Jason® membrane & collprotect® membrane

Natural collagen membranes for GBR/GTR technique

Scientific and clinical evidence

native
reliable
resorbable
Collagen – a multifaceted protein

Collagen is 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 constitutes ~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 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. 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

<table>
<thead>
<tr>
<th>Collagen Type</th>
<th>Location</th>
</tr>
</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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</table>

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.

Guided Tissue Regeneration (GTR) Guided Bone Regeneration (GBR)

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

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.

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 observed3.

Advantages of collagen membranes
- Exceptional biocompatibility
- Support of 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 wound4. 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® 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 colliprotect® membrane. This membrane possesses loosely structured areas (pores) that penetrate the compact collagen matrix and support a fast vascularization of the membrane.

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 (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

collprotect® membrane is a native collagen membrane made of porcine dermis. Its multistep cleaning process ensures the removal of all antigenic and non-collagenous components, at the same time preserving its natural collagen structure.

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
- Native collagen matrix with natural collagen structure
- Natural wound healing and blood clot support
- 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. of the Schneiderian membrane
- Sinus lift
- Socket and ridge preservation
- Horizontal ridge augmentation
- Fenestration and dehiscence defects
- Intraosseous defects (1 to 3 walls)
- Furcation defects (class I and II)
Jason® membrane
Native pericardium
GBR/GTR membrane

Jason® membrane is a native collagen membrane obtained from porcine pericardium, developed and manufactured for dental tissue regeneration. The advantageous biomechanical and biologic properties of the natural pericardium are preserved during the production process.

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
- Natural long barrier function
- Native, ultra-thin membrane
- Easy handling, may be applied dry or wet
- Supple but strong, with exceptional adaptation to surface contours
- No stickiness after rehydration
- Multidirectional strength and tear resistance

Indications:
- Implantology, Periodontology and Oral and CMF Surgery
- Fenestration and dehiscence defects
- Sinus lift
- Protection of the Schneiderian membrane
- Socket and ridge preservation
- Horizontal and vertical augmentation
- Alveolar ridge reconstruction
- Intraosseous defects (1-3 walls)
- Furcation defects (class I and II)

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

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

## Jason® membrane versus collprotect® membrane

<table>
<thead>
<tr>
<th>Origin</th>
<th>Jason®</th>
<th>collprotect®</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pericardium</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Degradation</td>
<td>8-12 weeks in a rat model, naturally long barrier function due to slow degradation</td>
<td>4-8 weeks in a rat model, intermediate barrier function</td>
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<tr>
<td>Structure</td>
<td>Multi-oriented collagen fibres providing strong tear resistance</td>
<td>Dense network of collagen bundles with pores for better vascularization</td>
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## Product Specifications

<table>
<thead>
<tr>
<th>Art.No.</th>
<th>Size</th>
<th>Content</th>
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<tbody>
<tr>
<td>Jason® membrane</td>
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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>
<td>1 membrane</td>
</tr>
<tr>
<td>683040</td>
<td>30 x 40 mm</td>
<td>1 membrane</td>
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</table>

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<tr>
<td>collprotect® membrane</td>
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<td></td>
</tr>
<tr>
<td>601520</td>
<td>15 x 20 mm</td>
<td>1 membrane</td>
</tr>
<tr>
<td>602030</td>
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</table>
The Jason® membrane supports attachment and proliferation of osteoblast-like cells

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

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 highlights its suitability as scaffold for osteoblast guidance which supports of the bony regeneration of covered defects.

**In vivo** pre-clinical testing

Results from a degradation study in a rat model, Prof. Dr. Dr. D. Rothamel, 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 the Jason® membrane and the 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.

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In vivo pre-clinical testing

Jason® membrane – Excellent biocompatibility and tissue integration
Results from an animal model, Prof. Dr. Dr. D. Rothamel, University of Düsseldorf

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.7

Four 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.

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

Jason® membrane was still intact, serving as barrier against ingrowth of surrounding soft tissue.

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, 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.

Seven 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

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 application of collprotect® membrane

Clinical case by 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

Pre-operative defect measurement

Pre-operative x-ray showing intrabony defect

Defect presentation after preparation of mucoperiosteal flap

Rehydration of cerabone® particles

collprotect® membrane cut to shape

Filling of intrabony defect with cerabone®

collprotect® membrane in place

Wound closure

X-ray control at 12 months post-operatively

X-ray at 24 months post-operatively

Final prosthetic restoration
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. 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

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 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 Prof. Dr. Dr. Daniel Rothamel,
University of Düsseldorf, 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 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 maxresorb® particles within the newly formed bony matrix
Post-operative radiograph
Clinical application of Jason® membrane

Clinical case by Dr. Sebastian Stavar, Houten, Netherlands

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 Prof. Dr. Dr. Daniel Rothamel, University of Düsseldorf, Germany

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
- Mucoperiosteal flap elevation reveals a self-containing defect at tooth 15 and a non-containing lateral bone defect at teeth 14 to 12
- Bone spreading at tooth 12 for lateral widening of the crest
- Internal sinus grafting to compensate the vertical deficiency at tooth 15
- After implant installation, 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-operatively
- Radiological situation at one year post-operatively
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.
Clinical application of Jason® membrane

Clinical case by Prof. Dr. Dr. Daniel Rothamel, University of Düsseldorf, Germany
Sinus lift with two-stage implantation

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.

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