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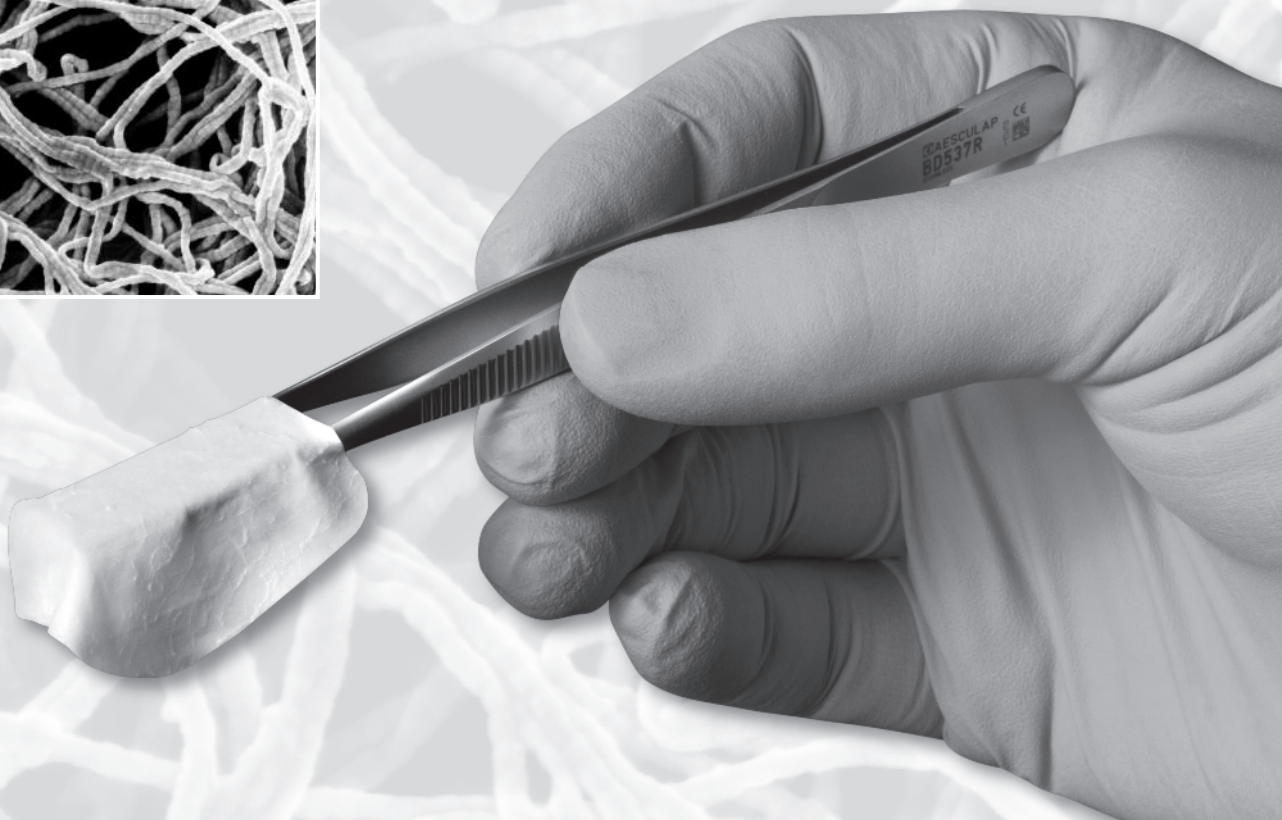
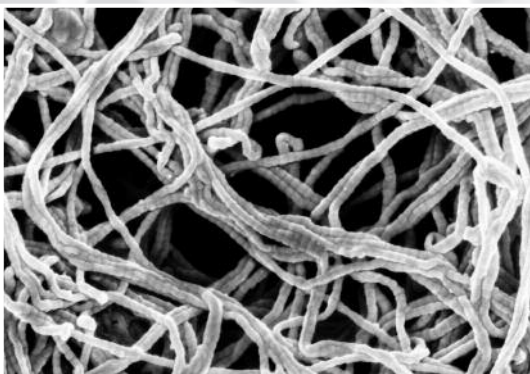
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“New Materials in GBR” and “Safe Bone Regeneration through a new Collagen Membrane”

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New Materials in GBR

Given the current general guidelines for dental implantation with regard to aesthetic aspects and the required long-term prognoses, it is frequently necessary to use augmentative measures to improve the implant site before or during implant placement.

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■ Augmentation using various techniques has been developed since the paradigm shift from bone-driven implantation techniques to “backward planning” in order to avoid an unfavourable crown-implant length relationship in general, or to avoid for example pink ceramic in the aesthetically visible area.

In planning the replacement of a lost or extracted tooth with an implant, the aesthetic and static final result must be taken into consideration. According to the current academic opinion, the bony and gingival tissue around the implant site must be restored in many cases—at least in the visible area. Disregarding such prerequisites can lead to serious failure.

Membranes are frequently required in implantology and periodontology for protection and for fixation of augmented sites, or in “Guided Bone Regeneration” (GBR). In the USA, the FDA recommends using suitable membranes when building up bone in order to prevent the migration of bone replacement material into the soft tissue. Resorbable membranes are superior to non-resorbable membranes as they show higher tissue compatibility, have a lower dehiscence rate and are easier to handle.^{4,26} They show a higher biocompatibility to the PDL fibroblasts as well as to osteoblasts,²² and are significantly more biocompatible than PTFE membranes.²⁴

For this reason, in Germany, resorbable membranes derived from collagen from an animal source are most frequently used. The use of such membranes has been well documented and has demonstrated a high probability of success.^{9,13,14}

The barrier function is particularly important in the augmentation of larger bony defects, especially in case of early exposures of the membrane (dehiscence). Because of bacterial contamination, non-resorbable membranes should be removed at an early stage if there is exposure to the oral cavity. Dehiscence with a resorbable membrane does not necessarily lead to contamination of the augmentation site, but results, however, in a reduced volume of the augmented bone due to a faster disintegration of the membrane itself.²⁶

Non-cross-linked collagen membranes show a dehiscence rate of 22–32 %, ^{18,20,25} with a stable barrier function of approximately four to six weeks.^{5,19} By chemical cross-linking processes, the stability of a membrane against degradation can be increased, leading to a slower resorption. There is, however, a significantly higher dehiscence rate of 39–64 % of cross-linked membranes.^{10,20,25}

The non-cross-linked collagen membrane (Remaix, Matricel GmbH, Herzogenrath, Germany/creos™ xeno.pro-

tect, Nobel Biocare, Gothenburg, Sweden) that was used in this study is a novel bio-resorbable barrier membrane derived from porcine collagen and elastin. It was clinically approved in Germany in 2009 and is marketed as a CE certified class III medical device. It is a highly purified natural membrane that is not chemically cross-linked.

The membrane development was based on Matricel's experience with the collagen membrane ACI-Maix in the field of orthopaedics. ACI-Maix has been used clinically for the tissue engineering of cartilage according to the matrix-induced autologous chondrocyte implantation (MACI) technique in more than 10,000 patients since 2002.^{3,6,16} It has been specifically optimised for the indicated use as a dental barrier membrane.

The membrane has a homogenous structure on both sides, which obviates a risk of confusing the sides during surgery. *In vitro* studies show a significantly higher collagen stability of the membrane in comparison to non-cross-linked reference membranes (unpublished Matricel data). Comparative studies with rats also show a lower degradation rate of the membrane compared to other non-cross-linked membranes *in vivo*. Rothamel et al. determined a degradation time of 2–4 weeks for Bio-Gide® (Geistlich Biomaterials); Jäger et al. observed a degradation time of 6–12 weeks for ACI-Remaix.^{17,23} Unpublished results from animal implantation studies conducted by Matricel have shown a degradation time of 12–16 weeks for the membrane.

There is definitely a need for a degradable collagen membrane without clinical side effects and risk of infection with a low dehiscence rate and high stability against degradation, in order to guarantee, also for ma-

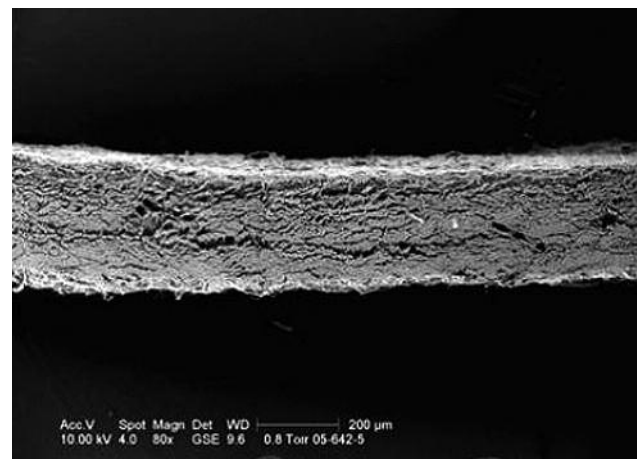


Fig. 1: Electronmicroscopic scan: cross section of the membrane showing both surfaces.



Fig. 2: Orthopantomograph of the first consultation.

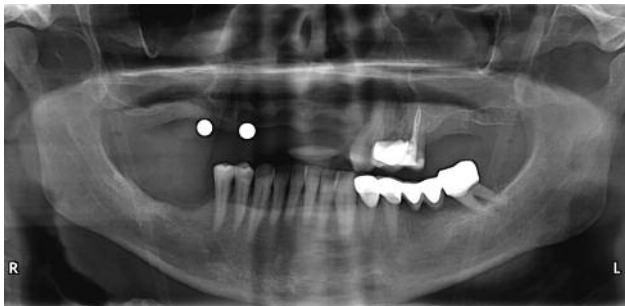


Fig. 3: Orthopantomograph with X-ray measuring template and 5 mm steel balls in regions 13,15.

for guided bone augmentation procedures, the necessary mechanical stability and a sufficiently protected space during bone regeneration.

We have been using the Rемаix/creos™ xeno.protect membrane (Matricel/Nobel Biocare) in our clinic as our clinical standard for augmentative operations of the jaw or maxillary sinus since October 2010. These or similar operations in our clinic were previously carried out using the Bio-Gide® (Geistlich Biomaterials) collagen membrane. Apart from this, the operative procedure has not been changed. The success of augmentation

with the aid of the GBR technique depends largely on primary, tension-free wound closure as well as on a stable positioning of the augmented volume.^{11,12,21} “Guided Bone Regeneration” can be used for both horizontal and vertical augmentation. It is significantly more successful if it is combined with bone or bone graft material.⁷

The GBR method is a minimally invasive method with a high success rate which is commonly used in everyday practice.¹ For this reason, we use this technique frequently. However, it has its limitations, particularly in the field of vertical augmentations of atrophied jaws. Especially in a severely atrophied lower mandible, other measures are thus required for bone construction. If a vertical bone construction with GBR is carried out, its success depends largely on whether a mechanically stable space for regenerating bone can be maintained (for example by using titanium meshes).²

Precautions against the previously described bone resorption processes can already be taken directly after tooth extraction if there is no acute apical inflammation. In such cases, especially in the region of front teeth in the upper jaw, we frequently perform a “socket preservation” by filling the alveolus with bone replacement material. When filling defects larger than 2 mm or even entire alveoli, the success rate is higher if an additional barrier membrane is used.¹⁵

Case 1 (Figs. 2–11)

The 61-year-old patient consulted our clinic with the wish for an aesthetic improvement of the situation of his upper front teeth. He was diagnosed to have severe periodontitis. The prognosis following periodontitis

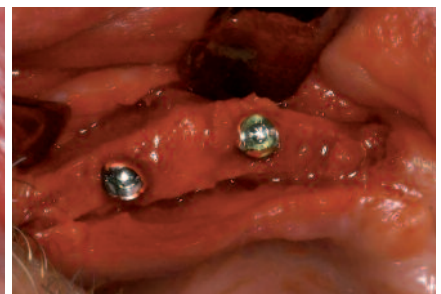
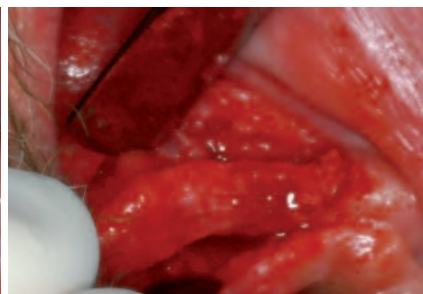


Fig. 4: The jaw crest in the implant area seems to be wide enough prior to surgical opening of the operation site. – **Fig. 5:** The jaw crest in the implant area after the formation of a muco-periosteal flap. After a vertical alveolotomy to create a plateau, the jaw crest is just wide enough for the insertion of implants with a diameter of 3.75 mm. – **Fig. 6:** View of the thin buccal bone lamellae after insertion of the implant.

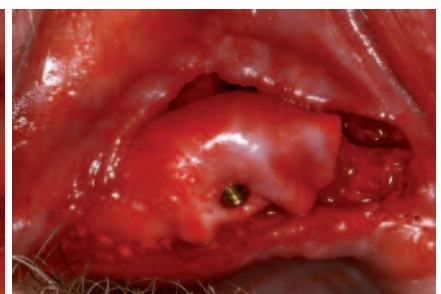


Fig. 7: Positioning the creos™ xeno.protect/Rемаix membrane (Nobel Biocare/Matricel), size 25 x 30 mm. – **Fig. 8:** Filling the “membrane pocket” with BioOss® bone replacement material (Geistlich Biomaterials). – **Fig. 9:** Crest fixation of the membrane with titanium pins.



Fig. 10: Tension-free closure of the mucous membrane.

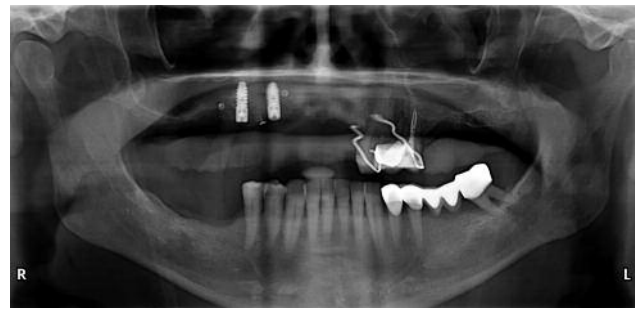


Fig. 11: Postoperative orthopantomograph.

treatment and root canal treatment (tooth 25) stated that only three teeth (teeth 23–25) were in a states to be preserved permanently. The teeth which could not be preserved were extracted during the preliminary periodontitis treatment and a temporary prosthesis was fitted for two months.

As a consequence, the patient decided on a telescopic, removable model cast prosthesis via strategic additional supports with implantation in regions 13 and 15. Two Templant ICX implants (Medentis Medical) with a size of 4.1 mm x 12.5 mm were planned. However, during implantation it became obvious that the implant region in the jaw was not wide enough, even after the creation of a plateau through vertical reduction. Thus two implants of the same type but with a width of 3.75 mm were placed. As the buccal bone lamella prior to implantation was only approx. 0.5 mm thick, particularly at the level of the final apical third, there was a risk of absorption of the buccal bone around the implants. For this reason, we decided on a prophylactic buccal augmentation with Bio-Oss® (Geistlich Biomaterials) as well as a Remaix/creos™ xeno.protect membrane (Matricel/Nobel Biocare) according to “Guided Bone Regeneration” (GBR) guidelines. Before bone augmentation, the buccal bone was perforated into the spongiosa at several locations using a rose-head bur, in order to allow a blood and cell migration into the bone augmentation material. The membrane was fixed with titanium pins in order to form a stable pocket. After periosteal incision, the gingiva was closed with sutures. There were no negative side-effects during wound healing; everything proceeded as planned with no signs of inflammation.

Case 2 (Figs. 12–21)

The 75-year-old female patient consulted our clinic with the wish for a prosthesis with implants in the upper jaw, as her denture was becoming increasingly loose, especially during eating, due to a pronounced resorption processes. Due to the health situation and the advanced age of the patient and in spite of the expected major GBR augmentation, we decided against taking a bone block from the lower jaw or even from the iliac crest. The implantation was to be performed in the regions of 12, 14, 22 and 24, as the patient also did not want a sinus lift operation. In the orthopantomograph,

an adequate height of remaining bone for the insertion of implants with a length of 11.5 mm was shown. The insertion of four 11.5 mm/3.75 mm ICX Templant implants (Medentis Medical) was planned simultaneously to a ridge augmentation by means of GBR, or a sole augmentation without implant insertion if the width of the existing bone should be absolutely insufficient. Surgical opening of the jaw revealed that both sides of the jaw were too narrow for a single-stage procedure with simultaneous augmentation in the planned area. For this reason, we decided on vertical and horizontal ridge augmentation according to the GBR technique. As a large amount of bone needed to be regenerated, we harvested autologous bone chips from the mandibular ramus on the right side with the aid of the Safescraper (Imtegra). These were mixed with approximately the same amount of Bio-Oss® (Geistlich Biomaterials). After buccal perforation of the area to be augmented with a Rose-head bur, a stable pocket for the bone mixture was formed on both sides with a



Fig. 12: Preoperative orthopantomograph.



Fig. 13: Toothless upper jaw.

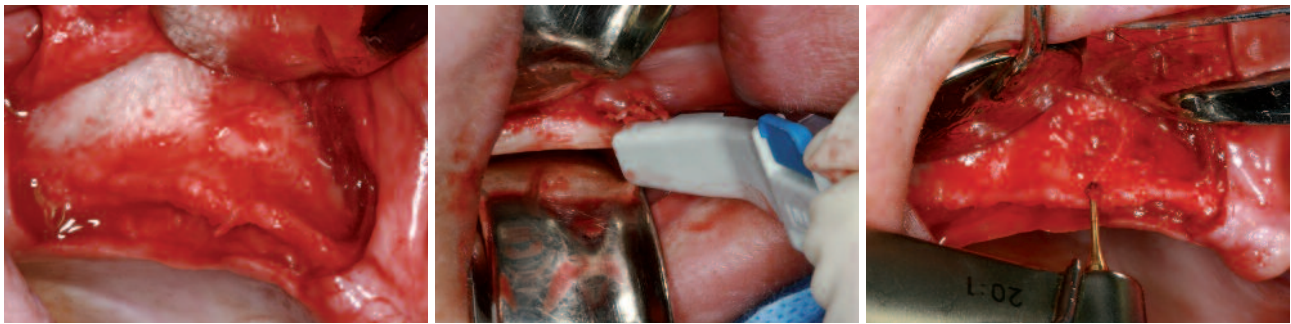


Fig. 14: Presentation of the operation site in regions 11–15 after formation of a mucoperiosteal flap. Implantation is not possible because the jaw crest is too narrow. – **Fig. 15:** Removal of autologous bone chips from the right mandibular ramus with the Safescraper (Imtegra). – **Fig. 16:** Buccal perforation of the jaw crest for the extraction of blood and cells from the bone.

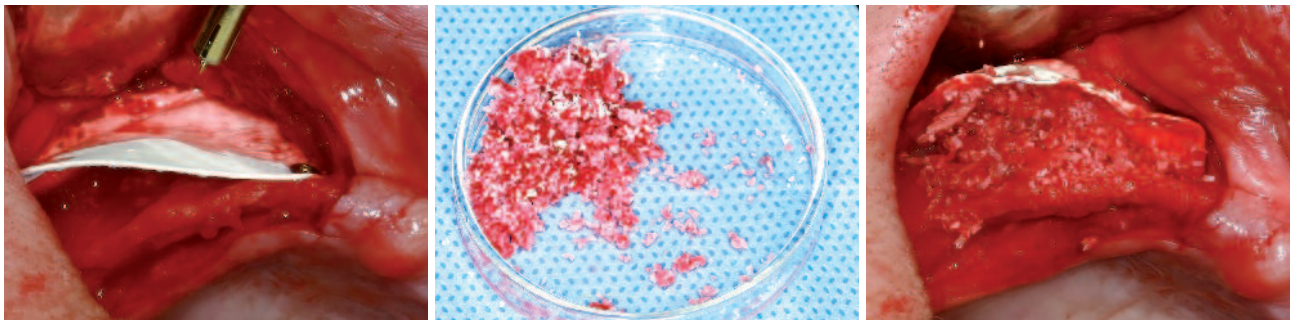


Fig. 17: Positioning and fixation of the membrane with titanium pins. – **Fig. 18:** Extracted bone chips mixed with Bio-Oss® (Geistlich Biomaterials). – **Fig. 19:** “Membrane pocket” filled with bone mixture.

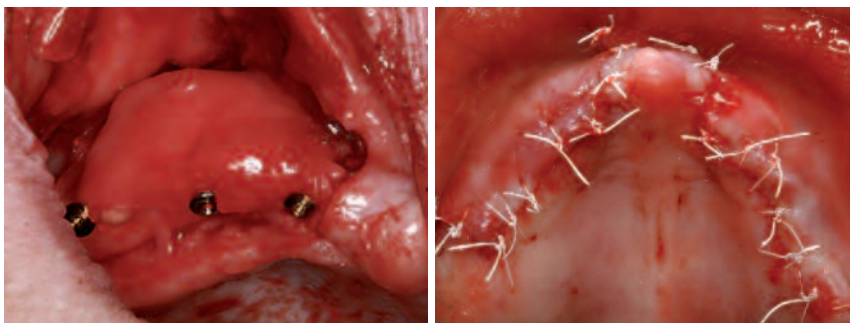


Fig. 20: Crest fixation of the membrane with titanium pins. – **Fig. 21:** Tension-free closure of the mucoperiosteal flaps. Note the increase in width of the jaw crest!

One advantage of the new membrane is that during surgery, in contrast to other competitive products, there can be no mix-up of the membrane surfaces. Even when wetted, the membrane has a higher stability than the collagen membranes we have used previously, enabling safer covering and adaptation during GBR.

The clinical implementation of the Rемаix/creos™ xeno.protect membrane for augmentation in

25 x 30 mm Rемаix/creos™ xeno.protect membrane (Matricel/Nobel Biocare) using titanium pins. After substantial, repeated periosteal incision, the wound edges were closed again and sutured tension-free. The patient was prescribed a temporary prosthesis for a ten-day period of primary healing. When sutures were removed after ten days, the prosthesis was ground down massively in the augmented region and lined with soft material.

The wound healing phase proceeded without any problems, and implants will be inserted in the augmented area after a healing time of at least six months.

the field of implantation shows promising first results. However, evidence-based data from larger-scale clinical case studies need to be collected. Here, the significantly higher membrane stability against degradation that has been confirmed in laboratory experiments should also be substantiated clinically. ■

Discussion

Since we substituted the previously-used barrier membranes by the new membrane in our clinic, we have not seen any increase in wound healing problems, pain or failure.

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Safe Bone Regeneration through a new Collagen Membrane

Guided bone regeneration (GBR) as a standard procedure in implant surgery is a well described and well investigated procedure for the restoration of an adequate implant bed and aesthetically pleasing results. The use of a barrier membrane to prevent quickly proliferating epithelial and connective tissue cells from growing into the implant site is a basic prerequisite for a sufficient regeneration of bony defects or alveolar ridge augmentation using guided bone regeneration (GBR).

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■ The US Food and Drug Administration recommends the use of suitable membranes for bone augmentation in order to prevent bone substitute material from migrating into the soft tissue. Resorbable membranes are superior to non-resorbable membranes due to their improved histocompatibility, lower rates of dehiscence, and easier handling. They have high cell compatibility with respect to PDL fibroblasts as well as osteoblasts, and are clearly more biocompatible than PTFE membranes. This translates to improved tissue integration, reduced foreign body reactions and, as a result, lower rates of dehiscence. Moreover, quick transmembranous angiogenesis has been observed, which was associated with faster bone regeneration in animal studies. Finally, good form stability of the augmented area is required in order to prevent collapse of the the space created during GBR. When using collagen membranes, this is generally achieved by applying the patient's own bone or bone substitute material under the membrane. The membrane itself, however, should be of sufficient mechanical stability to keep the augmentation material safely in place until remodelling has advanced to the point that a new bone precursor tissue of stable position is present.

Therefore, membranes made of resorbable collagen of animal origin are used in most cases in Germany today. The use of such membranes is well documented and backed up by results showing a high probability of success.

Non-chemically cross-linked collagen membranes have a rate of dehiscence ranging between 22 and 32 per cent with a stable barrier function of approximately four to



Patient case 1 – Fig. 1: Preoperative panoramic radiograph.

six months. It is true that an additional chemical cross-linking results in a longer in situ function of the membrane before its resorption, but this is also associated with increased rates of dehiscence ranging from 39 to 64 per cent.

Bioresorbable barrier membrane

The novel collagen membrane presented here is a bioresorbable barrier membrane made of porcine collagen and elastin. It was marketed as a CE-certified class-3 medical device in Germany in 2009 under the name Remaix (Matricel GmbH, Herzogenrath Germany) and since 2013 it is distributed as creos™ xeno.protect (Nobel Biocare, Gothenburg, Sweden). The membrane is based on a Matricel development for the orthopaedic field, where it has been used under the name of ACI-Maix for matrix-induced autologous chondrocyte implantation (MACI) in more than 10,000 patients already since 2002.

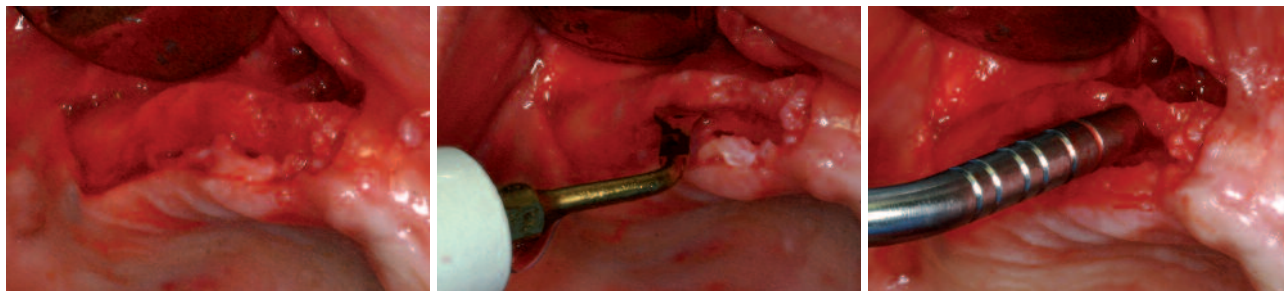


Fig. 2: Presentation of the alveolar ridge region 11–15. – **Fig. 3:** Bone splitting region 11–15 using piezosurgery. – **Fig. 4:** Formation of the implant bed using osteotomes.

This membrane has been further optimised for use as a dental barrier membrane. It has a bilaterally homogeneous structure which eliminates the danger of confusing the sides during the operation.

In vitro studies show a clearly increased collagenase stability of creos™ xeno.protect/Remaix membrane compared to, among others, the Bio-Gide® membrane (Geistlich Biomaterials AG) as an example of another non-cross-linked reference product (unpublished data, Matricel GmbH). When comparing different studies performed on rats, a longer resorption rate is found *in vivo* as well. For example, Rothamel et al. report a resorption period of two to six weeks for Bio-Gide®, Jäger et al. report a resorption period of six to twelve weeks for the ACI-Maix. Still unpublished data from animal implant studies performed by Matricel GmbH resulted in a resorption time of 12 to 16 weeks for the creos™ xeno.protect/Remaix membrane. Such a resorbable collagen membrane without clinically adverse effects and risk of infection with a low rate of dehiscence and higher rate of stability through longer resorption periods is needed in order to ensure the required mechanical stability as well as a longer healing period for large bone augmentations.

We have been using this membrane in our clinic as a standard for augmentation procedures in the alveolar ridge or in the maxillary sinus since October 2010. Prior, we performed these or similar procedures in our clinic using the collagen membrane Bio-Gide®. Apart from that, the surgical procedure has not been changed. The success of augmentations using the GBR technology mainly depends primarily upon achieving a tension-free wound closure as well as on a stable positioning of the augmentation material.

Success of GBR

Guided Bone Regeneration can be used both for horizontal and vertical augmentation. Here, it shows significantly increased success when combined with bone or bone substitute material.

The GBR method is a standard procedure for everyday use in practice, offering high probability of success and low invasiveness for the patient. That is why we often use this technique. However, it reaches its limits quite

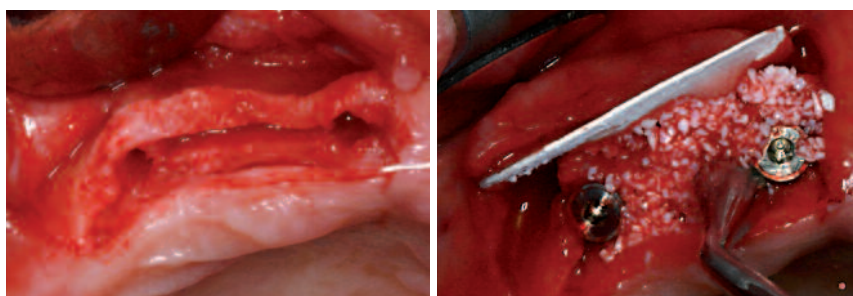


Fig. 5: Presentation of the alveolar ridge region 11–15 after bone spreading and formation of the implant bed. – **Fig. 6:** Situation after insertion of the ICX-templant® implants in the regions 12 and 14 (medentis medical), augmentation with Bio-Oss® (Geistlich Biomaterials AG) and membrane fixation (creos™ xeno.protect, Nobel Biocare/Remaix, Matricel GmbH) using titanium pins.

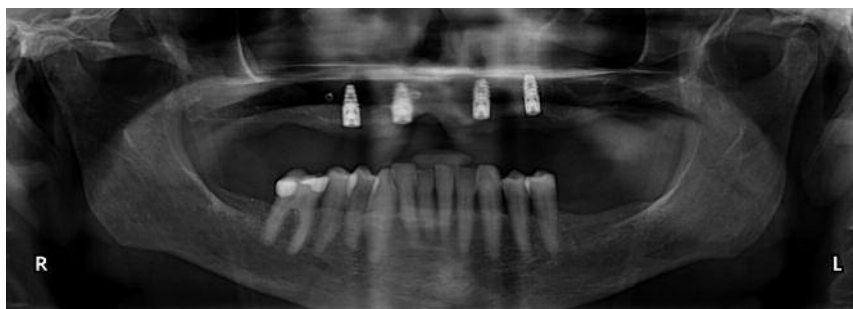


Fig. 7: Postoperative panoramic radiograph.

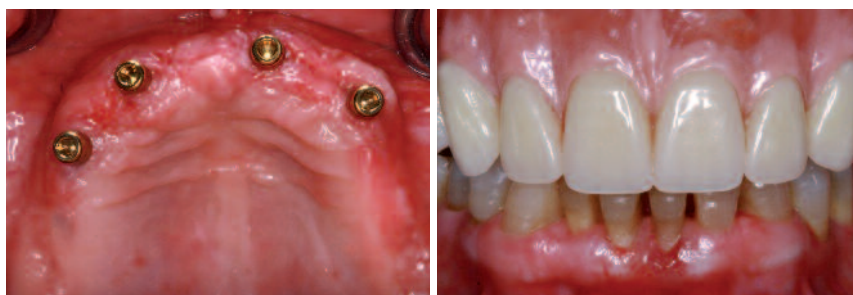


Fig. 8: Overall situation after healing and opening of the implants as well as installation of locator structures. – **Fig. 9:** En-face situation of completed palate-reduced overdenture prosthesis and individualised gingival situation.

fast in connection with vertical augmentation of atrophied alveolar ridges.

When a vertical bone augmentation is performed using the GBR technique, the success will highly depend on the ability to create a stable augmentation. Often, additional measures for bone augmentation are required, particularly with highly atrophied mandibles.

The resorption processes in such cases can already be prevented during tooth extraction, unless acute apical inflammation is present. In such case, we often perform socket preservation by filling of the alveoli with a bone substitute material, above all in the region of the maxillary anterior teeth. Here, the probability of success when filling defects larger than 2 mm or even whole alveoli is higher than that of using a barrier membrane.

Patient case 1

A 71-year-old female patient with full maxillary dentures presented herself at the clinic and stated the re-

quest of a palate-reduced prosthetic treatment. Due to the financial situation of the patient, it was decided to perform the minimal version of a palate-reduced denture in the maxilla. Implantation was to be made in regions 13, 15, 23, 25. The panoramic radiograph (Fig. 1) showed a sufficient residual bone height for the insertion of implants with a length of 11.5 mm. It was planned to insert four 11.5 mm/4.1 mm ICX-templant® implants (medentis medical). The operative presentation of the alveolar ridge (Fig. 2) showed the alveolar ridge to have a width of only 4 mm on both sides at the planned area, thus insufficient even for thinner implants of this type. Therefore, the decision was made to perform bone splitting with simultaneous implantation and augmentation (Fig. 3). The planned area was opened in the centre up to approx. two thirds of the implant length by using a piezo-electronic bone saw, and then expanded with a chisel. After performing a pilot bore, the implant bed was formed with the desired length and width by using osteotomes (Fig. 4). The four planned implants could be inserted at 30 Ncm. The remaining bone gap as well as the buccal bone lamella were augmented with Bio-Oss® (Geistlich Biomaterials AG) and previously collected blood from the bone bore. Each augmentation was covered with a creos™ xeno.protect/Remaix 25x30 mm membrane (Figs. 5–7). The region 13, 15 required significant augmentation. Here, the membrane was fixed with three titanium pins. Region 23, 25 was augmented safely and closed without strain or the necessity to use titanium pins.



Patient case 2 – Fig. 10: En-face situation of the patient at time of presentation at the practice clinic. – **Fig. 11:** Situation after dropping out of pin structure shortly before surgery date.

After a covered healing time of six months, the osseointegrated implants were opened and provided with locator structures. The patient was provided with a palate-free overdenture prosthesis on four locators (Figs. 8 and 9).

Patient case 2

A 49-year-old male patient presented himself at the clinic and stated the request of aesthetic improvement of his maxillary anterior teeth (Fig. 10). Tooth 21 showed a dark region above the marginal gingival edge. X-ray showed an oversized pin design with (after 15 years) insufficient metal-ceramic crown treatment. New treatment of the tooth with adherence to the biological width and simultaneous aesthetic improvement of this situation was not possible (Figs. 11 and 12). The patient was advised to have tooth 21 replaced by an implant. Given the fact that no apical infection was present, the patient and the attending dentist decided to perform an initial augmentation at extraction through socket preservation. Furthermore, the patient stated the request for a fixed temporary adhesive bridge. Tooth 21 was



Fig. 12: Dropped-out massive pin structure with cemented crown, alio loco, no consideration of biological width. – **Fig. 13:** Atraumatic loosening of periodontal fibres by using a narrow periosteal elevator. – **Fig. 14:** "Removal" of root residues.

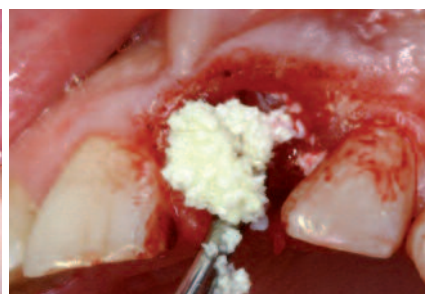


Fig. 15: Probing of alveolus using a periodontal probe; the buccal lamella is still completely present. – **Fig. 16:** Formation of a buccal muco-periosteal pocket. – **Fig. 17:** Filling of alveolus with Bio-Oss® (Geistlich Biomaterials AG).

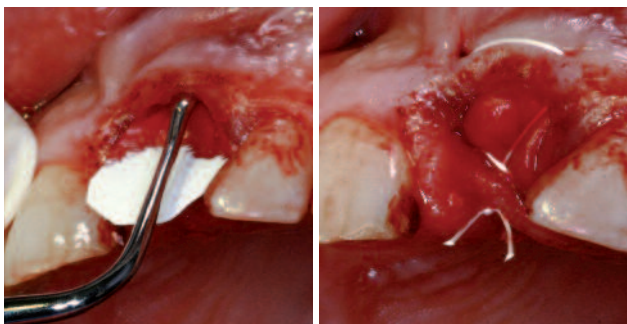


Fig. 18: Placement of creos™ xeno.protect/Remaix (Nobel Biocare/Matritel GmbH) membrane using a narrow raspatory, and subsequent filling of buccal “pocket” with bone substitute material as resorption protection of the buccal lamella. – **Fig. 19:** Fixation suture above augmentation and membrane.

removed in a tissue-conserving manner by using narrow periostomes, and the alveolus was filled with Bio-Oss® (Geistlich Biomaterials AG) (Figs. 13–17). The alveolus was closed with a Remaix membrane as well as an Ovate Pontic adhesive bridge (Figs. 18–21). After opening of the surgery site four months after surgery, there was a completely ossified alveolus with conservation of the whole alveolar ridge width (Figs. 22 and 23). An implant sized 4.3 mm x 13 mm (NobelReplace™ Straight Groovy, Nobel Biocare) was inserted safely at 40 Ncm (Fig. 24).

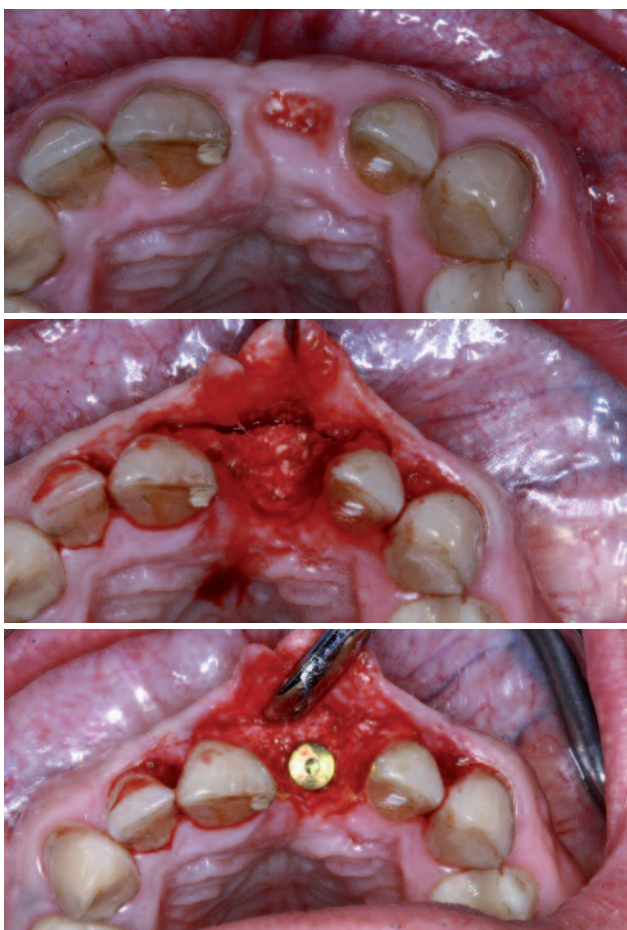


Fig. 22: Occlusal view of the healed extraction alveolus after a healing period of four months. – **Fig. 23:** Operation site of the ossified alveolus. – **Fig. 24:** NobelReplace™ Straight Groovy 4.3 mm x 13 mm implant inserted at 40 Ncm.



Fig. 20: Adhesive bridge fixed with Panavia F (Kuraray company) after socket preservation. – **Fig. 21:** En-face situation six weeks after surgery. Please note the regenerated soft tissue situation (as compared to the mucosal colour, Fig. 10).

Discussion

Since the change to this novel membrane at our clinic, we have not recorded any increased wound healing disturbance, pain, or failure in treatment. The operative handling of the new membranes is beneficial, as the membrane—contrary to some products of competitors—prevents a mix-up of surfaces. The membrane also shows a higher strength after wetting than the previously used collagen membrane; therefore, covering and shaping within the context of GBR can be performed more safely.

The clinical use of the creos™ xeno.protect/Remaix membrane for augmentation in the field of implantology shows promising first results. However, well-designed clinical studies should be performed to collect evidence-based data. Here, above all, the significantly increased implantation duration of this membrane as compared to products of competitors—confirmed within the scope of laboratory tests—should be verified clinically. ■

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