Jason® membrane &
collprotect® membrane

Natural collagen membranes for GBR/GTR technique

SCIENTIFIC AND CLINICAL EVIDENCE
Collagen – a multifaceted protein

Collagens are a family of structural proteins that are found in the extracellular matrix, and which represent the main component of the skin, blood vessels, tendons, cartilage and bone. Collagens account for approximately 30% of the total protein content within the body. In the connective tissue, collagen constitute ~80% of all proteins. The 29 types of collagen, which are known, differ in the primary sequence of their peptide chains.

Three collagen molecules are twisted together into a triple helix, thus forming the collagen fibril. The fibrils aggregate and form collagen fibers. These fibers show a remarkable tear resistance, and provide the basis for the structural properties of many tissues, such as the tensile strength of tendons as well as the flexible properties of the bone. Collagens are synthesized by specific cells, such as fibroblasts and osteoblasts.

Collagen types

Collagen type I is the most abundant protein in the body, with the largest quantitative share. It is a fibrous protein of the connective tissue, most frequently found in the skin, bone, tendons, ligaments and fibrous cartilage, but also in internal organs and their fibrous membranes, for example the pericardium and the peritoneum. Gingival connective tissue is composed of approximately 60% collagen type I. Other important collagens are collagen type II, III and IV.

Collagen type II is an important component of the extracellular matrix found in hyaline- and elastic cartilage, while collagen type III is responsible for the elastic properties of blood vessels, the skin, and the lung. Collagen type IV is the major structural element of the basal lamina.

The most common types of collagen

- **COLLAGEN TYPE I** skin, bone, tendons, ligaments, fibrous cartilage, cornea
- **COLLAGEN TYPE II** cartilage (hyaline and elastic), spinal discs, vitreous body
- **COLLAGEN TYPE III** skin, cardiovascular system
- **COLLAGEN TYPE IV** basal lamina

Collagen membranes for the GBR and GTR technique

The GBR and GTR technique

Collagen membranes have been used in Guided Tissue Regeneration (GTR) and Guided Bone Regeneration (GBR) for many years. The principle of these techniques is based on the placement of a barrier membrane for separation of slowly proliferating regenerative cell types, such as osteoblasts and periodontal cells, from fast proliferating epithelial and connective tissue cells, thus enabling the regeneration of lost tissue.

GTR aims at the regeneration of the periodontium. A barrier membrane is placed between the epithelium and the tooth, to provide space and time for regeneration of the periodontal ligament. In GBR procedures, membranes are normally applied in combination with a bone graft material. The membrane is placed over a bony defect filled with a bone graft material. The bone graft material prevents collapse of the membrane and serves as an osteoconductive scaffold for ingrowth of bone and precursor cells. The barrier membrane prevents migration of bone graft particles into the oral cavity and ingrowth of soft tissue into the defect area, thus enabling bony regeneration.

MEMBRANE TYPES

The first generation of barrier membranes was based on non-resorbable materials e.g. cellulose acetate, titanium and expanded polytetrafluoroethylene (ePTFE). These membranes gained satisfying results but had disadvantages such as the secondary surgery required for removal, which is associated with graft site morbidity. To avoid the limitations of the non-resorbable membranes, resorbable membranes were developed. Resorbable membranes are either synthetic polymers such as polyglycolides, polylactides (acidic degradation) or animal-derived, e.g. collagen. Due to the manifold positive natural properties of collagen, collagen membranes are commonly the material of choice.

Barrier membrane requirements:
- Biocompatibility
- Tissue integration
- Cell occlusiveness
- Dimensional stability
- Easy handling

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ADVANTAGES of collagen membranes
- Exceptional biocompatibility
- Support of hemostasis
- Low antigenicity
- Degradation by specific enzymes
- Chemotactic attraction of regenerative cells

Collagens are resistant to any unspecific proteolytic degradation and are only degraded by specific enzymes called collagenases. Collagens are involved in the primary hemostatic reaction. Thus, collagen membranes contribute to a fast stabilization of the wound area. Another advantage of collagen is its chemotactic attraction of regenerative cells such as osteoblasts, gingival fibroblasts and periodontal ligament cells. Following dehiscence, the exposure of a collagen membrane leads to its quick proteolytic degradation. However, a secondary granulation without any inflammatory reaction may be observed.

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Collagen a natural hemostatic agent

Damage to the blood vessel wall leads to subendothelial collagen exposure. The collagen directly or indirectly interacts with the surface receptors on thrombocytes. The binding of collagen initiates a reaction cascade leading to transformation and aggregation of the thrombocytes. Additionally, the thrombocytes are cross-linked by fibrinogen. The resulting (white) thrombus initially stabilizes the wound. Accordingly, collagen membranes support the formation of a blood coagulum and contribute to a rapid stabilization of the wound area. Due to their hemostatic effect, collagens are not only used as barrier membranes, but also as collagen sponges and cones for stabilization of biopsy harvesting sites or covering of minor oral wounds and extraction sockets, respectively.


Origin of collagen membranes

The first collagen membranes available on the market were of bovine origin (Achilles tendon and pericardium). Nowadays, porcine membranes are more widely used because their usage excludes the risk of BSE transmission.

Moreover, porcine collagen exhibits a high homology to human collagen and therefore a very low antigenicity. Due to these reasons, botiss membranes are exclusively produced from porcine collagen.

Collagen membranes may be derived from various tissues, ranging from dermis, to peritoneum and pericardium. Accordingly, these membranes differ in their handling and degradation properties, as well as their barrier function.

PROPERTIES OF BARRIER MEMBRANES – vascularization versus barrier function

Many collagen membranes have a limited barrier function due to their rapid enzymatic degradation. The stability and barrier function of collagen membranes are tightly linked to the properties of the native tissue from which they originate. The Jason® membrane is produced from pericardium. Due to its structural characteristics it undergoes slow degradation and thus offers a prolonged barrier function. Furthermore, Jason® membrane is distinguished by its extraordinarily high tear resistance and excellent handling properties (e.g. good adaptation to surface contours, no sticking).

The barrier function may also be influenced by the density of the membrane. Denser collagen structures offer longer barrier functions. However, extremely dense collagen structures may hinder early angiogenesis of the grafting site. The ingrowth of blood vessels into the augmentation area is important not only for the nutrition of the grafting site, but also for attraction of circulating progenitor cells (pericytes). These cells have the potency to differentiate into osteoblasts, which produce new bone matrix. Therefore, the selective permeability of membranes for blood vessels is desirable. One example of such a membrane is collprotect® membrane. This membrane possesses loosely structured areas (pores) that penetrate the compact collagen matrix and support a fast vascularization of the membrane.

PROVIDE EXCELLENT HANDLING AND STABILITY

All botiss soft tissue products consist of natural porcine collagen originating from animals destined for the food industry and certified according to EN ISO 22442.

botiss’ barrier membranes are native membranes, the natural properties of the original tissue (dermis or pericardium) are preserved during the production process. The inherent architecture of the collagen structure provides superior handling properties, such as tear resistance, tensile strength, and adaptation to surface contours, in comparison to „non-native“ collagen membranes (e.g. made from a solution).

The particular multi-stage cleaning process effectively removes all non-collagenic proteins and antigenic components. The resulting membranes exhibit a natural three-dimensional collagen structure mainly composed of collagen type I and a lower share of collagen type III.
collprotect® membrane
NATIVE COLLAGEN MEMBRANE

The unique processing as well as the dense but open-porous collagen structure of collprotect® membrane are the basis for its safe application in dental bone and tissue regeneration. Owing to its natural hemostyptic function, the membrane enables early wound stabilization, thus supporting the natural wound healing. The rough surface of collprotect® membrane facilitates a fast integration into the surrounding soft tissue.

Properties
- Natural compact, open-porous collagen structure
- No artificial cross-linking
- Natural rough surface for cell adhesion and migration
- Pores for blood vessel ingrowth, support of vascularization
- Controlled degradation
- Natural collagen to support blood clot formation / natural healing
- Easy handling in dry and wet status

INDICATIONS:
- Implantology, Periodontology, Oral and CMF Surgery
- Horizontal augmentation
- Socket and ridge preservation
- Sinus lift
- Protection and covering of minor perforations of the Schneiderian membrane
- Fenestration and dehiscence defects
- Intrabony defects (1 to 3 walls)
- Furcation defects (class I and II)

Jason® membrane
NATIVE PERICARDIUM GBR/GTR MEMBRANE

Owing to these unique properties, Jason® membrane exhibits beneficial handling characteristics such as a remarkable tear resistance and effective surface adaptation. Due to its pericardial origin Jason® membrane also exhibits a long barrier function, making Jason® membrane our recommended choice particularly for large augmentative procedures.

Properties
- Naturally long barrier function
- Multidirectional strength and tear resistance
- No sticking after hydration
- Excellent surface adaptation
- Very thin membrane
- Fast vascularization due to three-dimensional structure

INDICATIONS:
- Implantology, Periodontology and Oral and CMF Surgery
- Fenestration and dehiscence defects
- Sinus lift
- Socket and ridge preservation
- Alveolar ridge augmentation and reconstruction
- Intrabony defects (1 to 3 walls)
- Furcation defects (class I and II)

Histology six weeks after implantation of collprotect® membrane in a rat model. Blood vessels have penetrated the porous structure. Collagen fibers are visible and the degradation proceeds without any inflammatory response.

SEM image of collprotect® membrane

SEM image of Jason® membrane

Jason® membrane maintains the barrier function 56 days after subcutaneous implantation in rats.
**Jason® membrane**

**collprotect® membrane**

**Origin**
- **Porcine Pericardium**
- **Porcine Dermis**

**Degradation**
- 8-12 weeks in a rat model,
  naturally long barrier function due to slow degradation
- 4-8 weeks in a rat model,
  intermediate barrier function

**Structure**
- Multi-oriented collagen fibres providing strong tear resistance
- Dense network of collagen bundles with pores for better vascularization

**Pre-clinical testing**

**Jason® Membrane Supports Attachment and Proliferation of Osteoblast-Like Cells**

Results of *in vitro* cell cultures. Dr. M. Herten, University of Münster and Prof. Dr. D. Rothamel, Mönchengladbach Hospital, University of Düsseldorf

Incubation of the multi-layered Jason® membrane and a competitive bilayer membrane with osteoblast-like SaOs-2 cells showed a significantly higher cell proliferation on the Jason® membrane after seven days.

The excellent cell attachment and proliferation on Jason® membrane highlights its suitability as scaffold for osteoblast guidance which supports the bony regeneration of covered defects.

**Product Specifications**

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**In vivo pre-clinical testing**

Results from a degradation study in a rat model.

Prof. Dr. D. Rothamel, Mönchengladbach Hospital, University of Düsseldorf

Resorption time and tissue integration of collagen membranes not only depend on the animal origin, but also differ between tissues. Tissue integration and degradation of Jason® membrane and collprotect® membrane were tested by subcutaneous implantation in rats. Jason® membrane, which originates from pericardium, was integrated within the first weeks and remained stable for a healing period of eight to 12 weeks (please note the different metabolic rates for rats and humans). The cell invasion of the dermal collagen of the collprotect® membrane took a little longer, but the membrane was mostly degraded within the first four to eight weeks.

In vivo pre-clinical testing

Jason® membrane – EXCELLENT BIOCOMPATIBILITY AND TISSUE INTEGRATION
Results from an animal model, Prof. Dr. Dr. D. Rothamel, Mönchengladbach Hospital, University of Düsseldorf

Analysis of the tissue integration and morphological structure of Jason® membrane at four to 12 weeks after lateral augmentation in a dog model.

The membrane was integrated into the surrounding tissue without any inflammation. Significant degradation of the membrane started at week eight and proceeded until week 12. A bilayer membrane that was tested in the same model showed a comparably good tissue integration, but was almost completely degraded after eight weeks.7

Jason® membrane after four weeks healing time
The bilayer membrane after four weeks healing time
4 weeks healing time
Both membranes showed good tissue integration without any inflammatory reaction, as demonstrated by Toluidine staining. Initial ingrowth of blood vessels improves nutrition of the graft and osseous regeneration.

8 weeks healing time
The bilayer membrane was almost completely resorbed.
Jason® membrane was still intact, serving as barrier against ingrowth of surrounding soft tissue.

Jason® membrane after eight weeks healing time
12 weeks healing time
Jason® membrane was almost completely degraded and replaced by a periosteum rich in collagen fibers.
The collagen of the membrane is partially visible as cloudy fibrous areas.


In vivo pre-clinical testing

collprotect® membrane – RAPID ANGIOGENESIS AND TRANSMEMBRANOUS VASCULARIZATION
In vivo results from a rat model, Prof. Dr. Dr. D. Rothamel, Mönchengladbach Hospital, University of Düsseldorf

One week after subcutaneous implantation of collprotect® membrane in rats, cells started to superficially invade the membrane. No signs of inflammatory reactions were observed. collprotect® membrane exhibits good integration into the well-vascularized peri-implant tissue.

After four weeks, blood vessels within the pores of the membrane indicate transmembranous vascularization. Early vascularization of the membrane supports the nutrition and integration of the grafted site, thereby promoting osseous regeneration. Furthermore, the regeneration is promoted by circulating progenitor cells that reside in the blood vessels and evolve into bone forming osteoblasts.

7 days after implantation
28 days after implantation
Seven days after implantation, only superficial invasion of cells into the membrane can be observed, an empty pore in the membrane in the lower left part is recognizable.

28 days after implantation, ingrowth of blood vessels into the pores of the membrane can be observed.

Areas of a fibrillary structure within the dense collagen fiber network of the collprotect® membrane (pores, see right picture and arrow in left picture) facilitate the ingrowth of blood vessels into the defect area through the membrane.

CLINICAL CASE BY
PD Dr. Raluca Cosgarea and Prof. Dr. Dr. Anton Sculean,
University Cluj-Napoca, Romania and University Bern, Switzerland

REGENERATION OF INTRABONY DEFECTS WITH CERABONE® AND COLLPROTECT® MEMBRANE

CLINICAL CASE BY
Dr. Dominiki Chatzopoulou, University College London (UCL), England

GTR WITH CERABONE® AND COLLPROTECT® MEMBRANE USING THE SIMPLIFIED PAPILLA PRESERVATION TECHNIQUE
In cases involving an unstable soft tissue situation, or if wound dehiscence is expected, a Jason® fleece is recommended to cover the barrier membrane in order to provide extra protection for the healing area. Where applicable, Jason® fleece can be loaded with antibiotics.
CLINICAL APPLICATION OF COLLPROTECT® MEMBRANE

CLINICAL CASE BY
Dr. Georg Bayer, Landsberg am Lech, Germany

LATERAL AUGMENTATION

- CBCT image showing the reduced amount of bone available in the area of the mental foramen
- Lateral bone defect following root tip resection
- After preparation of the implant bed the thin vestibular wall is visible
- Insertion of implant in the reduced bone amount
- Lateral augmentation with maxresorb® and application of a dry colprotect® membrane
- Complete covering of the augmentation site and implant with the membrane
- Wound closure by soft tissue expansion without vertical releasing incisions
- Post-operative x-ray
- Stable keratinized gingiva after insertion of healing abutment at re-entry
- X-ray control at re-entry

CLINICAL APPLICATION OF JASON® MEMBRANE

CLINICAL CASE BY
Prof. Dr. Dr. Daniel Rothamel, Mönchengladbach Hospital, University of Düsseldorf, Germany

SINUS LIFT WITH TWO-STAGE IMPLANT PLACEMENT

- Clinical situation before sinus lift
- Clinical situation before sinus lift, occlusal view
- Clinical situation following preparation of the mucoperiosteal flap
- Preparation of a lateral sinus window
- Placing of Jason® membrane in the sinus cavity
- Jason® membrane serves as protection for the Schneiderian membrane
- Filling the sinus cavity with cerabone®
- cerabone® in the sinus cavity
- Excellent osseous integration of the cerabone® particles without soft tissue ingrowth at re-entry, six months post-operative
- Additional lateral augmentation with cerabone®
- Covering of the augmentation area with Jason® membrane
- Tension-free wound closure with single interrupted sutures
- CBCT image showing the reduced amount of bone available in the area of the mental foramen
- Stable insertion of two implants into sufficient bone matrix
- Histological sections of biopsy taken at the time of implantation
- Magnification of the histological sample demonstrating complete integration of cerabone® particles within the newly formed bone matrix
- Post-operative x-ray
**CLINICAL CASE BY**
Dr. Sebastian Stavar, Houten, Netherlands

**DEHISCENCE DEFECT**

- Initial clinical situation with broken bridge abutment in regio 12, tooth 21 not worth preserving and tooth 11 lost by a front teeth trauma several years ago.
- Situation after atraumatic tooth extraction and suturing of wound margins.
- Clinical situation five weeks after extraction.
- Preparation of a mucoperiosteal flap - extensive bone deficit in horizontal and vertical dimension.
- Horizontal and vertical augmentation with cerabone® and autologous bone after placement of two implants.
- Coverage of the augmentation site with Jason® membrane.
- Tension-free wound closure.
- Clinical view two weeks post-operative.
- Complication free healing eleven weeks after augmentation.
- Exposure of implants and insertion of healing abutments.
- Shaping of the emergence profile using the temporary prosthesis.
- Final prosthetic restoration with implant-borne bridge in regio 12-21 and crown on tooth 22.

**RIDGE AUGMENTATION**

- Instable bridge situation with abscess formation at tooth 15 after apicoectomy.
- OPG six months after tooth extraction shows vertical deficiency at tooth 15.
- Clinical situation showing scar tissue formation at former abscess incision site.
- Bone spreading at tooth 12 for lateral widening of the crest.
- Internal sinus grafting to compensate the vertical deficiency at tooth 15.
- After implant placement, lateral bone defects require further augmentation.
- Application of cerabone® and autologous bone (mixture 1:2) on the lateral aspect.
- Covering of the augmentation site with Jason® membrane.
- Tension-free soft tissue closure.
- Post-operative x-ray showing the internal sinus grafting and implant positions.
- Stable soft tissue condition after six months of healing.
- Perfect integration of the cerabone® particles into the newly formed bone matrix.
- Implant uncovering, and insertion of gingiva formers.
- Prosthetic situation following professional dental hygiene treatment at one year post-operative.
- X-ray control one year post-operative.

**CLINICAL CASE BY**
Prof. Dr. Dr. Daniel Rothamel, Mönchengladbach Hospital, University of Düsseldorf, Germany

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CLINICAL CASE BY
Prof. Dr. Dr. Daniel Rothamel, Mönchengladbach Hospital, University of Düsseldorf, Germany

LATERAL AUGMENTATION

- Lateral defect in regio 24 at six months after extraction
- Dehiscence defect at palatal side
- Soft tissue closure
- Lateral augmentation with cerabone® and autologous bone (mixture 1:1)
- Lateral view of defect
- Surgical presentation of the bone defect
- Further augmentation at the palatal side
- Satisfactory bone formation and volume maintenance
- Stable hard tissue conditions on both buccal and palatal side
- Thin buccal bone after implant installation
- Application of Jason® membrane
- Fixation of maxgraft® bonebuilder and contouring with allogenic particulated material
- Fixation of two more maxgraft® bonebuilder blocks on upper right maxillary ridge

CLINICAL CASE BY
Dr. Dr. Dr. Oliver Blume, Munich, Germany

RIDGE AUGMENTATION IN THE MAXILLA

- Preoperative clinical situation - severe atrophy of the maxillary bone
- Fixation of maxgraft® bonebuilder blocks (blue)
- Fixation of two more maxgraft® bonebuilder blocks on upper right maxillary ridge
- Three dimensional reconstruction of the bone defect and planned maxgraft® bonebuilder blocks (blue)
- X-ray six months post-operative
- Temporary provision
- Clinical situation six months after augmentation
- Implant placement
- Tension-free and saliva-proof wound closure
- Covering with Jason® membrane and one layer of PRF matrices
- Upper left maxilla - severe atrophic ridge

CLINICAL APPLICATION OF JASON® MEMBRANE
Innovation.
Regeneration.
Aesthetics.