Jason® membrane
collprotect® membrane
Natural collagen membranes for GBR/GTR
Scientific and clinical evidence
by PD Dr. Dr. Daniel Rothamel et al.
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University of Cologne, Germany

- Since 2010 Assistant Professor at the Department of Oral and Maxillofacial Plastic Surgery (Prof. Dr. Dr. J. Zöller), University of Cologne, Germany
- 2009, habilitation (post-doctoral lecturing qualification), University of Cologne
  Thesis: “Reconstruction of defects of the alveolar ridge using artificial and autogenous bone blocks and growth factors”
- 2008, doctorate in human medicine (Dr. med.), Heinrich-Heine University of Düsseldorf
  Thesis: “Biocompatibility, biodegradation and angiogenetic aspects of native and cross-linked collagen membranes”
- Since 2007 specialist in Oral Surgery
- 2004, doctorate in dental medicine (Dr. med. dent.), Heinrich-Heine University of Düsseldorf, Germany
  Thesis: „Establishing a new method for quantification of tooth hypersensitivity”

Already during his medicine studies, PD Dr. Dr. Daniel Rothamel was focused on scientific subjects in the field of bone regeneration and implantology. He has published more than 80 articles, many of them in renowned international scientific journals. He acts as a reviewer for several journals and frequently participates as a lecturer on congresses and training courses in Germany as well as other countries. His research and lecture activities are focused on subjects such as Guided Bone Regeneration (GBR), socket preservation, implant surfaces, collagen membranes, bone substitute materials, growth factors, face trauma, cancer rehabilitation and hemostyptics.
Collagen – a multifaceted protein

Collagens are a family of structural proteins that are found in the extracellular matrix and represent the main component of the skin, blood vessels, tendons, cartilage and bone. Approx. 25% of all proteins found in the body are collagens, in the connective tissue collagens account for ~80% of all proteins. About 28 types of collagen are known that differ in the primary sequence of their peptide chains.

Three collagen molecules are packed together as a triple helix, thus forming the collagen fibril. Collagen fibers then evolve from the aggregation of several fibrils. These fibers show a remarkable tear resistance providing 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 or osteoblasts.

Collagen types

Collagen type I is the most broadly distributed protein and has the largest quantitative share in the body. 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 or the peritoneum. The gingival connective tissue is made up of up to 60% of 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 type III, also called elastine, is responsible for the elastic properties of blood vessels and many tissues such as the skin and lunge tissue. Type IV collagen is the major structural element of the basal lamina.

Most common types of collagens

<table>
<thead>
<tr>
<th>Collagen type</th>
<th>Tissues</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>
</tr>
</tbody>
</table>

Collagen membranes for the GBR and GTR technique

**The GRB/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 to separate the slowly proliferating regenerative cell types like osteoblasts and periodontal cells from the fast proliferating epithelial and connective tissue cells, thus enabling the predictable regeneration of lost tissue.

GTR aims at the regeneration of the periodontium. A barrier membrane is placed between the epithelium and the tooth, therefore giving the cells of the periodontal ligament the time and space for regeneration. 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, which prevents the collapse of the membrane and serves as an osteoconductive scaffold for the ingrowth of bone cells (or bone precursor cells). The barrier membrane prevents the ingrowth of soft tissue into the defect area and the encapsulation of the bone graft material, thus enabling the bony regeneration.

**Membrane types**

The first generation of barrier membranes was based on non-resorbable materials like expanded polytetrafluorethylene (ePTFE) and cellulose acetate or titanium. These membranes gained predictable good results, but had the disadvantage of a secondary surgery for removal associated with a potential grafting site morbidity. Therefore, the development proceeded in the direction of resorbable membranes. As material for resorbable membranes synthetic polymers such as polylactides and polyglycolides (acidic degradation) and the natural polymer collagen were used. Due to the manifold positive natural properties of collagen the use of collagen membranes has emerged as the material of choice.

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The advantages of collagen

Several factors make collagen an optimal biologic material for resorbable barrier membranes. One important characteristic is the excellent biocompatibility and also the degradation products of collagens are biocompatible. Collagen is widely distributed throughout the body, making up approx. 60% of all proteins of the gingival connective tissue. Furthermore, it exhibits a very low antigenicity.

Therefore, collagens can be transferred from animal to human without problems. Collagens are degraded only by specific enzymes called collagenases and are resistant to an unspecific proteolytic degradation. Collagens are involved in the primary haemostatic reaction. Thus, collagen membranes can contribute to a fast stabilization of the wound area. Another advantage is the chemotactic attraction of regenerative cells like osteoblasts, gingival fibroblasts and periodontal ligament cells by collagen. An exposure following dehiscence leads to a quick proteolytic degradation of collagen membranes, yet a secondary granulation without any inflammatory reactions can be observed³.

Collagen as a natural haemostypt

A damage of the walls of blood vessels leads to the release of subendothelial collagen that directly or indirectly interacts with surface receptors of thrombocytes. This 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 the blood coagulum and contribute to a rapid stabilization of the wound area. Based on their haemostatic effect, collagens are not only used as barrier membranes, but also as collagen sponges and collagen cones for the stabilization of extraction sockets and biopsy harvesting sites or to cover minor oral wounds 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 a BSE transmission. Moreover, porcine collagen exhibits a high homology to human collagen and therefore a very good biocompatibility. Due to these reasons botiss membranes are produced from porcine collagen.

Collagen membranes can originate from various tissues ranging from dermis, to peritoneum or pericardium. Accordingly, these membranes differ in their handling and degradation properties and the resulting barrier function.

Properties of barrier membranes – vascularization versus barrier function

The disadvantage of most collagen membranes, other than the botiss membranes, lays in their rapid enzymatic degradation by collagenases, resulting in a limited stability and correspondingly short barrier function. A possibility to influence the barrier function is to choose a specific original tissue to impart the membranes with a better stability. In that way membranes made of pericardium, such as the Jason® membrane, due to a structural speciality, exhibit a slowed degradation and thus offer a prolonged barrier function. Furthermore, pericardium membranes can be distinguished by an extraordinarily high tear resistance and excellent handling properties (e.g. good adaptation to surface contours, no sticking).

Histology of a big blood vessel and some smaller ones

The barrier function can also be extended by the use of membranes with a very dense collagen structure, but this dense structure might oppose the 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 because the surrounding connective tissue of small capillaries contains undifferentiated progenitor cells (pericytes). These cells can evolve into osteoblasts that are responsible for new bone formation. Therefore, the selective permeability of membranes for blood vessels is desirable. One example of such a semi-permeable membrane is the collprotect® membrane. This membrane possesses loosely structured areas (pores) punctuating the compact collagen matrix and supporting a fast vascularization.


Histology of a big blood vessel and some smaller ones
botiss membranes provide better handling and stability

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

The botiss membranes are native materials, meaning that the natural collagen structure of the original tissue (pericardium or dermis) and thus their natural properties are preserved in the special production process. Naturally grown membranes exhibit especially good handling properties, such as pull and tear resistance, and a good adaptation to surface contours compared to membranes made of pressed collagen.

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 of collagen type I and a lower proportion of collagen type III.
collprotect® membrane is a natural collagen membrane. Due to the rough and porous three-dimensional collagen structure, controlled wound healing in combination with Guided Bone and Tissue Regeneration achieves optimal treatment results. During the regeneration process collprotect® membrane offers the necessary barrier function balanced with a controlled degradation time without inflammatory reaction.

The soft tissue around a collprotect® membrane usually heals without any problems, even if postoperative dehiscences occur. The biologic structure of the collprotect® membrane surface prevents ingrowth of soft tissue, but allows cell and blood vessel penetration and quick integration into the surrounding tissue. This unique biologic function provides a perfect basis for hard and soft tissue healing.

### Properties

- Three-dimensional natural collagen matrix
- Controlled wound healing and blood clot support
- Optimal barrier function in GBR/GTR procedures
- Degradation time approx. 8-12 weeks
- Easy application and handling in dry or wet status
- Rough and porous structure for cell guidance
- Natural collagen structure

### Indications:

- Implantology, Periodontology, Oral Surgery & CMF
- Protection or covering of minor perforations of the Schneiderian membrane
- Sinus lift
- Socket preservation
- Horizontal and/or vertical ridge augmentation
- GBR/GTR simultaneous use with bone substitutes
- Fenestration and dehiscence defects
- Intraosseous and furcation defects
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, maintaining the characteristics of this natural tissue.

Easy handling, optimal wound healing and the natural biomechanics combined with highly predictable results are the essential properties of the Jason® membrane.

Due to the natural, strong multidirectional-linking of the collagen network, Jason® membrane provides a long-lasting, adequate barrier function for 3-6 months. The use of Jason® membrane for regeneration of bone and tissue is an essential component of the GBR and GTR concept.

Properties
- Long-lasting barrier function for ~12-28 weeks
- Natural structure and low thickness
- Easy manipulation, can be applied dry and wet
- Supple but strong, with exceptional adaptability to surface contours
- No stickiness after rehydration
- Fast vascularization due to 3-dimensional structure
- Multidirectional strength and tear resistance

Indications:
- Implantology,
- Periodontology,
- Oral Surgery & CMF
- Implant dehiscence
- Sinus lift
- Protection of Schneiderian membrane
- Fenestration defects
- Extraction sockets
- Ridge preservation
- Horizontal & vertical augmentation
- Alveolar ridge reconstruction
- Intraosseous defects (1-3 walls)
- Furcation defects (class I-II)
## Product comparison

### Jason® membrane versus collprotect® membrane

<table>
<thead>
<tr>
<th>Origin</th>
<th>Pericardium</th>
<th>Dermis</th>
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</thead>
<tbody>
<tr>
<td>Degradation</td>
<td>12-28 weeks</td>
<td>8-12 weeks</td>
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<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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</table>

### Key factors for barrier membranes

- **PHPEUDQHB**

### Product Specifications

<table>
<thead>
<tr>
<th>Jason® membrane</th>
<th>Art.-No.</th>
<th>Size</th>
<th>Content</th>
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<td>681520</td>
<td>15x20mm</td>
<td>1 Membrane</td>
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<tr>
<td></td>
<td>682030</td>
<td>20x30mm</td>
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<tr>
<td></td>
<td>683040</td>
<td>30x40mm</td>
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<table>
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<th>Size</th>
<th>Content</th>
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</thead>
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<td>15x20mm</td>
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<td></td>
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<td>30x40mm</td>
<td>1 Membrane</td>
</tr>
</tbody>
</table>
In vitro testing

Jason® membrane supports attachment and proliferation of osteoblast-like cells
Results from cell culture, Dr. M. Herten, University of Düsseldorf and PD Dr. Dr. D. Rothamel, University of Cologne

The incubation of Jason® membrane (multilayer) and a bilayer membrane with osteoblast-like SaOs-2 cells showed a significantly superior proliferation of the cells on Jason® membrane after 7 days.

This excellent cell attachment makes Jason® membrane a good scaffold for the guidance of osteoblasts, therefore supporting 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 differs between tissues. Tissue integration and degradation of Jason® membrane and collprotect® membrane were tested by subcutaneous implantation in rats. Jason® membrane that originates from pericardium was integrated within the first weeks and remained stable for a healing period of 8-12 weeks (please note the different metabolism rates for rats and humans).

For the dermal collagen of collprotect® membrane cell invasion took a little longer, but the membrane was degraded in the first 4-8 weeks.

6 Biodegradation patterns of native and cross-linked porcine collagen matrices – an experimental study in rats. Daniel Rothamel, Tim Fenitz, Marcel Benner, Arndt Happe, Matthias Kreppel, Martin Scheer and Joachim Zöller, University Hospital of Cologne, Cologne, Germany, Poster EAO 2011
In vivo pre-clinical testing

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

Analysis of the tissue integration and morphological structure of Jason® membrane 4 to 24 weeks after lateral augmentation in a dog model (Toluidine blue staining)

The membrane was integrated into the surrounding tissue without any inflammation. Significant degradation of the membrane started at week 8 and proceeded until week 12. A bilayer membrane that was tested in the same model showed a comparably good tissue integration, but was nearly completely degraded after 8 weeks.

4 weeks healing time
Both membranes show good tissue integration without any inflammatory reaction.
Initial ingrowth of blood vessels improves nutrition of the graft and osseous regeneration.

Jason® membrane after 4 weeks healing time Bilayer membrane after 4 weeks healing time

8 weeks healing time
The bilayer membrane is nearly completely resorbed.
Jason® membrane is still intact, providing barrier against ingrowth of surrounding soft tissue.

Bilayer membrane after 8 weeks healing time Jason® membrane after 8 weeks healing time

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

Jason® membrane after 12 weeks healing time
In vivo pre-clinical testing

collprotect® membrane –
rapid angiogenesis and transmembranous vascularization

In vitro results from a rat model, PD Dr. Dr. D. Rothamel,
University of Cologne

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

After four weeks, blood vessels in the pores of the membrane indicate a trans-
membranous vascularization. The early vascularization of the membrane supports
the blood supply and nutrition of the grafting site, therefore promoting the osseous
regeneration. Furthermore, the regeneration is promoted by progenitor cells lining
the blood vessels and evolving into bone forming osteoblasts.

7 days after implantation

28 days after implantation

7 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 a pore of the membrane can be ob-
served.

Areas of a fibrillary structure
within the dense collagen fiber
network of collprotect® mem-
brane (pores, see green arrow
and right picture) facilitate the in-
growth of blood vessels into the
defect area through the memb-
brane.
Clinical application of collprotect® membrane

Clinical Cases by Dr. Raluca Cosgarea and
Prof. Dr. Dr. Anton Sculean Cluj, Romania and Bern, Switzerland

Regeneration of intraosseous defects

Pre-operative x-ray showing intrabony defect

Situation before surgery

Defect presentation after preparation of mucoperiosteal flap

Intraoperative measurement of intrabony defect

collprotect® membrane cut to shape

Filling of intrabony defect with cerabone®

collprotect® membrane in place

Saliva-proof wound closure

Preoperative x-ray control

Situation before surgery

Defect presentation after preparation of mucoperiosteal flap

Intraoperative measurement of intrabony defect

Defect filling with cerabone®

Adaptation of collprotect® membrane

Saliva-proof wound closure

X-ray control 6 months post-op
Clinical application of collprotect® membrane

Clinical case by Dr. Roland Török, Nuremberg, Germany

Ridge augmentation

For lateral augmentation the initial placement of the dry membrane and following application of the graft material is advantageous. After rehydration the membrane can 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 case of an unstable soft tissue situation or when you expect a wound dehiscence to occur, we recommend to cover the membrane with a Jason® fleece (where applicable, soaked with antibiotics), to protect the healing area by the fast resorbing fleece.
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 can be introduced before filling the sinus cavity with the bone graft material.
Clinical application of Jason® membrane

Clinical case by PD Dr. Dr. Daniel Rothamel, University of 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 Jason® membrane into the sinus cavity
Jason® membrane 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
Good osseous integration of the maxresorb® particles without soft tissue ingrowth 6 months post-OP at re-entry

Stable insertion of two implants into sufficient bone matrix
Histology of biopsy taken at implantation
Detail image of histology showing complete integration of particle in new bone matrix
Post-operative radiograph
Clinical application of Jason® membrane

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

Dehiscence defect

4 months after tooth extraction, resorption of the vestibular wall visible after flap elevation

Implant in place showing large buccal dehiscence defect

Augmentation of the defect with cerabone®

Covering of the augmentation site with Jason® membrane

Good soft tissue situation 6 months after implantation, occlusal view

Good soft tissue situation 6 months after implantation, vestibular view

Excellent bone formation at re-entry, implant covered by new bone matrix

Uncovering of implant

Histology of biopsy taken at implant uncovering showing stable integration of cerabone® particles

When using bone graft materials, the application of a barrier membrane is highly recommended, otherwise the fast proliferating soft tissue will oppose the complete osseous regeneration of the defect.
Clinical application of Jason® membrane

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

Ridge augmentation

- Instable bridge situation with abscess formation at tooth 15 after apicectomy
- OPG 6 months after tooth extraction shows vertical deficiency at 15
- Clinical situation with scar formation at former abscess incision site
- Mucoperiosteal flap elevation reveals a self-containing defect at 15 and a non-containing lateral bone defect at 14 – 12
- Bone spreading at 12 for lateral widening of the crest
- Internal sinus grafting to compensate the vertical deficiency at 15
- After implant installation, lateral bone defects need 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 position of implants and internal sinus grafting
- Stable conditions after 6 months healing period
- Perfect integration of the cerabone® particles into newly formed bone matrix
- Implant uncovering and insertion of gingiva formers
- Prosthetic situation after one year following professional dental hygiene
- Radiological situation after one year
Clinical application of Jason® membrane

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

Lateral augmentation

Studies showed that highest implant survival rates were achieved with the GBR technique, combining the use of a bone graft material and a barrier membrane.
In case of a small perforation (< 5 mm) of the Schneiderian membrane in progress of sinus floor elevation, the application of a collagen membrane is a useful tool for perforation coverage. Make sure that the patient doesn’t sneeze for two weeks and prescribe antibiotics and swelling prophylaxis (e.g. Xylometazoline). Never continue if you find an acute sinusitis with presence of pus.
Innovation.
Regeneration.
Aesthetics.

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