20 years of membrane-protected bone regeneration

A report

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_Dental implantology has developed to a reliable and successful clinical routine procedure for all those cases where an adequate bone material is available. But this precondition is not always met. Nevertheless, today also patients with a bone situation which is not optimal for implant insertion do wish an improvement of function and aesthetics—they actually consider this to be granted.

_Introduction

The use of barrier membranes for the regeneration of bone defects has changed dental implantology in the course of the last 20 years a lot. The principle titled as "membrane-protected bone regeneration" was first described by Hurley et al. in 1959. Already in the 1960s, a research group around Bassett and Boyne tested and described micro porous cellulose acetate laboratory filters (Millipore) for the treatment of cortical defects on long bones and the osseous reconstruction of the jaw. The basic idea of the authors was to use filter material for the isolation of bone defects against the cells of the adjacent, fibrous soft tissue and to create an appropriate milieu for osteogenesis. However, these pioneering studies did not immediately lead to a broad clinical application of barrier membranes on patients. Actually, the clinical possibilities of the membrane technology were not recognised until the early 1980s where the research group around Karring and Nyman systematically investigated the use of barrier membranes in different experimental and clinical studies on parodontal regeneration.

Already at the end of my studies about stomatology, especially the possibilities for periodontal regen-

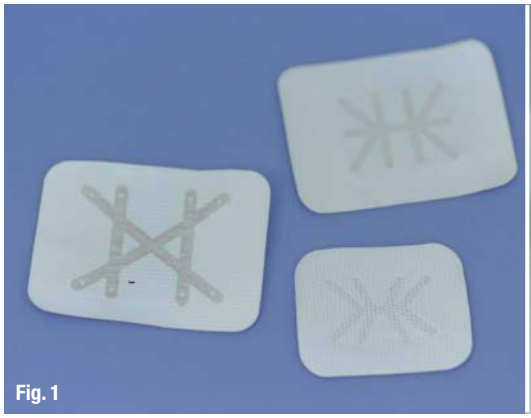
Fig. 1

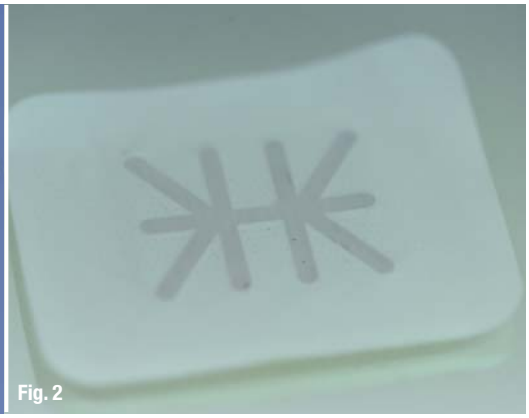
Fig. 2

Fig. 1_Example for different non-resorbable, titanium-mesh-reinforced ePTFE membranes, which are available in different forms and sizes depending on the manufacturer.
Fig. 2_Close up clearly shows the titanium-mesh reinforcement in the non-resorbable membrane material.

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Membrane types	Amount of patients questioned	First surgery	Second surgery for membrane removal	Overall assessment three month after membrane augmentation
Non-resorbable, titanium-mesh-reinforced ePTFE membrane	32	7	5	7
Resorbable ePTFE membrane	52	8	0	8
Collagen membrane	196	9	0	10

Tab. 1_Subjective patient satisfaction during and after augmentative procedures in our practice from 1994 to 1999, five years, total number of cases *n* = 280, average satisfaction based on a subjective satisfaction scale 0 = very unsatisfied … 10 = very satisfied.

eration were of great interest to me. At this time, great hopes were placed on the so-called GTR (Guided Tissue Regeneration) technique for treating extensive periodontal bone defects. A few years later, the membrane technique was tested as part of experimental studies on bone regeneration for larger alveolar ridge defects. Based on the studies' promising findings, the clinical use of membranes on implant patients started in the late 1980s (Nyman et al. 1990).

Despite this, it was not before the beginning of the 1990s until the discussion of this application found its way to congresses. From this time, works by Wachtel and Bernimoulin are to be named (Wachtel 1990, Wachtel and Bernimoulin 1991). In 1994, I purchased the first book dealing with this issue by Buser, Dahlin and Schenk for my private, scientific library. Under the title "Guided Bone Regeneration in Implant Industry", the authors published after five years of intensive experimental and clinical preparation the first English-speaking issue of this book in 1994, which could rouse a large interest for this topic on my side as well as among implantological experts. Since then, the GBR technique has constantly developed.

Always about to find better and for the patient more gentle treatment methods, in the last 20 years I applied different membrane types in the clinical daily routine (Tab. 3), compared their suitability and application parameters and based on the outcomes, discarded or kept them (Tab. 2). Thereby, an important criterion for the selection of the operation method and the used type of membrane was also the patient's subjective feeling (Tab. 1).

_Aims of membrane application

- Undisturbed regeneration of bone through a barrier function against the adjacent soft tissue.
- Avoidance of graft resorption particularly in autologous bone transplants.
- Protection against loss or dislocation of bone or bone graft substitute particles.
- Protection of the regenerate in case of wound dehiscence.

Depending on the used membrane type, the desired bone regeneration is given the required time and rest in a defined area. Especially the reservation of space volume defined by a surgeon can be perfectly ensured by the use of titanium-reinforced membranes (Figs. 1 & 2). Before the insertion into the operation area, these membranes can be tailored and also bended, as shown in Fig. 3 only exemplarily.

From 1994 to 1996, I thus used non-resorbable, titanium-mesh-reinforced membranes from the company W. L. Gore and Associates, Inc. USA, at first. Although, I as an operator was very satisfied with the clinical outcomes of the bone regeneration in

Tab. 2_Assessment of the handling for the operator and subjective evaluation of the plastic coverage and healing process, total amount of cases *n* = 280.

Membrane type	First surgery		Second surgery		Wound dehiscence	
	simple	difficult	simple	difficult	after 8 days	after 30 days
Non-resorbable, titanium-mesh-reinforced ePTFE membrane	6,25 % (2)	93,8 % (30)	28,2 % (9)	71,9 % (23)	9,4 % (3)	21,9 % (7)
Resorbable ePTFE membrane	11,5 % (6)	88,5 % (46)	0	0	3,8 % (2)	11,5 % (6)
Collagen membrane	59,5 % (117)	40,5 % (79)	0	0	1,5 % (3)	5,1 % (10)

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Manufacturers/ Distributors	BEGO Implant Systems	BEGO Implant Systems	Geistlich Biomaterials
Product name	BEGO Collagen Membrane	BEGO Collagen Fleece	Geistlich Bio-Gide
Origin	porcine pericardium-collagen	porcine collagen	porcine (pig)
Resorption **a) Service life** **b) Behaviour on exposure** **c) Behaviour on exacerbation**	a) > 3 months b) stable c) can be left with appropriate oral hygiene	a) 2–4 weeks b) – c) –	a) on request by Geistlich b) normally without complications, healing by free granulation, removal of membrane unnecessary c) in case of exposure of membrane an antimicrobial treatment is recommended
Recommended treatment before use	–	–	membrane-cutting to defect size
Processing before use	cut to size, can be applied wet and dry	cut to size, apply dry, fast hydrogenation	no further processing needed
Recommended fixation	unnecessary, pin or suture if needed	ns.	sticks well to defect, additional fixation with titanium-pin or double-layer-technique (Buser) in case of bigger defects
Available sizes	15 x 20 mm 20 x 30 mm 30 x 40 mm	20 x 20 mm	25 x 25 mm (6,25 m²) 30 x 40 mm (12,0 m²)
Price per membrane	15 x 20 mm: 90 Euro 20 x 30 mm: 110 Euro 30 x 40 mm: 165 Euro	12 pieces = 200 Euro	from 122 Euro
Scientific references	on request	on request	on request (more than 80 publications)
Distribution in GER since	2009	2009	1996
Ranges of application	implantology, periodontology, sinus floor elevation, defect surgery, biological protective barrier also at risk of infection	reconstruction, protection of Schneider'sche extraction site, bleeding complication, biopsy points, bone defects	implantology, periodontology, defect surgery, sinus floor elevation, extraction sockets, GBR/GTR, resorption protection
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Tab. 3

94 per cent of the cases, for most patients the necessary second surgery was subjectively more burdensome than the first one. As a questionnaire of my patients had shown, they were relatively satisfied with the therapeutic measure—meaning the first surgery and the overall treatment. But there was also a remarkable number of patients who considered the second surgery for the removal of the non-resorbable membrane materials as disturbing and even more burdensome than the first one (Tab. 1). This has improved with the introduction and application of resorbable ePTFE membranes, which were and still are available in different configurations on the dental market—depending on the field of application. As long as there was no surgery for membrane removal, the patients were relatively satisfied with the therapy from the beginning to the end (Tab. 1). The handling of a titanium mesh reinforced ePTFE membrane with its complete plastic coverage puts enhanced requirements on the oral surgeon depending on the area of

Geistlich Biomaterials	RIEMSER Arzneimittel AG	RIEMSER Arzneimittel AG
Geistlich Bio-Gide Perio	Epi-Guide	Cytoplast TXT-200; Cytoplast TI-250 (titanium-reinforced)
porcine (pig)	synthetic (polylactid)	synthetic (PTFE)
a) on request by Geistlich b) normally without complications, healing by free granulation, removal of membrane unnecessary c) in case of exposure of membrane an antimicrobial treatment is recommended	resorbable a) barrier function: 2–4 months, complete resorption within 12 months b) depending on material only low bacterial colonisation in case of an exposition (special pore structure counteracts exposition), exposed areas usually resorb without complications within short time c) in the unlikely case of a renewed infection, the membrane should be removed and the infection eliminated	a) non-resorbable b) without complications. Membrane was designed for exposed surfaces c) in the unlikely case of a renewed infection, the infection should be eliminated first
membrane-cutting to defect size (possible with supplied sterile pattern)	remove focus of inflammation in the defect area, clean bone, maybe fill up with bone regeneration material	remove focus of inflammation in the defect area, clean bone, maybe fill up with bone regeneration material
no further processing needed	cutting with surgical scissor, briefly soak with blood from the defect	cut to size, round off edges
sticks well to defect, additional fixation with titanium-pin or double-layer-technique (Buser) in case of bigger defects	membrane can be fixed by blood contact, further fixation with resorbable suture or tacks if needed	overall suture with non-resorbable suture material, e.g. Cytoplast PTFE-Suture (do not perforate)
16 x 22 mm (3,52 m²)	18 x 30 mm	different cuttings and forms between 1,2 x 2,4 and 3,0 x 4,0 cm optionally titanium-reinforced
113 Euro	109 Euro	from 49,90 Euro (1,2 x 2,4 cm)
on request (more than 80 publications)	Arthur R. Vernino et al., Int. Journal of Periodontics and Restorative Dentistry 1999; 9(19):57–65	on request
1998	2001	2007
implantology, periodontology, GBR/GTR	periodontology, implantology, GBR/GTR	recovery surgery, defect surgery, GBR/GTR, no primary wound closure necessary
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lesion. The plastic and de-energised coverage often proves to be difficult (Tab. 2). However, the clear room stabilisation and the volume preservation (Fig. 3) are particularly to be highlighted as the core advantages.

For the sake of completeness, I want to mention my use of a direct applicable GTR barrier for the coverage of periodontal bone defects—which is especially indicated for an infestation of bifurcation—on the protection of augmentation material. In the then dental market, this barrier was available under the name Atrisorb® of the company Atrix Laboratories, Inc., Fort Collins, USA. Although the clinical healing process was unremarkable, a dimensional stability of this viscously applied barrier materials after hardening was not traceable. At least, there was no dislocation of particles from the materials placed into the defect. Due to the few patients treated in this way, these were not included into the evaluation of the questionnaire.


Fig. 3


Fig. 4

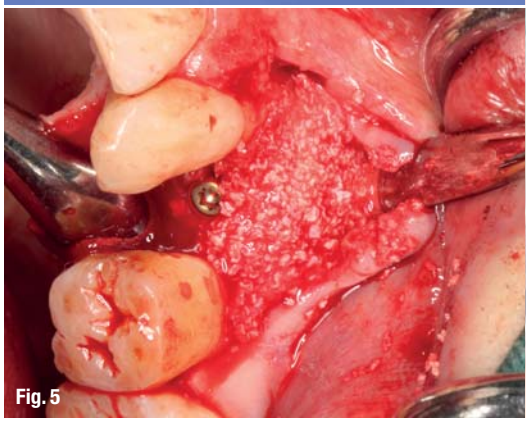
Fig. 5

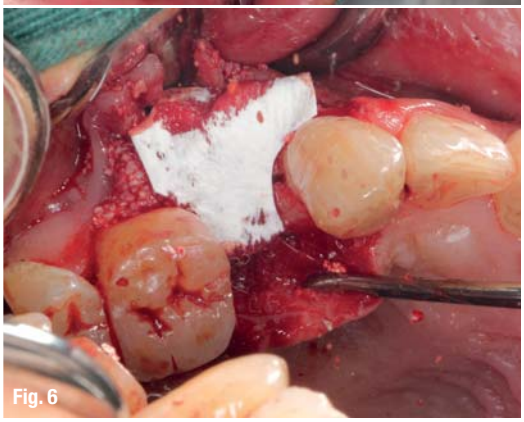
Fig. 6

Fig. 3_By bending the inner titanium frame, the desired room volume above the bone defect can be fixed and kept stable, similar to today's commercial tent poles.
Fig. 4_Patient with a clear buccal retraction of the processus alveolaris, about 18 years after loss of teeth and following bone resorption in regio 24, 25 as well as narrowing of gaps by a mesial migration of 26.
Fig. 5_After implant insertion 24 and simultaneous augmentation of the buccal defect area by a mixture of autologous bone chips and Bio-Oss granulate with a particle size 0,25 to 1,0 mm, Fa. Geistlich Pharma AG, Wolhusen, Switzerland, a clear widening of the processus alveolaris is prepared and the desired bone regeneration is supported evidence-based.
Fig. 6_After tailoring and examination, the Bio-Gide membrane is placed on the augmentation material.

Already since 1996, I increasingly switched to the clinical application of collagen membranes. Besides the effective barrier function, the good wound healing properties were and still are the reason why I am using these materials almost exclusively for my patients' treatment now. Both the handling as well as the patient compliance is in most cases superior to the old methods using titanium mesh reinforced ePTFE membranes (Tab. 1 & 2).

As Plöger described in 2003 already, natural collagen membranes do influence tissue integration in a positive way. Amongst our treatments, only 1.5 per cent of the cases of membrane application showed low dehiscence after eight days and about 5 per cent after 30 days. This was a revolutionary improvement compared to the titanium mesh reinforced, non-resorbable as well as resorbable ePTFE membranes. Under a local antiphlogistic treatment, the lowly exposed collagen membranes do heal without complications, whereas the other membrane types need be removed promptly in case of a wound dehiscence. In principle, all membrane expositions or wound dehiscence are clinically controllable. But they also require the frequent scheduling of patients and at least weekly follow-ups and wound cleaning, which is reflected by a lower patients rating (Tab. 1). For this, the reason can be seen in the fact that collagen chemotactically works on fibroblasts and thus enhances the primary wound closure. Today it seems to be undisputable that it supports the development and stabilisation of the wound coagulum and promotes the proliferation, migration and adhesion of cells. Furthermore, when reducing the membrane materials there is no need to fear irritations of the tissues or the desired regeneration processes, which in contrast can occur for synthetic materials. In Table 3, the membrane materials used in my practice from 2001 until 2014 are listed with their different properties.

In the direct clinical comparison, the handling of the native collagen membrane—in our case Bio-Gide® by Geistlich Pharma AG, Wolhusen, Switzerland—was remarkably easier. After unpacking out of the delivered sterile box, this material can be tailored without problems and thus adapted to the defect and configuration size (Figs. 4–6). Soaking or moistening with any liquids before application is not needed; shortly after the application, the membrane material becomes saturated with the surrounding blood and the below defect area (Figs. 7 & 8). Regardless of autologous bones or bone graft substitutes of different origins, the adhesion to bone walls and the adaption to the augmentation material is much better than for synthetic membranes—if it is possible at all. Thus, I used resorbable pins for membrane consolidation only in the beginning of my augmentative work. Today, I am adapting the barrier material below the adjacent periost (Fig. 7). However, collagen membranes do always need dimension stable bone graft substitutes or autologous bones to prevent the room volume from collapsing.


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Fig. 7_The Bio-Guide-membrane can be adapted well under the surrounding periost without absorbable pins and saturates itself with the patient's blood from the edges.
Fig. 8_The membrane is completely soaked with the patient's blood and can be plastically covered by mucoperiosteal flaps.
Fig. 9_Complete, primary wound closure from buccal.
Fig. 10_Also the occlusal view and examination confirms the de-energised closure of the mukosa which is not unimportant for the healing process; due to flap advancement, the vestibulum could be saved well.


Fig. 7

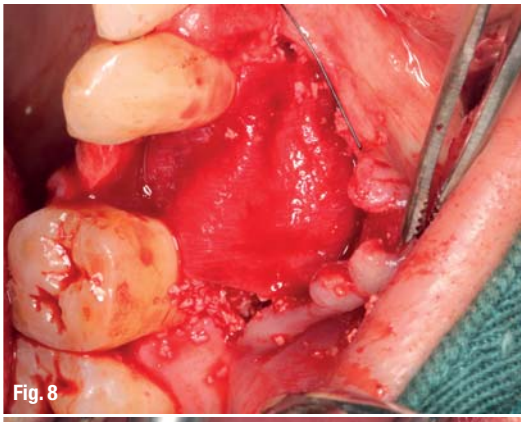
Fig. 8


Fig. 9


Fig. 10

If the operator can achieve a primary and de-energised wound closure, fissure dehiscence is a rare exception and possibly due to subjective patient factors. Usually, I use 5/0 or 6/0 fissure material in augmentation surgery, whereby the Bio-Gide membrane, which I am using oftentimes, is available in the dimensions 13 x 40 mm, 25 x 25 mm or even 30 x 40 mm. Thus, the operator has an option for almost every indication and can choose the most economic, i.e. most priceless option, which is also in the patient's interest.

I must not forget to point out the remarkably good material properties of this membrane regarding tensile strength and foldability, which is not granted for every competitor. Thus, I often perform external sinus lift operations with very small lateral bone space, whereby I fold the membrane—in the same way as a model ship is inserted into a bottle—and then unfold it before it becomes saturated with liquid. In this way, the Schneider'sche membrane in the paranasal sinus is stabilised for a long time and a perforation of undesired dislocation of augmentation material is prevented successfully (Liebaug & Wu, 2011).

_Conclusion

Without the application of augmentative treatment methods—particularly the membrane protected bone regeneration—I would have helped only few patients to get a fixed or high-quality implant-supported dental prosthesis in the past 20 years. In my therapy concept, a successful dental implantology begins already or at best with the socket preservation and ridge preservation simultaneously to the tooth removal. But these measures do make sense when afterwards a conventional prosthetic rehabilitation with fixed bridges or combined fixed and removable telescopic or bed-load prosthesis will be planned. The application of barrier membranes—particularly collagen membranes—has developed to a very reliable and successful clinical routine procedure for all those cases where an adequate bone material in height and width shall be generated for later therapy measures._

_contact implants

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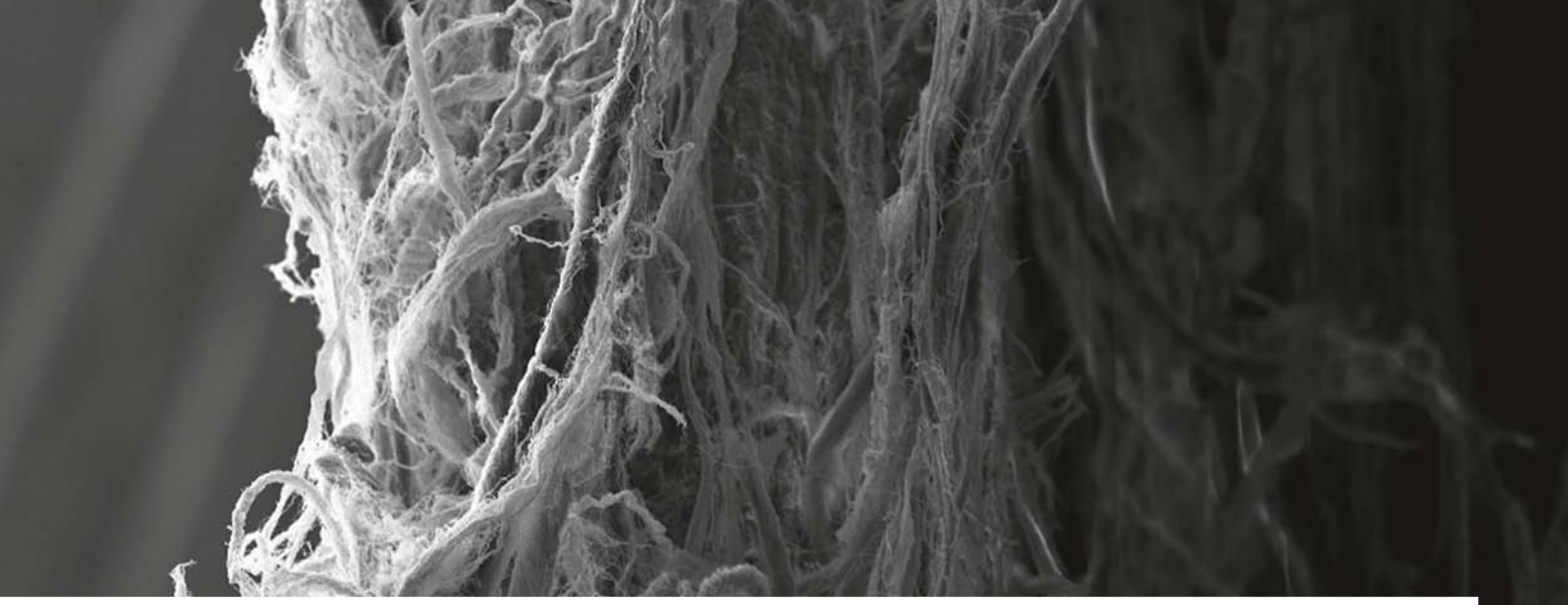

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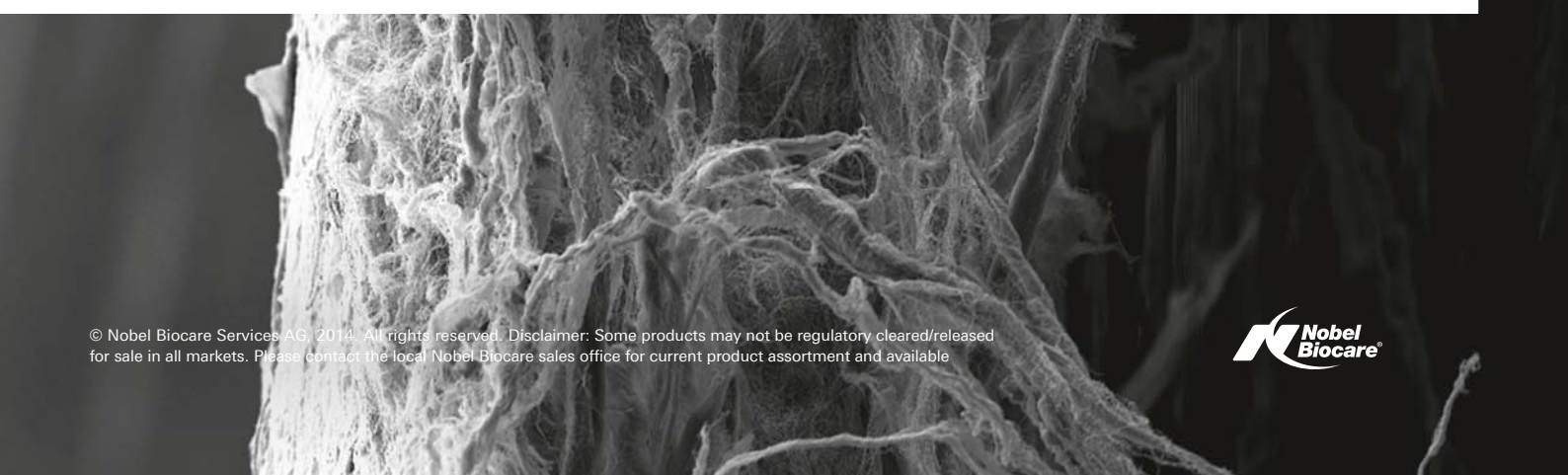

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