в стоматологической сфере. Это подразумевает своего рода «сделай сам» при закупке оборудования и материалов, что также может привести к нежелательным результатам, вызванным неизбежной несовместимостью между различными продуктами.

Вот почему в UBGEN мы создали OTiGEN SYSTEM: в то время как наши конкуренты предоставляют только некоторые компоненты, часто даже не предназначенные специально для стоматологической хирургии, мы создали первую полную систему продуктов и услуг, специально разработанных для удовлетворения потребностей тех, кто работает в тканевая инженерия с особым упором на стоматологию.



Таким образом, OTiGEN SYSTEM является связующим звеном, которое позволяет клиницисту иметь единственного коммерческого партнера, способного обслуживать его / его на 360 °: от начальных фаз с концентратами, полученными из крови, до ушивания раны через нашу кость.

Для наших партнеров это означает наличие первой и единственной интегрированной системы, в которой каждый компонент был разработан для взаимодействия с другими, обеспечивая полную совместимость и предсказуемость результатов.



# RE-BONE®

Специальная линия заменителей костей крупного рогатого скота, обработанных при низкой температуре для ускорения регенерации твердых ткани в хирургии костной реконструкции.



## RE-BONE® BONE SUBSTITUTE

RE-BONE ® - это костный заменитель бычьего происхождения, обработанный при низкой температуре с помощью инновационного производственного процесса Thermagen ®, сертифицированный CE и произведенный исключительно итальянской цепочкой поставок.

В то время как другие производители поставляют заменители костей бычьего происхождения, обработанные при высокой температуре, или не используют сырье бычьего происхождения (свиное, конское или синтетическое), мы улучшаем выигрышные характеристики заменителя костей крупного рогатого скота с помощью инновационного низкотемпературного производственного процесса Thermagen®. , гарантируя высокую биосовместимость, большую пористость гранул и отсутствие керамизации с относительной полной реабсорбцией сырья.

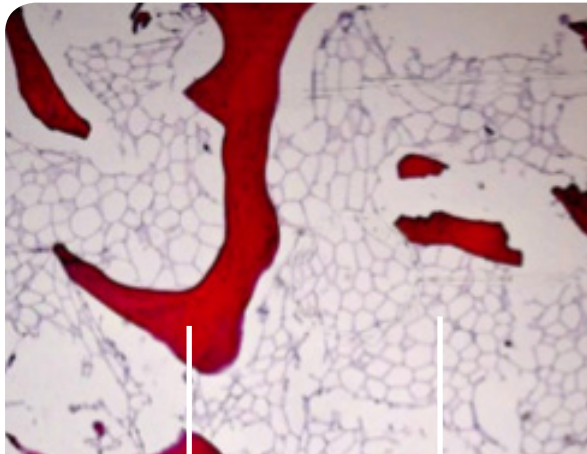
Эта технология децеллюляризации сырья была разработана нашей командой биоинженеров и впоследствии подтверждена испытаниями, проведенными Департаментом биологии Университета Падуи.

Помимо Thermagen ®, наш секрет заключается в выборе сырья. В UBGEN мы знаем каждый этап производственной цепочки: от качества земли, используемой для выпаса скота, до естественного возделывания, используемого для производства кормов, до здорового состояния помещений, в которых содержатся сами животные.

Если животные живут и растут хорошо, в здоровой окружающей среде, которая учитывается в их территориальных характеристиках, производные продукты по сути соответствуют требованиям здоровья и безопасности.

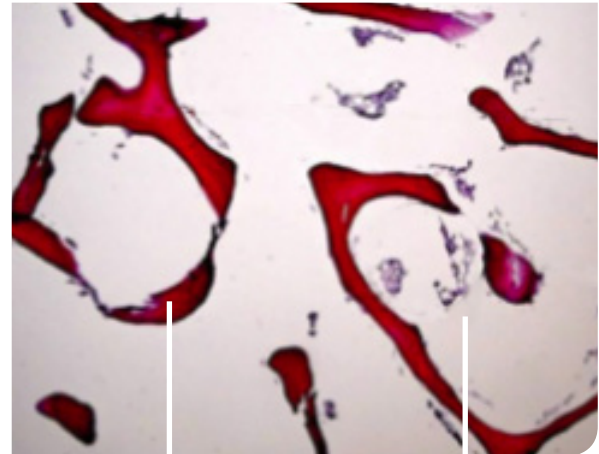
RE-BONE® - костный заменитель, очень похожий на костную ткань человека. Следовательно, он позволяет создать благоприятную среду для хемотаксиса, пролиферации остеобластов и неоангиогенеза благодаря поддержанию белков внеклеточного матрикса. 7

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



Bone Tissue      Adipose Tissue

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



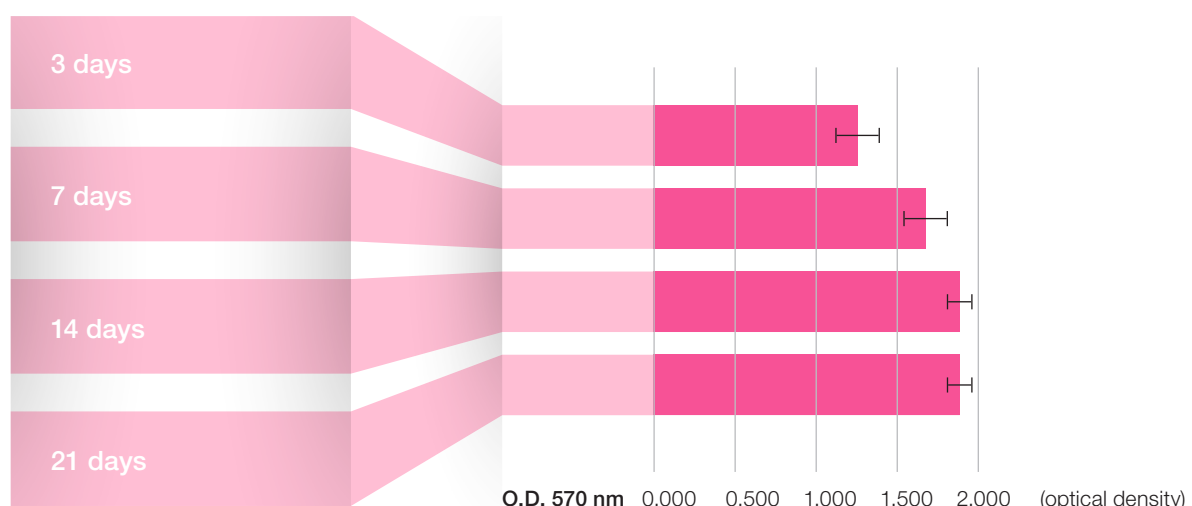
Bone Tissue      Adipose Tissue

## 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).

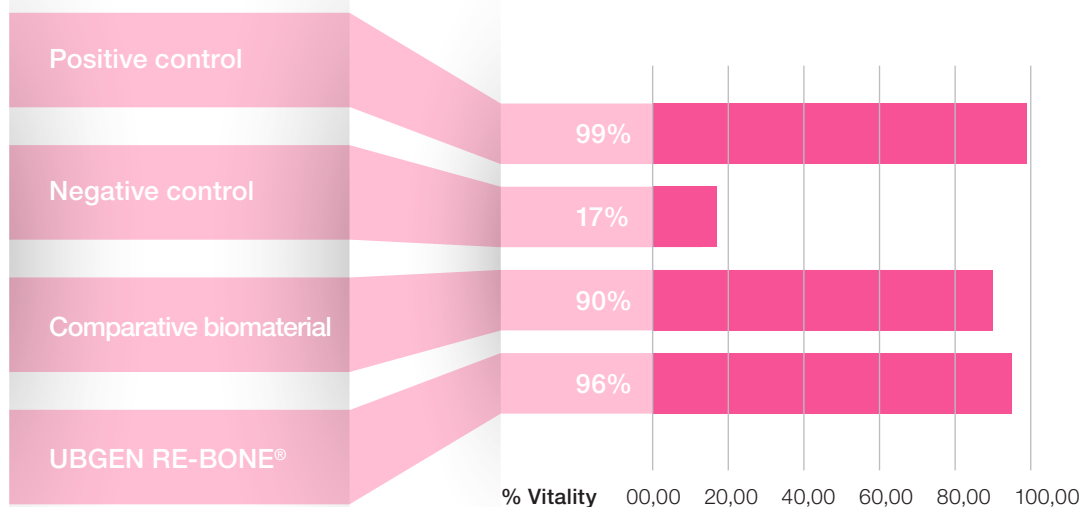


By growing adipose-derived mesenchymal stem cells with RE-BONE®, cell proliferation increased up to 35% after more than 14 days of culture.

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.



By comparing the cellular viability of the osteoblasts in contact with RE-BONE with other commercially available bovine derived biomaterials, a higher cell survival can be seen, from 90% (comparison sample) to 96% (RE-BONE sample).

## 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.<sup>5</sup>

*Studies on humans<sup>11</sup> 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)<sup>13</sup>, 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.

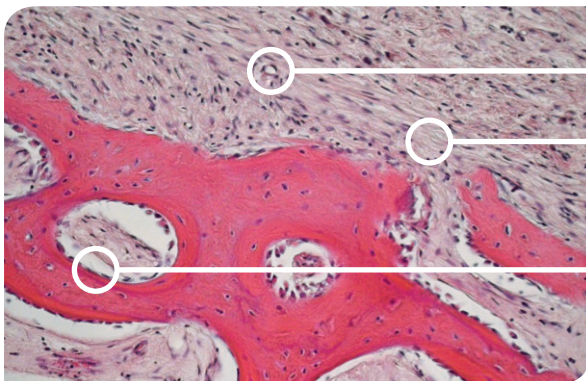
It is also possible to notice the approach of the osteoblasts towards the contact surface of the biomaterial/host tissue and their insertion in the structure of the biomaterial with the deposition of collagen fibers.

**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.<sup>9</sup>*

#### BIOMATERIAL



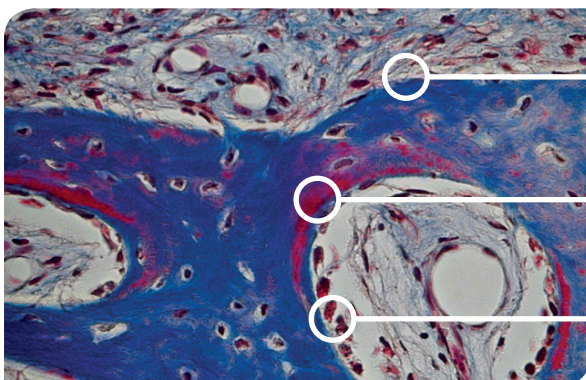
Vessel.

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.

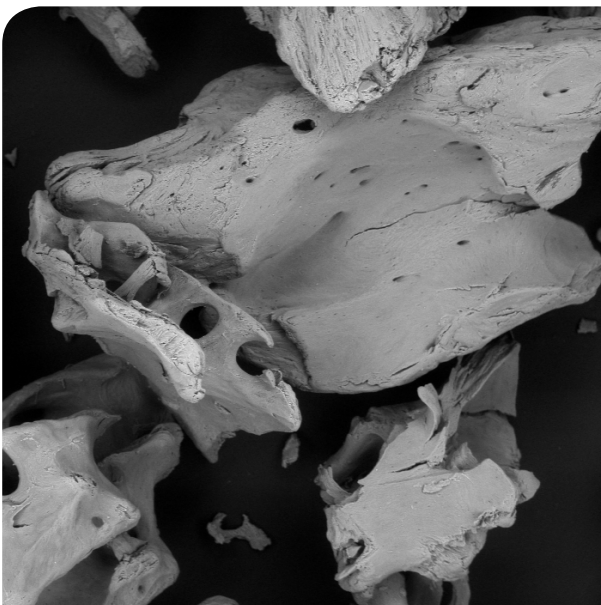
## Microporosity of the mineral structure

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.<sup>6</sup>

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.*



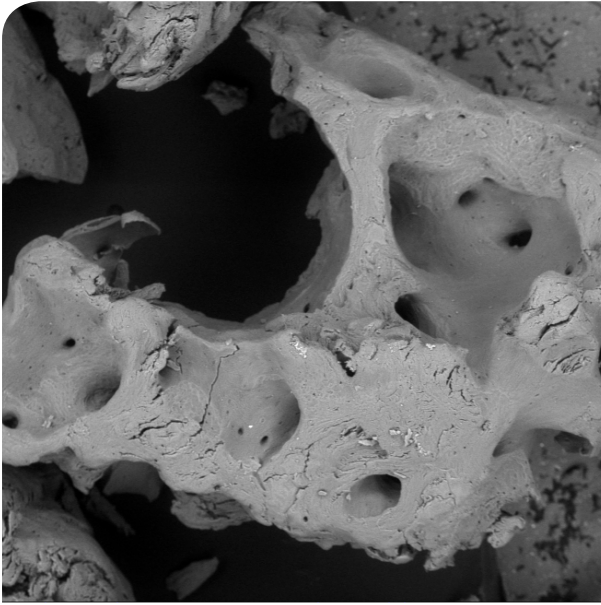
RE-BONE 100x granules



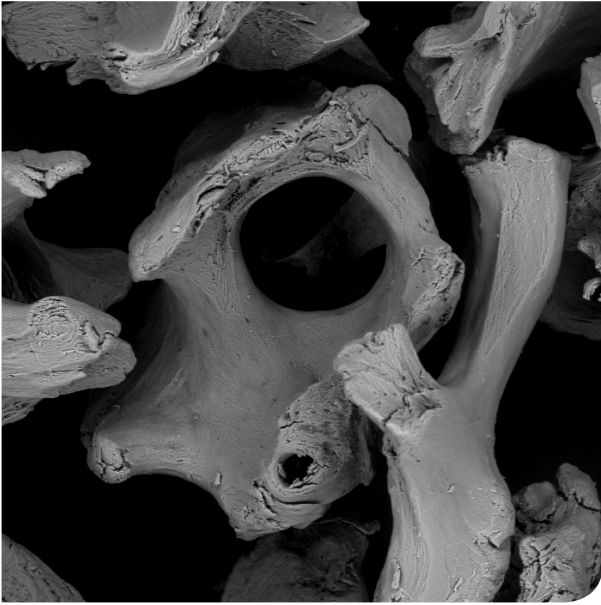
RE-BONE 100x granules

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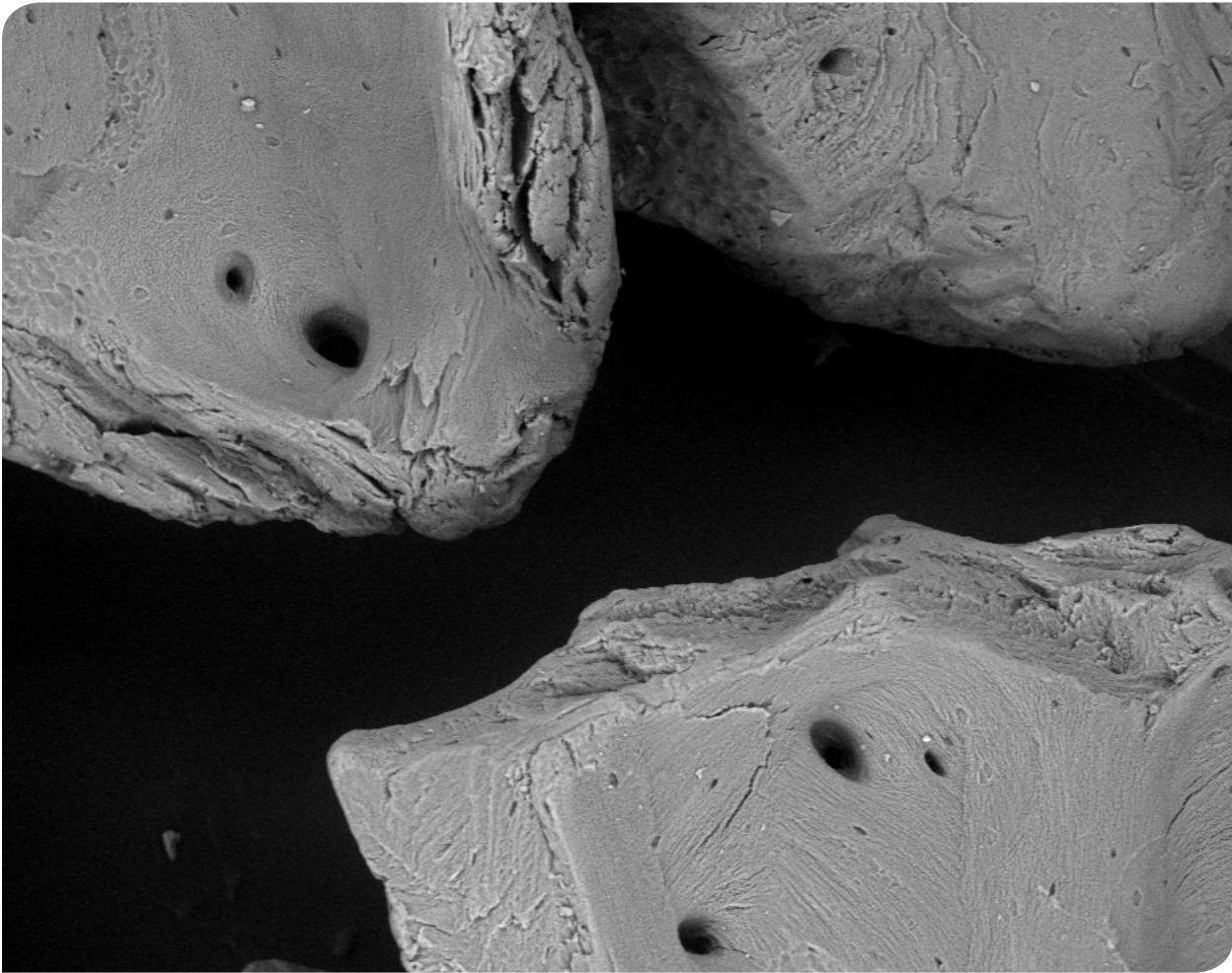
6. Gardin C, Ferroni L, Favero L, Stellini E, Stomaci D, Sivoiella S, Bressan E, Zavan B. Nanostructured Biomaterials for Tissue Engineered Bone Tissue Reconstruction. International Journal of Molecular Science. 2012, 13: 737-757.



RE-BONE 150x granules



RE-BONE 195x granules



RE-BONE 300x granules



# RE-BONE<sup>®</sup>

## clinical applications

Support of the alveolus and bone crest.

Sinus lift surgery.

Horizontal increase in two-wall defects.

Vertical increase in two-wall defects.

Dehiscences and fenestrations in peri-implant lesions.

Periodontal regeneration in intra-osseous defects and

2-or 3-wall furcation defects.

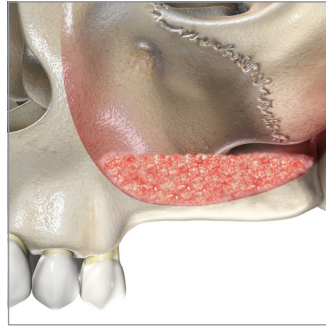
# RE-BONE® clinical applications

Support of the alveolus and bone crest.

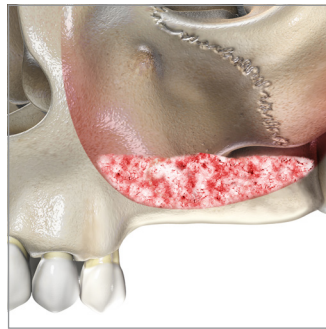
Sinus lift surgery.

Horizontal increase in 2-wall defects.

## Granules



## Syringe



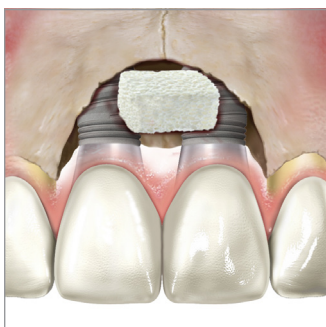
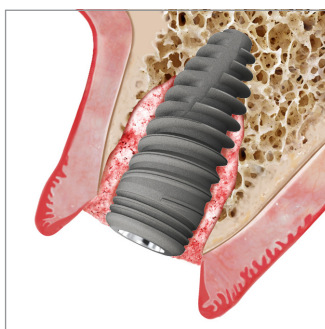
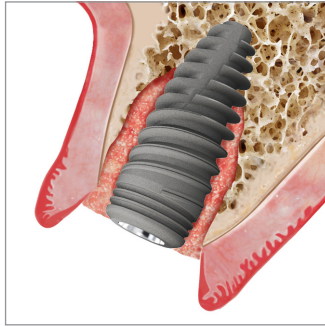
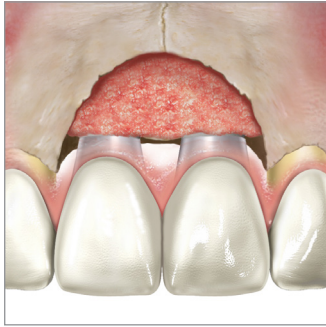
## Block



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.



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

RE-BONE®



PRODUCT	CODE
RE-BONE granules vial cortico-cancellous 0,25g - 0,25-1 mm	BM01A (pack of 1) BM01A6 (pack of 6)
RE-BONE granules vial cortico-cancellous 0,5g - 0,25-1 mm	BM01B (pack of 1) BM01B6 (pack of 6)
RE-BONE granules vial cortico-cancellous 1g - 0,25-1 mm	BM01C (pack of 1) BM01C6 (pack of 6)
RE-BONE granules vial cortico-cancellous 2g - 0,25-1 mm	BM01D (pack of 1) BM01D6 (pack of 6)
RE-BONE granules vial cortico-cancellous 0,5g - 1-2 mm	BM01E (pack of 1) BM01E6 (pack of 6)
RE-BONE granules vial cortico-cancellous 1g - 1-2 mm	BM01F (pack of 1) BM01F6 (pack of 6)
RE-BONE granules vial cortico-cancellous 2g - 1-2 mm	BM01G (pack of 1) BM01G6 (pack of 6)
RE-BONE granules vial cortico-cancellous 5g - 1-2 mm	BM01H (pack of 1) BM01H6 (pack of 6)
RE-BONE granules vial cancellous 0,25g - 0,25-1 mm	BM01I (pack of 1) BM01I6 (pack of 6)
RE-BONE granules vial cancellous 0,5g - 0,25-1 mm	BM01J (pack of 1) BM01J6 (pack of 6)
RE-BONE granules vial cancellous 1g - 0,25-1 mm	BM01K (pack of 1) BM01K6 (pack of 6)
RE-BONE granules vial cancellous 2g - 0,25-1 mm	BM01L (pack of 1) BM01L6 (pack of 6)
RE-BONE granules vial cancellous 0,5g - 1-2 mm	BM01M (pack of 1) BM01M6 (pack of 6)
RE-BONE granules vial cancellous 1g - 1-2 mm	BM01N (pack of 1) BM01N6 (pack of 6)
RE-BONE granules vial cancellous 2g - 1-2 mm	BM01O (pack of 1) BM01O6 (pack of 6)
RE-BONE granules vial cancellous 5g - 1-2 mm	BM01P (pack of 1) BM01P6 (pack of 6)

PRODUCT	CODE
RE-BONE 0.25g syringe for 0.25-1mm granules	BM03A
RE-BONE 0.5g syringe for 0.25-1 mm granules	BM03B
RE-BONE 0.5g syringe for 1-2 mm granules	BM03C

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



# SHELTER®

A complete line of bovine pericardium membranes with different resorption times designed to promote tissue regeneration in reconstructive bone surgery.

Shelter® - первая рассасывающаяся мембрана перикарда крупного рогатого скота, специально разработанная для костной хирургии в стоматологии и произведенная исключительно итальянской цепочкой поставок.

В UBGEN мы разработали два типа мембран, которые используют благотворное влияние перикарда крупного рогатого скота и действуют как естественный защитный барьер:

\_ **Shelter Fast**, мембрана с быстрым временем рассасывания (4-6 недель) благодаря особой структуре коллагена с широкой текстурой;

\_ **Shelter Slow**, мембрана с более медленным временем рассасывания (4-6 месяцев) из-за измененной трехмерной структуры коллагеновых волокон, которые более устойчивы из-за усиленных связей.

В частности, в нашем Shelter Slow используется инновационный процесс производства Pericross®, который делает его резорбируемым в течение более длительного времени, чем в Fast-версии и других мембранах перикарда, доступных на рынке.

Shelter Slow в версии 0,8 мм может заменить растворы ПТФЭ с тем преимуществом, что он полностью рассасывается, что позволяет избежать второй операции удаления.

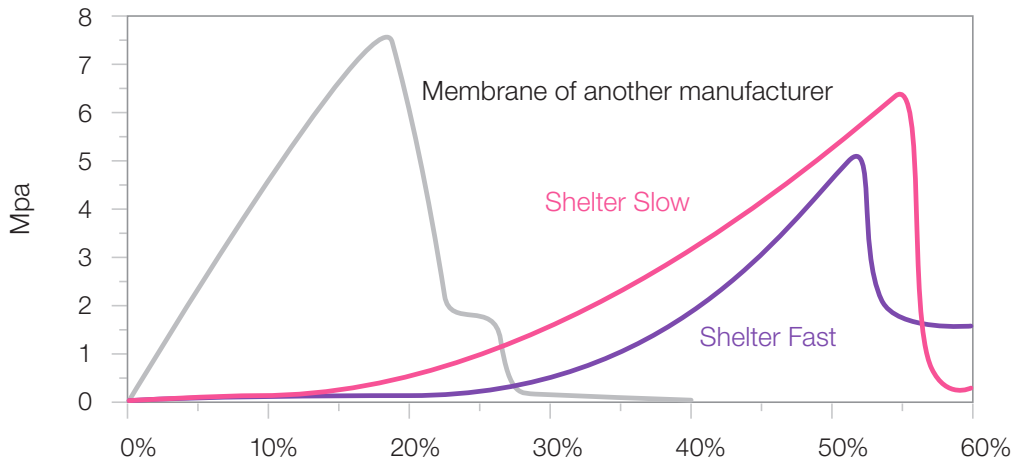
Shelter Fast и Shelter Slow препятствуют прохождению клеток. Они разработаны для стимулирования пролиферации клеток остеобластов и периодонтальной связки, защищая участок от колонизации мягких тканей; устойчивы и устойчивы к сцеплению, их легко и удобно устанавливать.

## Mechanical properties

Мембраны укрытия были испытаны механическими испытаниями на растяжение, из которых можно было получить кривые зависимости напряжения от деформации (график 1) с характерной тенденцией для коллагеновых материалов: это доказывает, что производственные процессы UBGEN и Pericross в частности поддерживают структуру фибрилл коллагена и другие компоненты, такие как эластин, не повреждены.

ГРАФИК 1

Bone Implant Contact



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

Despite having slightly different values, Shelter Fast and Shelter Slow come from tissues that allow to keep the fibrils of the collagen matrix and other components such as elastin undamaged.

Therefore, under hydrated conditions, Shelter Fast and Shelter Slow present the natural inclination of collagen:

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

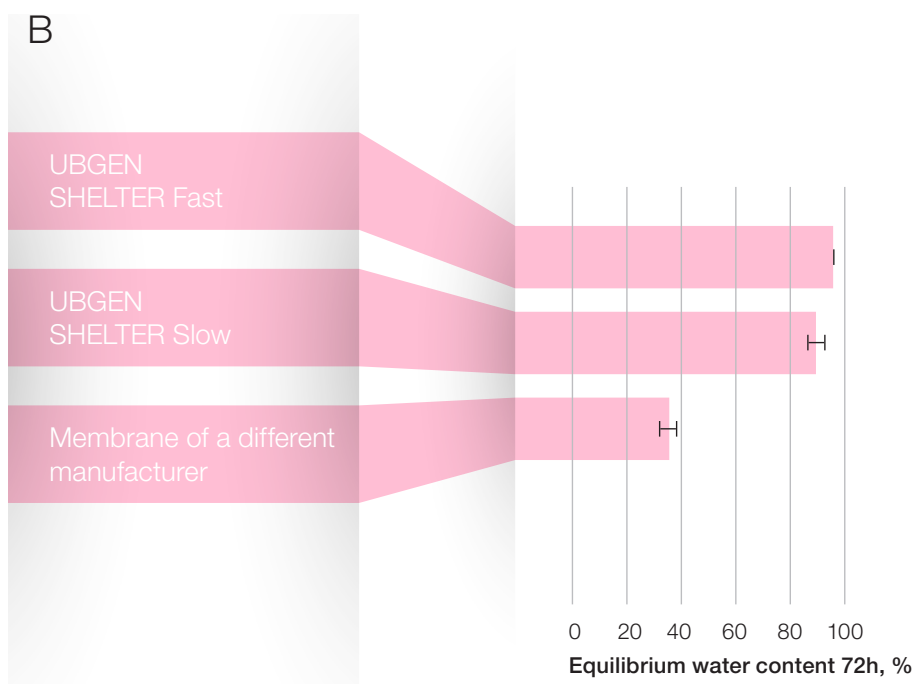
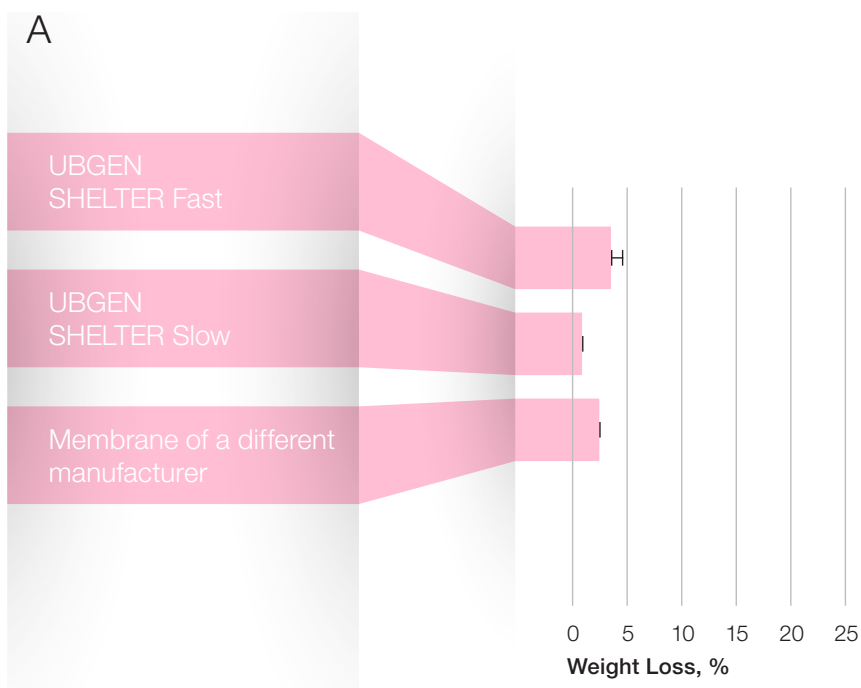
*The graph clearly shows that the Shelter Slow membrane requires a greater tensile stress to reach the breaking point, indicating a greater resistance to degradation.*

## Resorption properties

Shelter Fast and Shelter Slow have undergone in vitro degradation tests.

The process of cross-linking the Shelter Slow membrane allows it 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 (graphs A and B).

Shelter Fast, on the other hand, has a degradation time of 4-6 weeks.



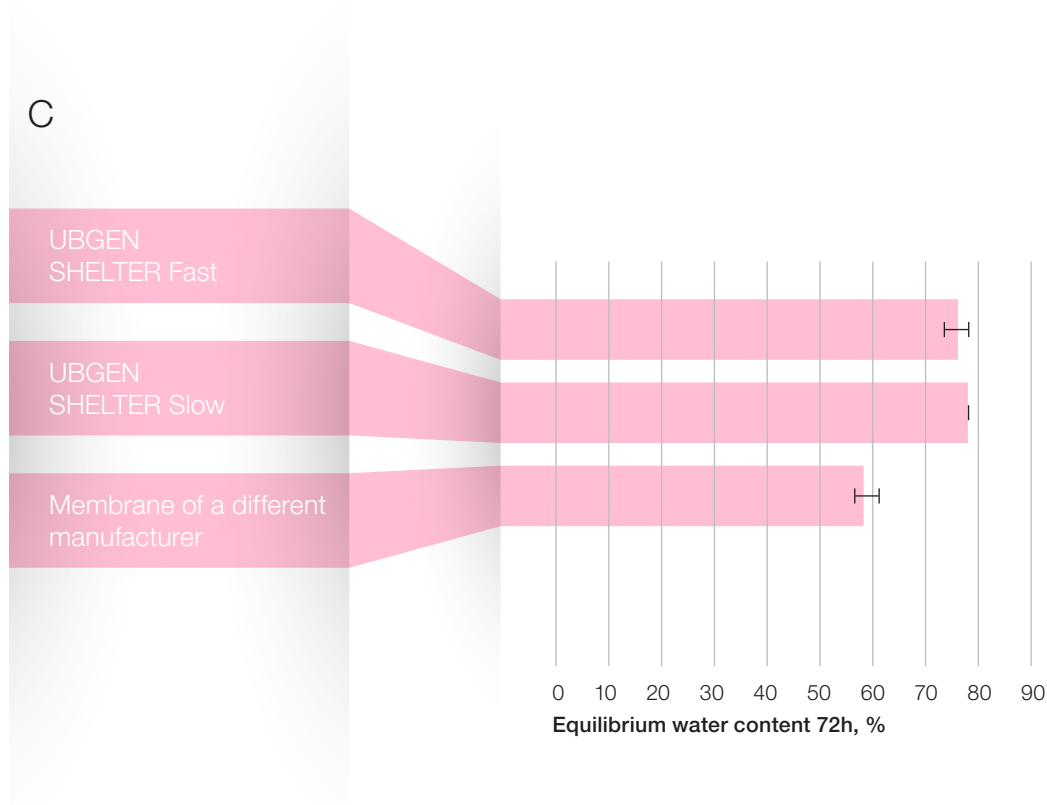
## Свойства увлажнения

Процесс производства Shelter позволяет мембране сохранять ретикулярную структуру коллагеновой матрицы, обеспечивая определенную пористость после обезвоживания (график С).

Мембрана оказывается очень гидрофильной, она быстро впитывает раствор, сохраняя хорошую структуру, и приобретает свойство адгезии и конформации на поверхностях, что чрезвычайно важно, когда мембрану необходимо укладывать и, следовательно, согласовывать даже с очень неровными поверхностями.

Shelter Slow, в отличие от Shelter Fast, более жесткий, прочный и немного менее гидрофильный, хотя сохраняет свои свойства эластичности и управляемости.

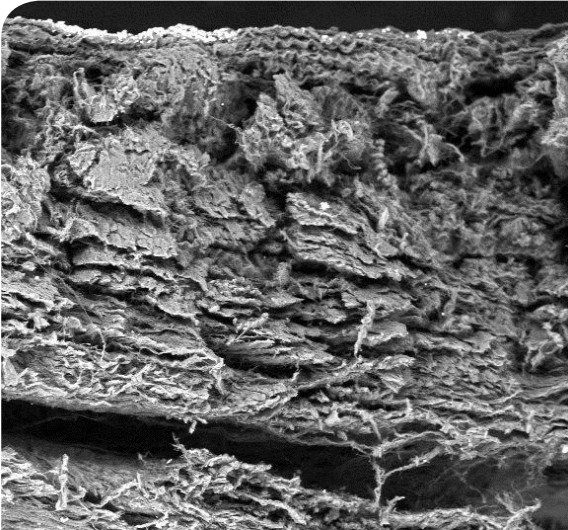
Процесс сшивания мембран Shelter Slow делает сетку мембраны более компактной, увеличивая прочность на разрыв и сохраняя неизменной эластичность.



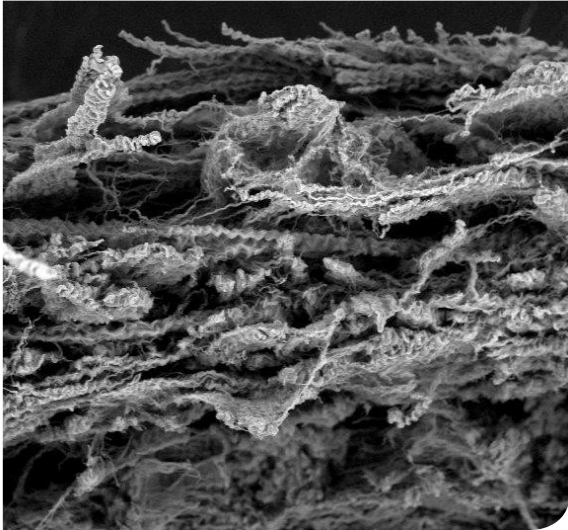
Из этого видно, что мембраны Shelter Fast и Shelter Slow подходят для применения при регенерации альвеолярной костной ткани с использованием метода управляемой регенерации ткани (GTR).

Их способность к гидратации делает их удобными в обращении, способными прилипать к неровным поверхностям даже в труднодоступных местах.

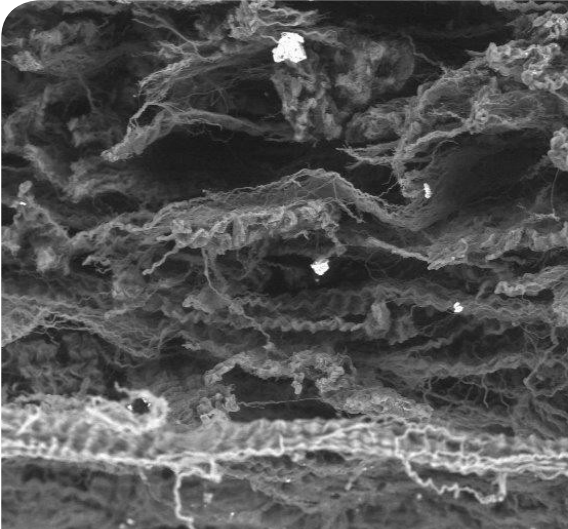
# Scanning electron microscope (SEM)



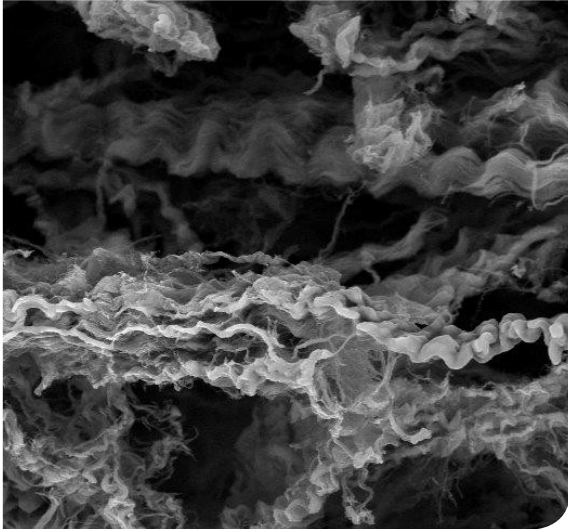
SHELTER Fast, cross-section, 100 μm



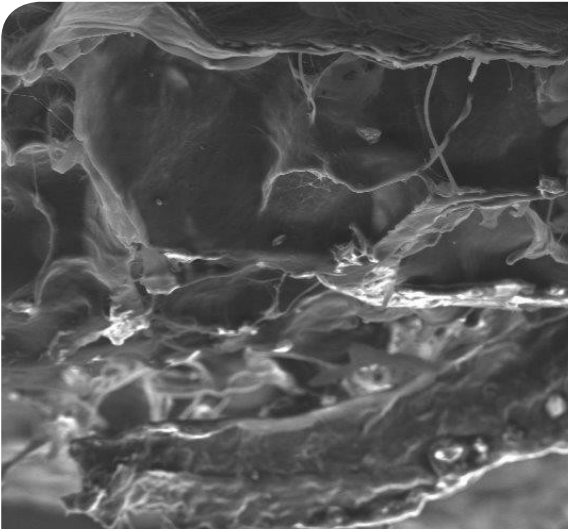
SHELTER Fast, cross-section, 100 μm



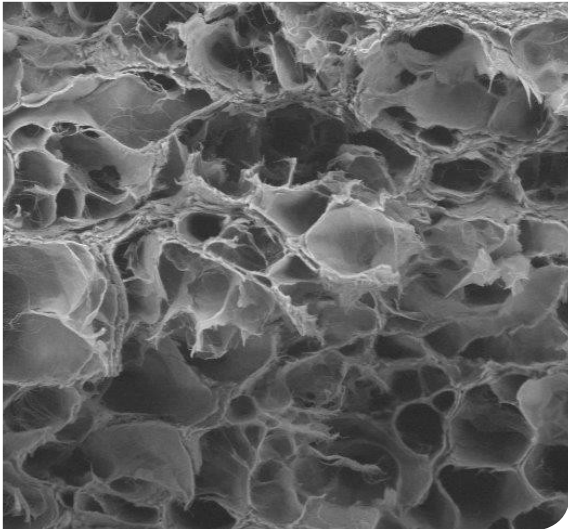
SHELTER Fast, cross-section, 100 μm



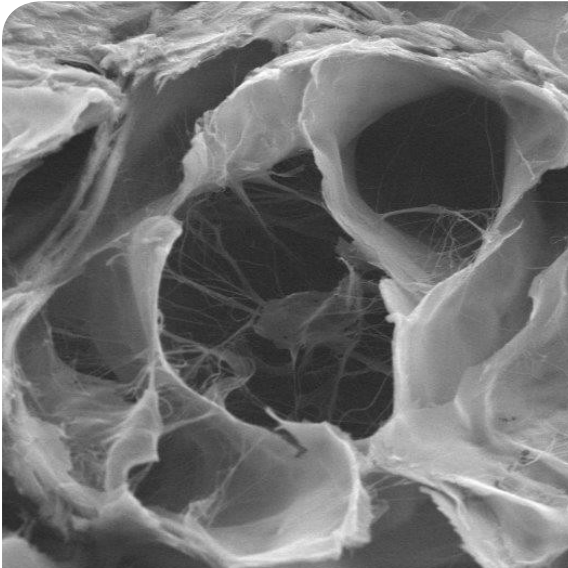
SHELTER Fast, cross-section, 10 μm



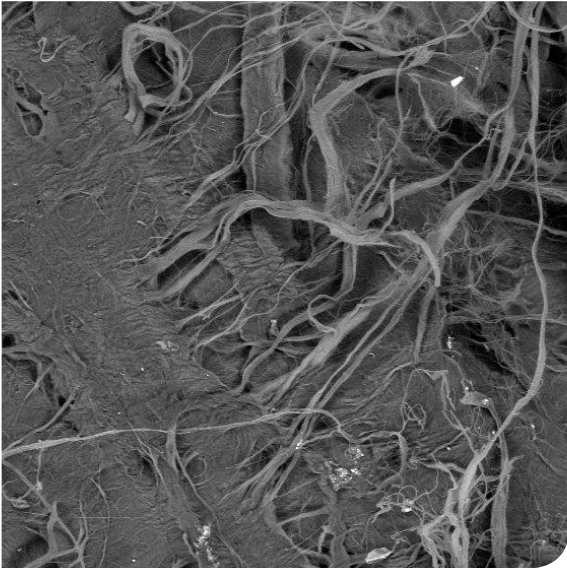
SHELTER Slow, cross-section, 100 μm



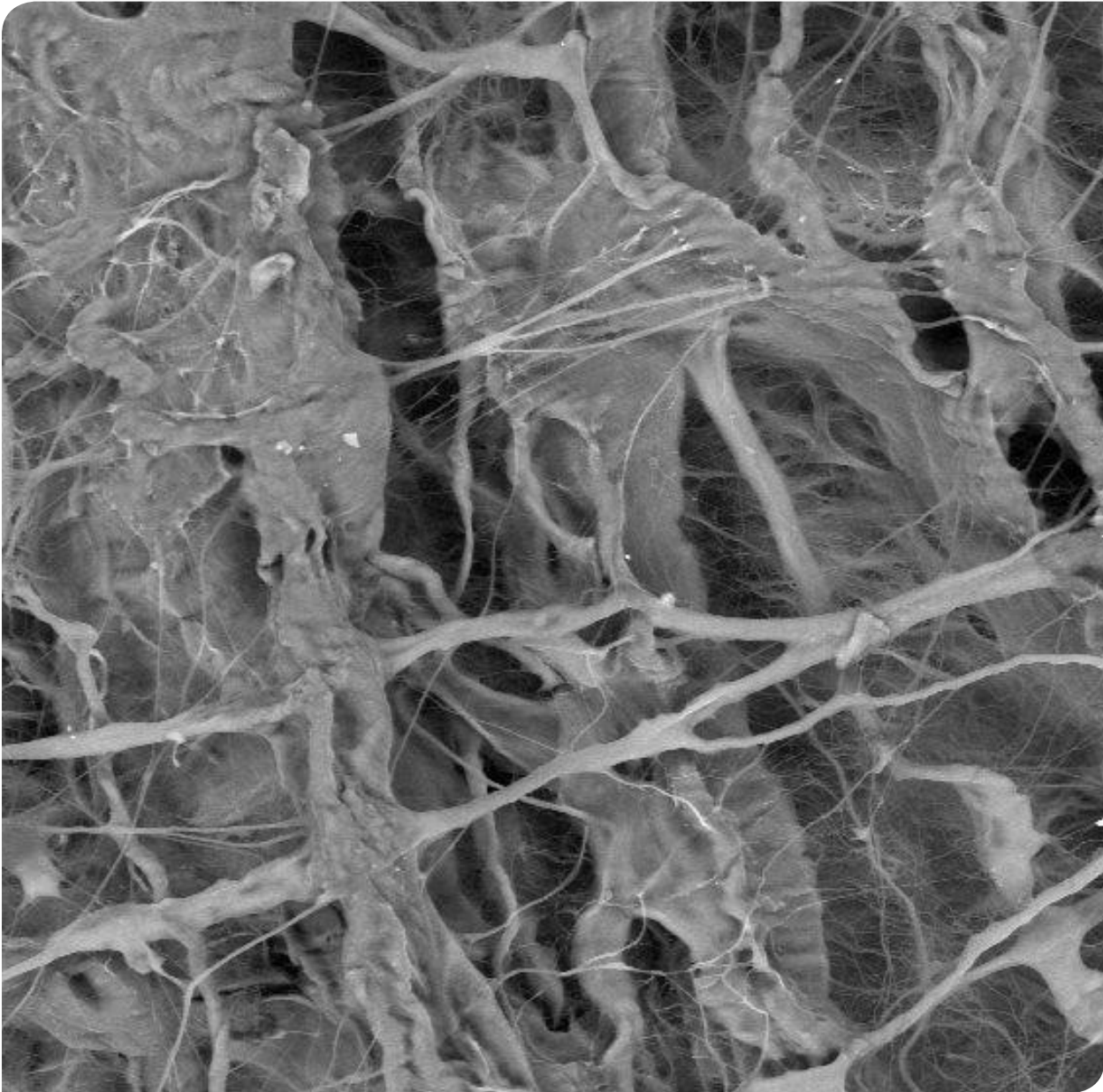
SHELTER Slow, cross-section, 100 μm



SHELTER Slow, cross-section, 20  $\mu\text{m}$



SHELTER Slow, plane, 100  $\mu\text{m}$



SHELTER Slow, plane, 10  $\mu\text{m}$



# SHELTER®

## клиническое применение

Поддержание альвеол и костного гребня.  
Горизонтальное увеличение двустенных дефектов.  
Расхождения Увеличение отверстий верхней челюсти и пазух в периимплантной  
хирургии. поражения.  
Регенерация пародонта при внутрикостных дефектах и  
Дефекты фуркации с двумя или тремя стенками.

Вертикальное дефектов. увеличение двустенных

# SHELTER<sup>®</sup> MEMBRANE: clinical applications

Support of the alveolus and bone crest.

Sinus lift surgery.

Horizontal increase in two-wall defects

Fast Membrane



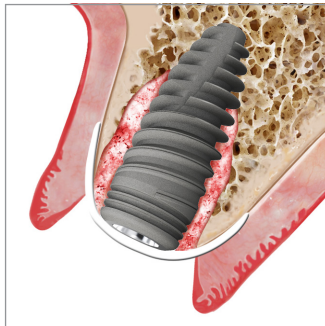
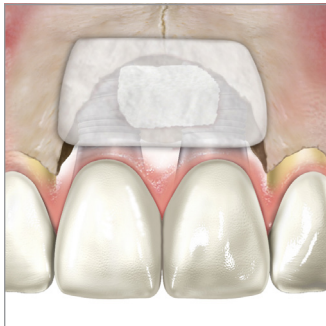
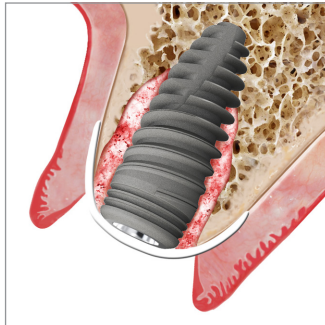
Slow Membrane



Vertical increase in 2-wall defects.

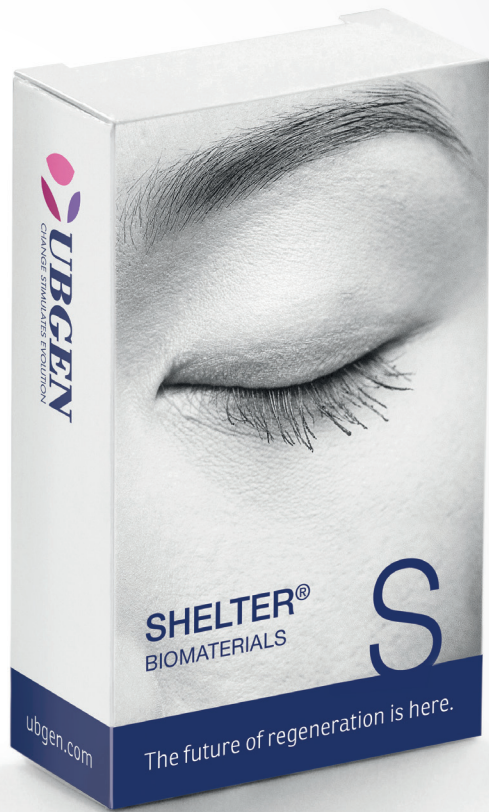
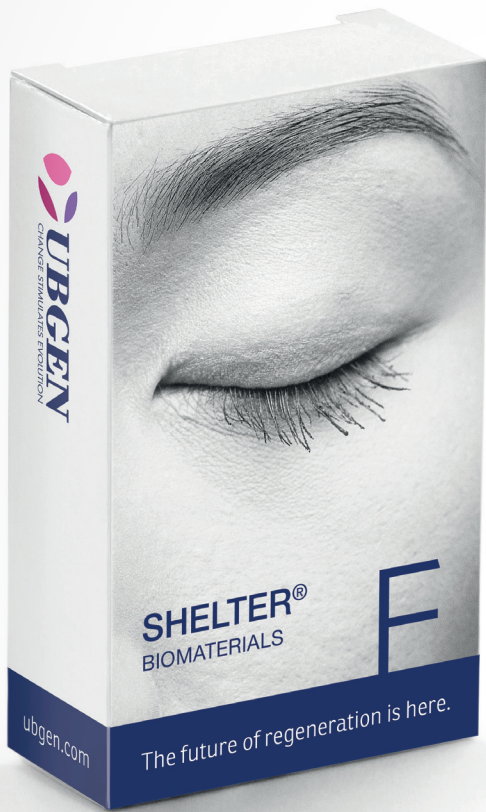
Dehiscences and fenestrations in peri-implant lesions.

Periodontal regeneration in intra-osseous defects and 2-or 3-wall furcation defects.<sup>10</sup>



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

# SHELTER® MEMBRANE



	PRODUCT	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

	PRODUCT	CODE
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

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13. Data on file with RE-BONE/UBGEN.





# GF-ONE®

APG® (Autologous Platelets Gel).

A cutting-edge technology that exploits the body's natural ability to regenerate after an injury.

A microscopic view of red blood cells, showing their characteristic biconcave disc shape. The cells are scattered across the field of view, with some appearing more prominent than others. The background is a soft, out-of-focus pinkish-red color.

Загляните в природу, и тогда вы поймете, что перемены лучше

GF-ONE® is the first integrated system for the preparation of platelet concentrates specially designed for bone surgery in dentistry.

Usually, in the blood separator market only the equipment for preparing platelet concentrates is provided, and these devices are normally designed for general use.

At UBGEN we have created instead a specific system to be used in dental surgery supported by technical training, start-up assistance and authorization of the dental practice.

This technology and its applications, which provide a unique and complete solution, allow 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 biochemical studies have shown a growth-stimulatory effect on different cell lines, with platelets acting as metabolic inducers: they release growth factors that immediately come into action, stimulating the regeneration of damaged tissues, and significantly accelerating the healing process.*

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 proactively act towards angiogenic processes;*
- \_ they are chemotactic towards biological steps and mitogenic towards the cells they encounter, activating a multiplier effect;*
- \_ they significantly increase cell membrane receptor expression.*

APG® GROWTH FACTORS	EXPECTED EFFECT
PDGF Platelet Derived Growth Factor	Chemotactic for fibroblasts and macrophages, mitogen for fibroblasts, smooth muscle cells, endothelial cells.
TGF-β1/β2 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.
Proinflammatory Cytokines IL1, IL6, TNF-α	Plays an important role in the early stages of tissue repair.
Serotonin, histamine, dopamine, calcium, adenosine	Impact on tissue regeneration.



## The APG<sup>®</sup> technique

The APG<sup>®</sup> (Autologous Platelets Gel) technique is the most advanced autologous system for obtaining a Platelets Concentrate both in liquid and gel.

*It is based on the activation of the patient's own platelets, which are concentrated through centrifugation of a small sample of autologous blood (7-10 ml) and used to stimulate and accelerate tissue regeneration.*

This methodology offers extraordinary results against many diseases, without side effects. Moreover, it reduces the recovery time after surgery.

## Patient benefits

Applying APG<sup>®</sup> to the area to be treated allows a faster and of better-quality healing process.

Technically, it is 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:*

- \_ Reduced risk of infection and pain relief;*
- \_ Improved healing time and quality of hard & soft tissue, thus accelerating osteogenetic processes;*
- \_ Possibility of combining it with medicaments and/or other biomaterials such as grafts, and implants.*

## Clinical studies with the University of Chieti-Pescara

In collaboration with Prof. Antonio Scarano of the University of Chieti-Pescara, UBGEN studies the effects of the APG® technique on different types of tissues.

Several studies<sup>17-18</sup>, including in vivo animal studies, suggest that platelet factors, such as growth factors, can be used to increase bone and soft tissue healing.

In particular, a recent in vitro<sup>19</sup> study conducted by the University of Chieti showed that the use of platelet concentrates mixed with granular bovine bone, allows the formation of a single block called *sticky graft block*.

This block has the property of increasing the mechanical resistance creating a real three-dimensional scaffold; inside it, the granules create a structural support to the tissue and act as a vector and model for the extracellular matrix; on the other hand, the autologous platelets act as a binding agent to hold the granules together.

The *sticky graft block* technique allows to easily fill the bone defect, reducing the migration of the inner particles and creates greater stability as it can be easily placed in defects of any size and shape.

Another advantage of using the *sticky graft block* technique is that it creates a network of fibrins, platelets and growth factors that are released slowly, leading to a better wound healing.

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17. Soft Tissue Augmentation with Autologous Platelet Gel and  $\beta$ -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

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# APG<sup>®</sup> applications

With its high concentration of growth factors, the APG<sup>®</sup> Platelet Concentrate can be used in multiple surgical procedures and clinical treatments.

## APG<sup>®</sup> concentrate in dentistry

Several studies suggest that the use of a platelet concentrate, either alone or combined with other surgical techniques, or even as a support to implant devices, improves the final success of operations, significantly increasing patient's comfort by reducing healing time.

In dentistry, the APG<sup>®</sup> method is used for:

- \_ Accelerating the healing of surgical wounds;
- \_ Reducing inflammation and post-operative discomfort;
- \_ The surgical treatment of post-extraction alveolus associated with biomaterials;
- \_ Maxillary sinus surgery;
- \_ Periodontal and muco-gingival surgery;
- \_ The surgical treatment of patients with bisphosphonates-induced osteonecrosis.

In all these treatments, the adhesive nature of APG<sup>®</sup> facilitates the handling of implant material, improving hemostasis and wound closure compared to the traditional technique.<sup>6</sup>

*Furthermore, recent studies have shown that the use of platelet-rich plasma increases microvascular proliferation in the early stages of healing, followed by a better osteoblastic activity.*

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6. 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<sup>®</sup> concentrate in cosmetic surgery

In the dermis, exposure to UVB rays stimulates collagenase production by fibroblasts present in the skin that degrade collagen.

This process causes the alteration of the disposition of the elastic tissue reducing the structural integrity of the dermis, the first cause of wrinkles and loss of skin elasticity.

*Since APG<sup>®</sup> 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 cells to rejuvenate.*

It has been shown that the use of APG<sup>®</sup> concentrate during cosmetic laser treatments increased skin elasticity, the amount of collagen and the number of fibroblasts, demonstrating a better cosmetic result and faster wound healing.<sup>7</sup>

The APG<sup>®</sup> method is used for:

- \_ Treating forehead wrinkles, wrinkles around the eyes, nasolabial wrinkles, wrinkles on the neck and on the neckline;
- \_ Treating acne scars;
- \_ Toning the skin and reducing sagging skin;
- \_ Treating stretch marks;
- \_ Treating and re-epithelialising skin wounds and ulcers.<sup>8</sup>

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7. 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.

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

## APG<sup>®</sup> concentrate in orthopedics

In recent years, clinical experience has shown that acute traumatic injuries of the muscles, tendons, and joint capsules significantly benefit from treatment with platelet growth factors, also in relation to the age of patients, the affected area of the body and its degree of functionality.

Young patients and athletes benefit from the use of platelet growth factors by reducing the time of functional damage, guaranteeing a faster recovery.

*More specifically, the application of APG<sup>®</sup> concentrate has proved particularly effective in the treatment of acute and chronic injuries of tendons, osteoarthritis, and epicondylitis.<sup>4-6</sup>*

- 
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>.
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  6. 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 trichology

It was recently found that treatments with platelet concentrate on patients affected by alopecia areata or baldness result in increased hair growth and thickness, as well as an increased number of hair follicles and improved microcapillary angiogenesis.<sup>10-12</sup>

*This treatment has no side effects; it is well tolerated and offers tangible results from the very first use and in a short time, both in terms of reduced hair loss and improved re-growth and thickening of the hair.*

- 
10. 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.
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# GF-ONE® CENTRIFUGE



## Multifunctional GF-ONE® blood separator for applications with medical devices

A counter-top device specifically designed for separating blood components. It is managed by a microprocessor which allows users to set speed and centrifugation time, with the ability to customise programmes.

GF-ONE® centrifuge options:

- \_ 8-position steel lamina rotor (10/15 ml)
- \_ 4-position steel lamina rotor (10/15 ml)
- \_ 4-position steel lamina rotor (30/50 ml)
- \_ 12-position steel lamina rotor (2.5/5 ml)
- \_ 10/15 ml tube holder
- \_ 30/50 ml tube holder
- \_ 10 ml vial adapters

The GF-ONE device also allows to set the rotation speed in RCF (Relative Centrifugal Force).

GF-ONE® KIT



There are choices in life  
that can be done with closed eyes.

**UBGEN**  
CHANGE IS THE BEST EVOLUTION

The future of regeneration is here.

## GF-ONE® KIT01

Disposable kit for the preparation and application of the Platelet Gel in the dental field containing:

- \_ 4 x 9 ml blue vials with anticoagulant
- \_ 4 x 9 ml white vials for fractionation
- \_ 2 x 9 ml red vials with serum activator
- \_ 1 x 2,5 ml syringe
- \_ 1 x 1 ml activator syringe
- \_ 1 butterfly needle 21G for blood collection with a safety device for withdrawal.
- \_ 1 needle 20G

## GF-ONE® KIT02

Disposable kit for the preparation and application of the Platelet Gel in aesthetic field containing:

- \_ 4 x 9 ml blue vials with anticoagulant
- \_ 4 x 9 ml white vials for fractionation
- \_ 1 x 2,5 ml syringe
- \_ 1 x 1 ml activator syringe
- \_ 1 butterfly needle 21G for blood collection with a safety device for withdrawal.
- \_ 4 ultra-fine needles 34G
- \_ 1 needle 20G

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10. 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.
11. Dae Hun Kim, M.D., Young Jin Je, M.S., Chang Deok Kim, Ph.D., Young Ho Lee, M.D.<sup>1</sup>, 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 <sup>1</sup>Anatomy, College of Medicine, Chungnam National University, Daejeon, Korea.
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17. Soft Tissue Augmentation with Autologous Platelet Gel and  $\beta$ -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
18. 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/SCS.0000000000002712
19. 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).



# ACTIGEN<sup>®</sup>

The new and exclusive implant surface coating with collagen.

A biological surface to promote implant osseointegration.



## THE STRENGTH OF COMPATIBILITY

ACTIGEN® is the exclusive collagen coating layer for implant surfaces that promotes osteogenesis. It is the only bioactive class III treatment on the market that has been rigorously certified to protect patient safety. It is only available at selected and certified implant manufacturers.

At UBGEN we have developed the only bioactive surface treatment of class III that has an osteoinductive effect.

It is a solution that:

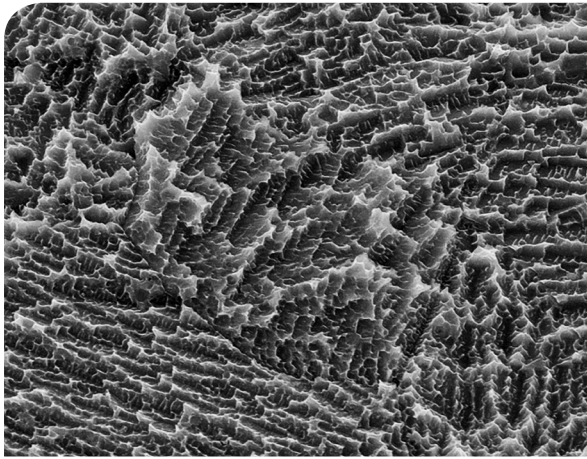
- \_ stimulates platelet activity;
- \_ predisposes the surface of the implants to be rapidly colonized by the bone;
- \_ increases the bone/implant contact area (BIC);
- \_ shortens recovery times.

This for our customers means being able to make a safe choice (product certified in class III), in order to obtain a predictable result even in high-risk patients.

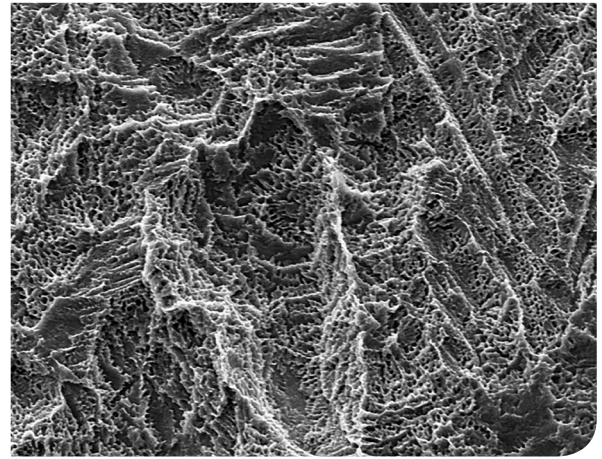
### The implant coating to date

Currently the most widespread dental implants have two types of surface coatings: DAE (Double Acid-Etched) and SLA (Sandblasted and Acid-Etched).

For this to happen, it is necessary that the cells perceive that the surface has a roughness compatible with their size.<sup>1-2</sup>



DAE (Double Acid-Etched)



SLA (Sandblasted and Acid-Etched)

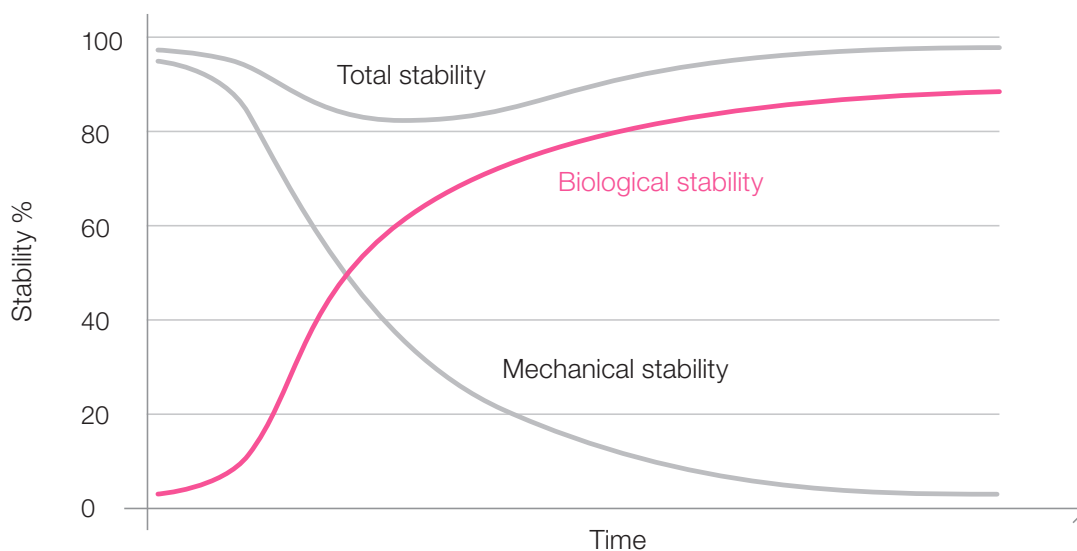
## Osseointegration and implant stability

The concepts and ideas that underlie SLA and DAE surfaces have represented a significant advance in the design of implant fixtures, but they have not yet solved the problem of positioning implants in immediate post-extraction alveolus with lower primary stability.

*Osseointegration is in fact favoured by the initial mechanical stability, subsequently reinforced by biological stability (graph 1).*

### GRAPH 1

Stability of dental implants over time



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.
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## Analysis and research of UBGEN process

Starting from today's implant coating technologies, UBGEN has invested in the research for a biological surface able to accelerating and increasing the osseointegration process of the implant fixture.

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.

It has been a while since 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.<sup>3-4</sup>

*UBGEN has researched in this direction for the development of Actigen, the exclusive coating for implant surface.*

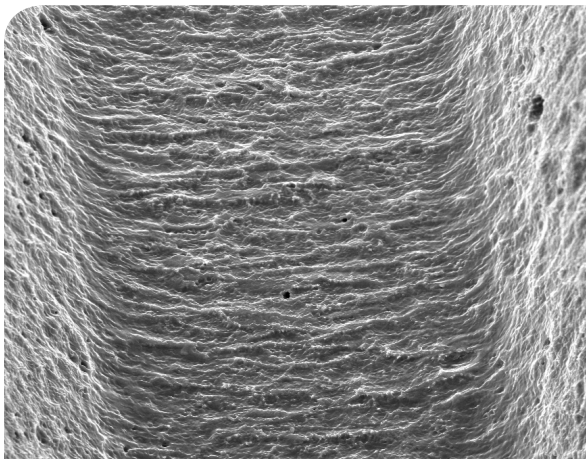
- 
3. Morra M. Biochemical modification fo titanium surfaces: peptides and ECM proteins. Eur Cell Mater. 2006 Jul 24;12:1-15.
  4. De Jonge LT et al. Organic-inorganic surface modifications for titanium implant surfaces. Pharm Res. 2008 Oct;25(10):2357-69. doi: 10.1007/s11095-008-9617-0. Epub 2008 May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

## ACTIGEN®: the evolution of the implant coating

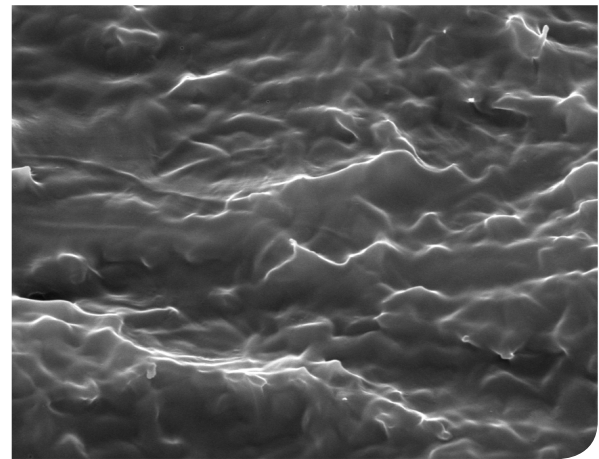
The most significant result in terms of osseointegration has been achieved by immobilising collagen of dermal origin (type I) on etched surfaces since the same type of collagen already constitutes to a large extent the organic portion of the bone and supports its vital processes.<sup>5-7</sup>

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: the adhesion of osteoblasts and osteoclasts, is a cofactor for many growth factors and many other mechanisms.<sup>5-16</sup>

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



Collagen loop detail - 100 µm

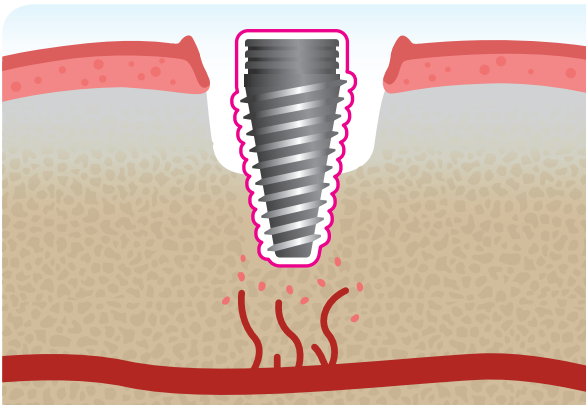


Collagen surface detail - 10 µm

- 
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.

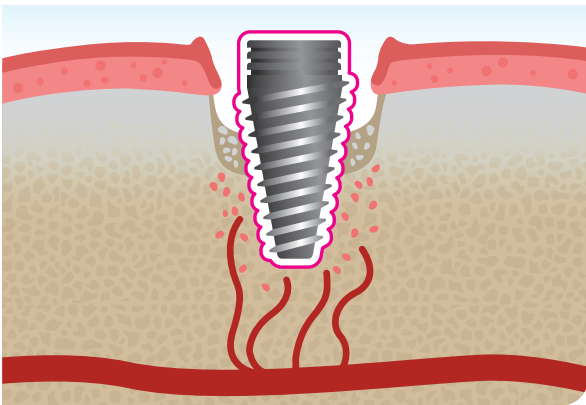
## Collagen functions

Stimulation mechanisms that allow the physiological development of bone regeneration.



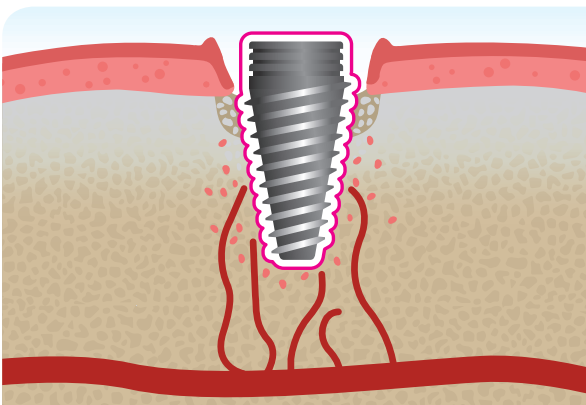
### Angiogenesis

Collagen plays a chemotactic action on the cell line of monocytes/macrophages, from which osteoclasts derive. These cells in turn stimulate angiogenesis, thanks to the secretion of angiogenic growth factors. Collagen is also able to activate the receptors on the cellular membrane of the platelets, thus facilitating haemostasis.



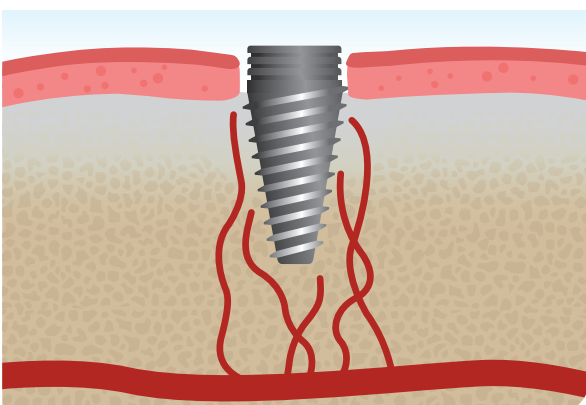
### Remodeling

Collagen stimulates a chemoattractant action on the precursors of osteoclasts, cells that through their action reabsorb the mineral component and collaborate with the osteoblasts in the rearrangement and remodelling of the bone in which the implant is placed.



### Osteoblastic activity

Collagen, by binding itself to fibronectin, promotes the anchoring of mesenchymal stem progenitor cells on which it exercises its chemotactic activity and induces the osteoblastic differentiation.



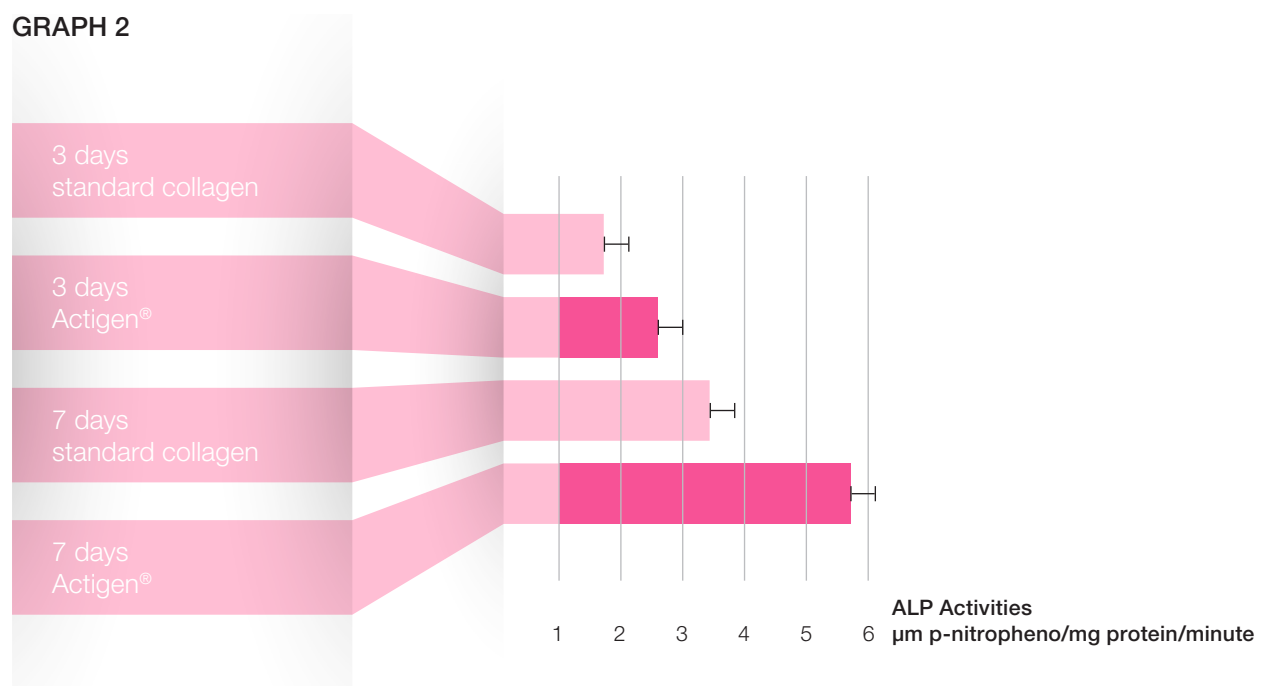
### Osteoconduction and guided regeneration

Collagen is able both to increase osteoblast proliferation speed and to guide the connective tissue regeneration.

*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, providing biochemical stimulation to osseointegration events.*

## In vitro tests

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



Graph 2: Tests 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.

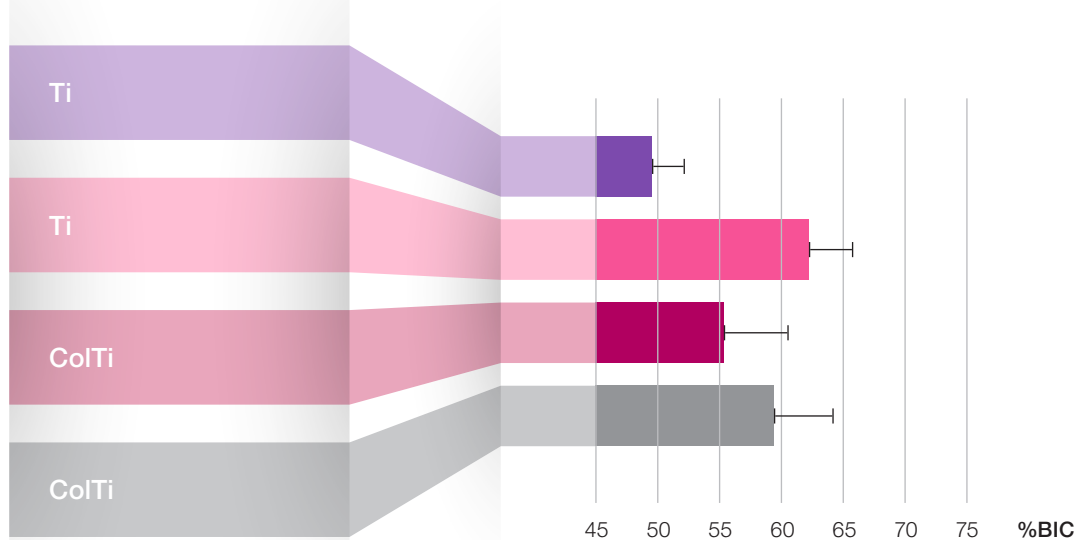
A second set of implants was inserted into rabbit femurs and histomorphometric analyses were performed at two and four weeks.

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.

### GRAPH 3

Histomorphometric evaluation of Ti and CoTi implants



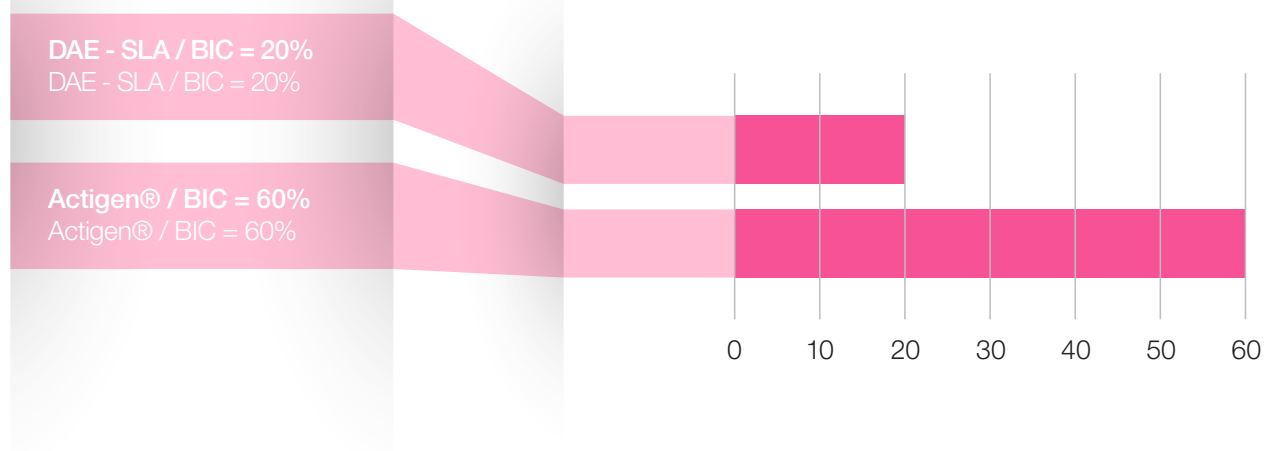
## Case report

In a case report 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 conditions:

- \_ placement in native bone D4;
- \_ uncovering after 10 weeks;
- \_ ASA 1 patient.

*Two tests were carried out to reveal the achievement of implant stability: the percussion test and the torque removal test at 20 N · cm. All the surgical phases have been documented with radiographs and photos. One year later, after uncovering the implant at ten weeks, all implants are correctly osseointegrated.*

**GRAPH 4**  
Bone Implant Contact



## 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 at the interface has increased both the percentage of bone-implant contact and bone growth within the coils in a statistically significant way.<sup>6</sup>

The results show that in just two weeks, ACTIGEN® allows the BIC (Bone Interface Contact) to be increased up to 3 times compared to traditional surfaces.

### Why collagen?

- \_ stimulates angiogenesis
- \_ promotes cell adhesion
- \_ promotes osteoblastic behavior
- \_ favors remodeling and mineralization

### What benefits does it involve?

- \_ predisposes the implant surface to be rapidly colonized by the bone
- \_ increases the BIC
- \_ allows faster bone growth
- \_ greater quantity and quality of bone
- \_ stimulates platelet activation
- \_ protection and safety of the patient (the class III certification provides a far more rigorous protocol compared to other classes)

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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.
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18. 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.

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# Bone & Tissue management

Surgical instruments and PTFE sutures to support the  
most advanced oral surgery techniques



## Bone & Tissue Management

*To complete the products offered, UBGEN manufactures and distributes a range of surgical instruments and PTFE sutures to support the most advanced oral surgery techniques.*

### **Surgical instruments**

UBGEN provides the clinician 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, ensuring high-quality and carefully selected products.

### **Sutures**

To complete our Bone & Tissue Management line we have at disposal an essential product for oral surgery: PTFE sutures, that are carefully selected to guarantee a precise and atraumatic adjustment of soft tissues wounds.



