Jason® membrane & collprotect® membrane

Natural collagen membranes for GBR/GTR technique

Scientific and clinical evidence

soft tissue
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 25% of the total protein content within the body. In the connective tissue, collagen constitute ~80% of all proteins. The 28 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 specialized 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. The 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, also called elastin, 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

<table>
<thead>
<tr>
<th>Collagen Type</th>
<th>Tissues/Structures</th>
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</thead>
<tbody>
<tr>
<td>collagen type I</td>
<td>skin, bone, tendons, ligaments, fibrous cartilage, cornea</td>
</tr>
<tr>
<td>collagen type II</td>
<td>cartilage (hyaline and elastic), spinal discs, vitreous body</td>
</tr>
<tr>
<td>collagen type III</td>
<td>skin, cardiovascular system</td>
</tr>
<tr>
<td>collagen type IV</td>
<td>basal lamina</td>
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Collagen membranes for the GBR and GTR technique

The GRB and GTR techniques

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 a predictable 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 predictable 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

The advantages of collagen

Several factors make collagen an optimal biologic material for use as barrier membranes. One important characteristic is the excellent biocompatibility of collagen and its degradation products. Collagen is widely distributed throughout the body, making up approx. 60% of all proteins within the gingival connective tissue. Due to their low antigenicity, animal collagens may be used in humans without causing tissue rejection.

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

Collagen as a natural hemostypt

Damage to the blood vessel wall leads to subendothelial collagen release. 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.

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. Yet a secondary granulation without any inflammatory reaction may be observed.

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, the Jason® pericardium 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 the collprotect® membrane. This membrane possesses loosely structured areas (pores) that penetrate the compact collagen matrix, and support a fast vascularization of the membrane.

Histology demonstrating the presence of blood vessels within a collagen membrane

Despite its thinness, the Jason® membrane exhibits an excellent multidirectional tear resistance.

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botiss membranes 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) being 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 (i.e. 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 of collagen type III.
collprotect® membrane
Native collagen membrane

collprotect® membrane is a native collagen membrane that supports wound healing and achieves optimal treatment results in GBR and GTR procedures due to its rough, porous structure. During the regeneration process, the collprotect® membrane provides the required barrier function and degrades without any inflammatory reaction.

The soft tissue overlying the collprotect® membrane usually heals without any problems, even if postoperative dehiscences occur. The inherent structure of the collprotect® membrane prevents ingrowth of soft tissue cells, but allows blood vessel penetration and quick integration into the surrounding tissue. This unique biologic function is ideal for hard and soft tissue healing.

Properties
- Three-dimensional native collagen matrix
- Controlled wound healing and blood clot support
- Optimal barrier function in GBR/GTR procedures
- Degradation time approx. eight to 12 weeks
- Easy application and handling in dry or wet status
- Rough and porous structure for cell guidance

Indications:
Implantology, Periodontology, Oral and CMF Surgery
- Protection and covering of minor perforations e.g. the Schneiderian membrane
- Sinus lift
- Socket preservation
- Horizontal and vertical ridge augmentation
- GBR/GTR simultaneous use with bone substitutes
- Fenestration and dehiscence defects
- Intraosseous and furcation defects
The Jason® membrane is a native collagen membrane originating from pericardium, developed and produced for dental tissue regeneration. Due to the unique, proprietary production process, the superior properties of the native pericardium are preserved.

The natural biomechanics and biological characteristics are the essential properties that give the Jason® membrane its ease of handling and highly predictable results.

Due to the strong, multidirectional linking of the natural collagen network, the Jason® membrane offers a long-lasting barrier function, which remains adequate for three to six months. This unique long-term degradation has made the Jason® membrane an essential component of the GBR/GTR concept.

**Properties**
- Long-lasting barrier function of ~12 to 28 weeks
- Native, ultra-thin membrane
- Easy manipulation, may be applied dry or wet
- Supple but strong, with exceptional adaptation to surface contours
- No stickiness after rehydration
- Fast vascularization due to three-dimensional structure
- Multidirectional strength and tear resistance

**Indications:**
- Implant dehiscence
- Sinus lift
- Protection of the Schneiderian membrane
- Fenestration defects
- Extraction sockets
- Ridge preservation
- Horizontal and vertical augmentation
- Alveolar ridge reconstruction
- Intraosseous defects (1-3 walls)
- Furcation defects (class I-II)

Jason® membrane – excellent drapeability and adaptation to surface contours
Product comparison

Jason® membrane versus collprotect® membrane

<table>
<thead>
<tr>
<th>Origin</th>
<th>Jason®</th>
<th>collprotect®</th>
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<tbody>
<tr>
<td>Pericardium</td>
<td></td>
<td>Dermis</td>
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<tr>
<td>Degradation</td>
<td>12 to 28 weeks</td>
<td>Eight to 12 weeks</td>
</tr>
<tr>
<td>Structure</td>
<td>Differently oriented collagen fibers providing multi-directional tear resistance</td>
<td>Dense network of collagen bundles with pores for better vascularization</td>
</tr>
<tr>
<td>Handling</td>
<td>Highly adaptive</td>
<td>Slightly rigid</td>
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**Product Specifications**

<table>
<thead>
<tr>
<th>Jason® membrane</th>
<th>Art.No.</th>
<th>Size</th>
<th>Content</th>
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<tr>
<td>681520</td>
<td>15 x 20 mm</td>
<td>1 membrane</td>
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<tr>
<td>682030</td>
<td>20 x 30 mm</td>
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<tr>
<td>683040</td>
<td>30 x 40 mm</td>
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<table>
<thead>
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<th>Art.No.</th>
<th>Size</th>
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Pre-clinical testing

The Jason® membrane supports attachment and proliferation of osteoblast-like cells

*In vitro* cell culture results. Dr. M. Herten, University of Düsseldorf and PD Dr. Dr. D. Rothamel, University of Cologne

Incubation of the multi-layered Jason® membrane and a competitive bi-layer 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 the Jason® membrane proves its suitability as scaffold for osteoblast guidance and support of the bony regeneration of covered defects.

*In vivo* pre-clinical testing

Results from a degradation study in a rat model⁶, PD Dr. Dr. D. Rothamel, University of Cologne

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 the Jason® membrane and the collprotect® membrane were tested by subcutaneous implantation in rats. The 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 degraded within the first four to eight weeks.

⁶ Rothamel et al. (2011). Biodegradation patterns of native and cross-linked porcine collagen matrices – an experimental study in rats. University Hospital of Cologne, Cologne, Germany. Poster EAO.
Analysis of the tissue integration and morphological structure of the 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.

Four weeks healing time
Both membranes showed good tissue integration without any inflammatory reaction, as demonstrated by Toluidine staining.

Eight weeks healing time
The bilayer membrane is almost completely resorbed.

The Jason® membrane is still intact, providing barrier against ingrowth of surrounding soft tissue.

12 weeks healing time
The 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, PD Dr. Dr. D. Rothamel, University of Cologne

One week after subcutaneous implantation of the collprotect® membrane in rats, cells start to superficially invade the membrane. No signs of inflammatory reactions may be observed. The 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. The 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.

Seven days after implantation

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

28 days after implantation

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

Areas of a fibrillary structure within the dense collagen fiber network of the collprotect® membrane (pores, see green arrow and right picture) facilitate the ingrowth of blood vessels into the defect area through the membrane.
Clinical application of \textit{collprotect®} membrane

Clinical case by
Dr. Raluca Cosgarea and Prof. Dr. Dr. Anton Sculean, Cluj-Napoca, Romania and Bern, Switzerland
Regeneration of intrabony defects with \textit{cerabone®} and \textit{collprotect®} membrane

Pre-operative defect measurement
Pre-operative x-ray showing intrabony defect
Defect presentation after preparation of mucoperiosteal flap
Rehydration of \textit{cerabone®} particles

\textit{collprotect®} membrane cut to shape
Filling of intrabony defect with \textit{cerabone®}
\textit{collprotect®} membrane in place
Wound closure

X-ray control at 12 months post-operatively
X-ray at 24 months post-operatively
Final prosthetic restoration
Clinical application of collprotect® membrane

Clinical case by Dr. Roland Török, Nuremberg, Germany

Ridge augmentation

Clinical situation before augmentation, thin alveolar ridge

Surgical presentation of the atrophic alveolar ridge

Perforation of the cortical bone and insertion of screws to support placement of bone graft material

Placement of collprotect® membrane at the buccal wall

Ridge augmentation with maxresorb® and maxgraft®, mixture 1:1

Covering of augmentation site with PRF matrices

The collprotect® membrane turned down over defect

Situation after wound healing, at three months post-operatively

Stable integration of maxresorb® particles at re-entry three months post-operatively

Situation after removal of screws and preparation of the implant beds

Insertion of two implants in sufficient bone amount

Tension-free wound closure

For lateral augmentation it is advantageous to place the dry membrane upright in the defect initially, and then fill the defect with a graft material. After rehydration the membrane may be turned down over the defect.
Clinical application of collprotect® membrane

Clinical case by Dr. Viktor Kalenchuk, Chernivtsi, Ukraine

Sinus lift with immediate implantation

In cases of unstable soft tissue situation, or if a wound dehiscence is expected, covering of the barrier membrane with a Jason® fleece (loaded with antibiotics where applicable) is recommended for extra protection of the healing area.
Clinical application of **collprotect®** membrane

Clinical case by Dr. Viktor Kalenchuk, Chernivtsi, Ukraine

Ridge augmentation with **maxgraft®** bonebuilder

To protect the Schneiderian membrane from damage, a membrane may be introduced before filling the sinus cavity with the bone graft material.
Clinical application of collprotect® membrane

Clinical case by Dr. Georg Bayer,
Landsberg am Lech, Germany

Lateral augmentation

- DVT 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 collprotect® membrane
- Complete covering of 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 PD Dr. Dr. Daniel Rothamel, Cologne, Germany

Sinus lift with two-stage implantation

Clinical situation before sinus lift

Clinical situation before sinus lift, occlusal view

Surgical presentation of the buccal wall

Preparation of a lateral sinus window

Introduction of the Jason® membrane into the sinus cavity

The Jason® membrane placed in the sinus cavity to protect the Schneiderian membrane

Filling of the sinus cavity with maxresorb®

maxresorb® in the sinus cavity

Additional lateral augmentation with maxresorb®

Covering of the augmentation area with Jason® membrane

Tension-free wound closure with single button sutures

Excellent osseous integration of the maxresorb® particles without soft tissue ingrowth at re-entry, six months post-operatively

Stable insertion of two implants into sufficient bone matrix

Histological sections of biopsy taken at the time of implantation

Detailed image demonstrates complete integration of the maxresorb® particles within the newly formed bony matrix

Post-operative radiograph
Clinical application of Jason® membrane

Clinical case by PD Dr. Dr. Daniel Rothamel, Cologne, Germany

Dehiscence defect

When using bone graft materials, the application of a barrier membrane is highly recommended to prevent the fast proliferating soft tissue from hindering complete osseous regeneration of the defect.
Clinical application of Jason® membrane

Clinical case by PD Dr. Dr. Daniel Rothamel, Cologne, Germany

Ridge augmentation

Instable bridge situation with abscess formation at tooth 15 after apicoectomy

Bone spreading at tooth 12 for lateral widening of the crest

Covering of the augmentation site with Jason® membrane

Perfect integration of the cerabone® particles into the newly formed bone matrix

OPG six months after tooth extraction shows vertical deficiency at tooth 15

Internal sinus grafting to compensate the vertical deficiency at tooth 15

Tension-free soft tissue closure

Implant uncovering, and insertion of gingiva formers

Clinical situation showing scar tissue formation at former abscess incision site

After implant installation, lateral bone defects require further augmentation

Post-operative x-ray showing the internal sinus grafting and implant positions

Application of cerabone® and autologous bone (mixture 1:2) on the lateral aspect

Stable soft tissue condition after six months of healing

Prosthetic situation following professional dental hygiene treatment at one year post-operatively

Radiological situation at one year post-operatively
Clinical application of Jason® membrane

Clinical case by PD Dr. Dr. Daniel Rothamel, Cologne, Germany

Lateral augmentation

Studies have shown that the highest implant survival rates with the GBR technique are achieved when combining the use of a bone graft material and a barrier membrane.
Small perforations (<5 mm) of the Schneiderian membrane during sinus floor elevation may be covered with a collagen membrane. The patient should be prescribed antibiotics and prophylaxis against swelling (e.g. Xylomethazoline), and must avoid sneezing for two weeks. The treatment must be terminated in case of an acute sinusitis with the presence of pus.
Innovation.
Regeneration.
Aesthetics.