Received: 13 March 2023 | Revised: 21 May 2023 | Accepted: 29 May 2023

DOI: 10.1111/prd.12502

Periodontology 2000 WILEY

REVIEW ARTICLE

Membrane barriers for guided bone regeneration: An overview of available biomaterials

Gabriel Mizraji[1] | Alon Davidzohn[2] | Mervi Gursoy[3,4] | Ulvi K. Gursoy[3] | Lior Shapira[1] | Asaf Wilensky[1]

[1]Department of Periodontology, Faculty of Dental Medicine, Hadassah Medical Center, Hebrew University of Jerusalem, Jerusalem, Israel

[2]Private Practice, Rishon LeZion, Israel

[3]Department of Periodontology, Institute of Dentistry, University of Turku, Turku, Finland

[4]Oral Health Care, Welfare Division, City of Turku, Turku, Finland

Correspondence
Asaf Wilensky, Department of Periodontology, Faculty of Dental Medicine, Hadassah Medical Center, Hebrew University of Jerusalem, P.O. Box 12272, Jerusalem 91120, Israel.
Email: asafw@ekmd.huji.ac.il

1 | INTRODUCTION

Missing teeth have posed a major challenge throughout dental history. The introduction of dental implants revolutionized the number of treatment possibilities for restoring form, function, and esthetics. Implant placement depends on the availability of sufficient residual bone. In many cases, lack of sufficient bone or ridge collapse, both horizontally and vertically, is a common outcome of advanced periodontal disease,[1,2] trauma or tooth loss. It was estimated that more than 40% of patients require bone augmentation procedure for optimal implant placement.[3] In these situations, reconstructive surgical techniques have been developed for creating new sufficient bone that will enable implant placement either simultaneously or with a delayed approach. To date, guided bone regeneration (GBR) constitutes a predictable and successful approach for lateral and vertical bone augmentation of atrophic ridges before or in conjunction with implant placement[4,5] with a success rate of approximately 95%.[6-10] To ensure predictable results, it is of utmost importance to maintain four major biological principles: primary wound closure, angiogenesis, space creation/maintenance and stability of the initial blood clot.[5] To achieve these principles, the use of barrier membranes has been suggested.[4] The hypothesis was based on the idea that different cellular components have distinct migration rates during wound healing, therefore, the membrane would help to maintain space, allowing the arrival of slow migrating osteogenic cells to the defect, while fast migrating epithelial and connective tissue cells will be excluded.[4] Etymologically, a membrane is defined as any thin pliable sheet of material,[11] while a barrier is an object or layer that physically prevents something from moving from one place to another.[11] Historically, the importance of space maintaining and barrier membranes was first described by Hurley et al.[12] in the late 50s for the treatment of spinal fusion. Orthopedic surgeons described then "osteosynthesis in the spine was surely achieved if the paraspinal muscles were elevated from the decorticated laminae, creating a space in which bone-forming granulation tissue could grow." Research in this field was first described for the field of dentistry by Nyman et al.[13] in which a Millipore® filter was used as a membrane to maintain space and separate the bone defect around a periodontal tooth from the surrounding soft tissue. Subsequently, Dahlin et al.[14] created a standard size bone defect in the angle of rat jaws and covered one side with a Teflon® membrane, while the other uncovered side served as a control. After 6 weeks, the membrane-covered defects resulted in complete bone healing, while little or no sign of bone formation took place in the control defects, with a follow-up of 22 weeks. This is the first recorded description of the foundation principles of GBR. From these early studies, we can define barrier membrane as a physical barrier placed over a bony defect to prevent soft tissue ingrowth and promote bone regeneration.

Since barrier membranes have a fundamental role in bone regeneration during GBR, ideal membrane characteristics, other than the barrier effect, include (a) biocompatibility, (b) biological activity,

[Correction added on December 26, 2023 after first online publication: Given names for all authors have been included.]

(c) porosity/occlusive properties, (d) mechanical properties, (e) exposure tolerance, and (f) biodegradability.[15] From a mechanical point of view, the ideal membrane for GBR should be sufficiently rigid to withstand the compression of the overlying tissues for a long duration, should possess simple handling properties such as elastic memory and plasticity, and they should be easily contoured and mold to adapt to the shape of the desired bone gain.[16,17] In pursuit of finding the perfect membrane, several materials had been suggested in the past. The first generation of membranes consisted of non-resorbable materials such as expanded polytetrafluoroethylene (e-PTFE) and high-density polytetrafluoroethylene (d-PTFE),[18] with e-PTFE membranes being widely utilized during the 1990s and considered as the gold standard.[19] While the first generation of membranes possessed excellent space-maintaining ability, they had major drawbacks such as relatively high exposure and bacterial infection rates and resulted in the need for a second surgery for membrane removal. To overcome these disadvantages, resorbable natural and synthetic membranes were fabricated, eliminating the need for a second surgery, decreasing patient morbidity, increasing cost-effectiveness,[19] and in some cases, avoiding soft tissue complications.[18,20] The second-generation membranes used presently include resorbable collagen membranes, non-cross-linked collagen membranes (NCLM), cross-linked collagen membranes (CLM), and resorbable synthetic membranes.[17,21] These membranes have variable resorption times, mechanical and biological properties and outcomes that are different from those of the non-resorbable, first-generation membranes. This review will focus on the characteristics, advantages, and disadvantages of available occlusive barrier membranes.

2 | METHODS

Electronic searches in Medline (PubMed) and in CrossRef databases were performed and complimented by manual searches of relevant recent articles representing original research or review papers. The search included the following key words: barrier membrane, guided bone regeneration, bone augmentation, and terms related to each of the membranes described below. Data were retrieved from in vitro, in vivo, preclinical, and clinical studies. Thorough reading of the articles included herein was done by the coauthors. Due to the vast number of published articles in the field, references were selected based on scientific and/or clinical relevance. No systematic search, meta-analysis, or statistic calculation were performed due to the descriptive nature of this review.

3 | NON-RESORBABLE MEMBRANES

3.1 | PTFE membranes

Polytetrafluoroethylene (PTFE), commonly known as Teflon®, was discovered in the late 1930s by Dr. Roy J. Plunkett at DuPont's Jackson Laboratory in New Jersey. While DuPont's laboratory was working with chlorofluorocarbon refrigerants, Dr. Plunkett discovered that tetrafluoroethylene (TET) polymerized spontaneously into a white, waxy solid form of PTFE. Since then, PTFE has been used in a wide variety of industries ranging from cooking pan coatings to aerospace crafts.[22]

Polytetrafluoroethylene is used extensively as a medical material due to its high biocompatibility, inertness, and resistance to breakdown.[16,23] In dentistry, e-PTFE or d-PTFE, with or without titanium reinforcement, are available in various forms and are used to manufacture products such as barrier membranes (Table 1A,B). The first e-PTFE membrane (Gore-Tex®) consisted of two different parts: an open microstructure portion (100–300 μm porosity) and an occlusive portion (<8 μm porosity). The open microstructure promotes an ingrowth of collagen fibrils on its surface, enhancing membrane stability, and allows for the diffusion of nutrients through the pores. The occlusive portion, relatively impermeable to fluids and cells, blocks the migration of soft tissue cells into the area of bone growth.[24,25] All e-PTFE membranes consist of a network of dense nodes interconnected by PTFE fibrils. The more multidirectional the fibril orientation is, the more open the structure becomes.[26] e-PTFE membranes also have good tissue integration, thereby possessing the ability to adhere to the surrounding connective tissue. Simion et al.[27] used SEM to demonstrate interlacing connective tissue within the membrane, and simultaneously observed a limited number of neutrophils. In addition to the aforementioned uses, expanded membranes have been applied extensively in periodontal and bone regeneration. During the 1990s, Hammerle et al.[19] considered e-PTFE membrane to be the gold standard for GBR, and suggested that new membranes should be compared to it. One of the main drawbacks of e-PTFE is that, if exposed during the healing process, an early bacterial infection can occur, affecting the outcome of regeneration.[4] This disadvantage led to the development of the d-PTFE membrane. This membrane is non-expandable, has high density structure, with very low porosity ranging from 0.2 to 0.3 μm,[28] and a thickness that ranges from 0.13 to 0.25 mm.[29] It contains a smooth surface that minimizes cell and fiber attachment.[30] Due to this characteristic, it integrates weakly into tissue or fails to integrate, although manufacturers created a textured outer surface, aiming for stability in tissues (Table 1A,B). The advantage of d-PTFE is that, due to its very low porosity, it is impervious to bacteria.[31-33] In light of this, some investigators and manufacturers claim that soft tissue coverage of d-PTFE is not needed since even if exposed to the oral cavity the risk of complications remains low, compared to e-PTFE membranes.[34-36] However, the low porosity of d-PTFE membranes can limit blood supply to the healing area.

Biologically, the balance between occlusive properties and porosity is extremely important. The desired effect is only achieved if the membrane is able to prevent unwanted cell migration into the bone chamber, without preventing the diffusion of oxygen, fluids, nutrients, and bioactive substances. Hence, the pore size has a direct impact on bone formation in the scaffold. Lundgren et al.[37] showed in a rat calvarial defect model, using e-PTFE membranes with increasing pore size, that pore sizes above 10 μm have no effect on the amount of augmented mineralized bone, whereas smaller pore size resulted in delayed bone formation. Zellin et al.[31] demonstrated that

TABLE 1A Commercially available non-resorbable synthetic membranes.

Classification	Commercial name	Main component[a]	Structure and layers[a]	Pros	Cons	Additional information provided by the manufacturer
e-PTFE	Cytoflex Tef-Guard®, Unicare Biomedical, USA	e-PTFE	Smooth or textured. Microporous design enhances gingival tissue attachment	Resists bacterial and cell penetration, good space maintainer	Requires second surgery, high exposure rate compared to CLM	
d-PTFE	Cytoplast™ TXT-200, Osteogenics Biomedical, Lubbock, USA	d-PTFE	Outer textured (Regentex ™) surface [hexagonal dimples] helps stabilize the membrane and the soft tissue flap	Impervious to bacteria and cell penetration	Requires second surgery, high exposure rate compared to CLM	
	NeoGen®, neoss, England	e-PTFE + d-PTFE	Inner layer of e-PTFE with fibrils streched in multiple directions, outer layer of d-PTFE with a tight texture			
	permamem®, Botiss Medical AG, Germany	d-PTFE	Ultra-thin membrane[a]. ~0.08 mm thickness			
	OsseoGuard PTFE®, Zimmer Biomet, USA	d-PTFE	100% d-PTFE. Textured surface (hexagonal) to increase membrane stabilization			Textured outer surface
Reinforced	Cytoplast Ti-150 or Ti-250®, Osteogenics Biomedical, Lubbock, USA	e-PTFE + titanium + d-PTFE	Outer part of d-PTFE textured surface (Regentex™), an intermediate grade 1 titanium structure, and an inner e-PTFE layer. Thickness: Ti-150: 150 microns, Ti-250: 250 microns	Optimal space maintenance	Difficult edge adaptation, requires second surgery, high exposure rate compared to CLM	No elastic memory, small pores (<0.3 um), allows diffusion of small organic molecules and nutrients. Outer part of d-PTFE textured surface (Regentex™), an intermediate grade 1 titanium structure, and an inner e-PTFE layer
	NeoGen Ti-reinforced ®, neoss, England	e-PTFE + titanium + d-PTFE	Inner layer of e-PTFE with fibrils stretched in multiple directions, middle titanium layer, outer layer of d-PTFE with a tight texture			
	OsseoGuard PTFE Ti-reinforced®, Zimmer Biomet, USA	e-PTFE + titanium + d-PTFE	Inner layer of e-PTFE, middle layer titanium framework, textured external layer of d-PTFE			
	Cytoflex Ti-reinforced®, Unicare Biomedical, USA	e-PTFE + titanium + e-PTFE	Titanium frame enclosed within two layers of e-PTFE. For submerged healing only			

[a]According to the manufacturer.

TABLE 1B Non-resorbable synthetic membranes. Biological and mechanical characteristics.

Commercial name	Biological characteristics		Mechanical characteristics	
	Immunogenicity	Resistance in exposure	Fixation[a]	Handling/tissue adaptation
Cytoflex Tef-Guard®, Unicare Biomedical, USA	Bio-inert material	High resistance	Pins and screws	Easy handling, tear-resistant
Cytoplast™ TXT-200, Osteogenics Biomedical, Lubbock, USA		Very high resistance		Easy handling, tear-resistant
NeoGen®, neoss, England				
permamem®, Botiss Medical AG, Germany				
OsseoGuard PTFE®, Zimmer Biomet, USA				
Cytoplast Ti-150 or Ti-250®, Osteogenics Biomedical, Lubbock, USA		Very high resistance		Easy handling, tear-resistant, some elastic memory, difficult tissue adaptation
NeoGen Ti-reinforced ®, neoss, England				
OsseoGuard PTFE Ti-reinforced®, Zimmer Biomet, USA				
Cytoflex Ti-reinforced®, Unicare Biomedical, USA				

[a]According to the manufacturer.

the rate of bone neogenesis is dependent upon membrane porosity, however, differences in pore size did not affect final bone volume. They concluded that lower porosity drives less efficient tissue integration, and may inhibit initial clot formation, wound stabilization, and membrane stability,[29] reaffirming the need for membrane fixation. It was reported that, due to the lack of tissue integration, it is easier to remove an exposed d-PTFE membrane without raising the flap. When elevation of the flap is needed, easier removal of d-PTFE compared to e-PTFE membrane was described.[38] d-PTFE has been proposed for use in regions with large ridge atrophies to prevent graft contamination in the case of undesired exposure of the membrane.[39] Another reported advantage of the d-PTFE membrane is the ability to preserve the full width of keratinized mucosa after GBR, while leaving the membrane intentionally exposed.[33,40] This occurs by virtue of the fact that the flap margins remain in their original anatomic position rather than being advanced over the socket or surgical site to achieve primary closure. Nevertheless, after 3–6 weeks, the membrane should be removed.

Experimental studies show that in large defects, PTFE membranes can be partially compressed by the soft tissue during the healing phase.[41-44] To prevent this from occurring, a titanium framework was included in between two layers of the membrane,[19] providing additional membrane stability during treatment of non-space-maintaining bone defects.[45,46] The main advantage of these barriers is space maintenance. Additionally, the titanium framework allows the membrane to shape and adapt to the defect, according to the desired final ridge volume.

3.1.1 | Bacterial contamination

As previously mentioned, bacterial contamination may lead to worse clinical outcome and sometimes results in failure of the overall procedure.[34,47] In vitro experiments showed that PTFE membranes accumulate less bacteria than collagen membranes.[48] Nevertheless, De Sanctis et al.[49] demonstrated that e-PTFE-exposed membranes contained high bacterial colonization. Interestingly, they also found that 66% of unexposed membranes were also colonized with bacteria. Simion et al.[27] showed, in vivo, that following membrane exposure, bacteria were found on both sides of the e-PTFE membrane, providing evidence that microorganisms do, indeed, migrate across it. Donos et al.[50] demonstrated in a murine model of GBR, that exposure of e-PTFE membranes was associated with substantial graft resorption and lack of bone continuity between the bone graft and the native bone at the recipient site, probably due to bacterial contamination.

Due to their low porosity, d-PTFE membranes are thought to harbor less bacteria than e-PTFE membranes.[29,34,35] Krauser et al.[51] demonstrated that 21 days after exposure of d-PTFE membrane, low bacterial colonization was found at the outer side of the membrane, while no bacteria were found attached to the inner surface. However, some reports showed that d-PTFE membranes exposed to oral biofilm accumulate greater biofilm biomass and thickness

during initial exposure compared to e-PTFE membranes.[52] Zlikman et al.[53] in an in vitro setting comparing oral bacterial accumulation on different d-PTFE membranes, demonstrated that different commercial membranes may have varying impact on bacterial growth of *Streptococcus sanguinis*, and no effect on *Fusobacterium nucleatum*. Trobos et al.[26] found no correlation between membrane characteristics (wettability, surface roughness) and the adhesion and growth of *Streptococcus oralis* (early colonizer bacteria) on both d-PTFE and e-PTFE membranes, whereas, they found more accumulation of *Streptococcus oralis* on d-PTFE membranes than on e-PTFE. Regardless of the structural differences, indications for the use of either e-PTFE or d-PTFE are similar.[29]

4 | RESORBABLE MEMBRANES

4.1 | Natural membranes

A resorbable natural membrane is made from natural materials and is designed to be gradually absorbed by the body over time. Depending on the source of the material, it is possible to classify them as allografts or xenografts. An allograft is a tissue graft obtained from a donor of the same species as the recipient but not genetically identical. A xenograft is a tissue graft obtained from a donor of a different species of the recipient.

4.1.1 | Collagen membranes

Natural resorbable collagen membranes are widely used in GBR procedures. Since collagen is a principal component of the connective tissue, it is biocompatible, causes low immunogenicity,[54] and enhances wound healing. Moreover, it promotes hemostasis and chemotaxis of periodontal ligament and gingival fibroblasts.[55,56] The main components of currently available collagen membranes are collagen type I and/or type III, derived mostly from bovine or porcine tissues. They contain a wide range of porosity, allowing selective cell migration and the passage of chemicals, biomolecules, and viruses. In general, the porosity ranges from micro-porosity (5–20 μm) to moderate porosity (non-resorbable materials of ≤100 μm that allow the passage of bacteria, cells, and tissue integration/migration, which occurs at ≥30–40 μm) to macro-porosity (non-resorbable materials of >100 μm, which permit unrestricted passage of chemicals, biomolecules, viruses, bacteria, cells in addition to enabling tissue integration and migration). The pore size may increase during the process of membrane degradation and affect its occlusive function.[15]

Available collagen membranes have different structures and thickness. The membranes consist of either a homogenous collagenous matrix or a bilayer structure. For example, some membranes consist of differently oriented collagen fibers that create a comb-like structure, characterized by strong multidirectional linking. Others have a bilayer structure with a compact outer layer that prevents infiltration of epithelial cells and a porous inner layer of collagen fiber bundles that allows tissue integration.[16] The membranes described above differ not only in their architecture but also in their thickness (Table 1A,B), which may affect bone formation. Bubalo et al.[57] evaluated the way in which the thickness of resorbable membranes affect bone formation in extraction sockets in dogs by covering defects with either 100 or 200 μm resorbable membranes; the third defect was left empty as a control. The results demonstrated that the thicker membrane showed the least soft tissue ingrowth and promoted better bone formation at 6 months. It is important to remember that membranes and their materials do not function solely as passive barriers, but may influence the process of bone regeneration through the characteristics that promote better osteoblastic cell migration.[58]

Biological aspects

Biocompatibility. The ideal membrane should be biocompatible, meaning that the material should not assert an adverse effect on the surrounding tissues, the intended healing result, or the safety of the patient. Ideally, biomaterials should be inherently bioactive in promoting the bone regeneration process[15] by supporting rapid recruitment of advantageous cell types into the defect, including osteoblastic and osteoclastic phenotypes. More importantly, the membrane should promote an environment that is conducive for the molecular cascade of bone formation coupled with remodeling in the underlying defect.[16] Rothamel et al. tested the biocompatibility of various collagen membranes in cultures of human periodontal ligament (PDL) fibroblasts and human osteoblast-like cells, and demonstrated that Bio-Gide® and Ossix® had significantly more PDL fibroblasts adhere to the membrane than Tutodent® and each of these three had significantly more than Biomend®. Osteoblast-like cells adhered significantly better to Bio-Gide® and Tutodent® than to Ossix®. Interestingly, there were no osteoblast-like cells detectable on the Biomend® membrane.[59] Bio-Gide® exhibited excellent cytocompatibility in cultures of human PDL fibroblasts and SaOs-2 osteoblasts.[60] While in some studies, collagen membranes exhibited no signs of pronounced inflammatory reactions in the adjacent tissue,[61] in other studies, infiltration of inflammatory cells was observed in the adjacent tissue to the collagen membranes at 2 and 4 weeks after surgery. These findings are attributed to the membrane degradation process. Eight weeks post-surgery, the infiltration of inflammatory cells was markedly reduced.[62,63] Collagen-based membranes are considered not only biocompatible, they also are bioactive, as they provide binding sites for migrating wound-healing cells which ultimately results in microenvironmental cues for promoting tissue regeneration, fostering a hospitable environment following surgical intervention.[59,64,65]

Vascularization. Angiogenesis is an important factor that strongly influences the positive outcome of GBR procedures. Schmid et al.[66] showed in a rabbit model that formation of blood capillaries precedes the formation of new bone. Adequate vascularization from the surrounding soft tissue is important in order to provide a substrate for the osteogenic cells and to promote bone

regeneration.[67] Lack of vascular supply may be a plausible explanation for membrane exposure.[16] Rothamel et al. found in a rat model that NCLM membranes exhibit faster vascularization than CLM membranes and there is also a rate difference within the groups. Native collagen membranes revealed a nearly complete homogenous vascularization of the membrane body after 2 weeks, while glutaraldehyde cross-linked collagen membranes showed only slight superficial vascularization at the same timepoint. After 4 weeks, glutaraldehyde cross-linked collagen membranes revealed nearly complete vascularization.[65] In contrast, sugar-based cross-linked membranes exhibited only superficial vascularization after 24 weeks.[61] The angiogenesis pattern is related to the specific structure of each membrane. The porous membrane properties of some NCLM membranes seem to be most suitable for the development of a premature transmembranous formation of blood vessels, as observed 2 weeks following implantation. In contrast, CLM membranes have a more stratified appearance and a dense membrane body, hence vascularization and biodegradation of chemical and enzymatic cross-linked collagen membranes were slower as compared to non-cross-linked membranes.[61,68]

Degradation. One of the major drawbacks of resorbable membranes is the rate of degradation, resulting in an early loss of barrier function[69,70] that may impede the osseous formation during GBR.[71] During the wound healing process, collagen undergoes degradation, which is mediated by the enzymatic activity of matrix metalloproteases (MMP), that are released by recruited macrophages, neutrophils, eosinophils, and fibroblasts.[72-75] It has been proposed that an ideal GBR membrane should preserve its barrier function for 16–24 weeks.[76] The available collagen membranes that are used for regeneration possess different degradation times (Table 2A,B). Histomorphometric analysis shows that the thickness of the membrane significantly decreases 2–4 weeks post-surgery, partial degradation of the membrane is observed 1 month after implantation and severe degradation is detected at 3–4 months.[69] Among the available membranes in the market, some of the NCLM membranes begin the degradation process as early as 2–4 weeks following surgery[74] (Table 2A,B), while in others, the degradation process begins at 8 weeks (Table 2A,B).[60,61,68,69] As the degradation process begins, there is a breach in the integrity of the membranes, and its occlusive properties cease to exist. To prolong the resorption time of the native collagen, various cross-linking techniques have been developed. Cross-linking involves the multiplication of naturally occurring links between collagen molecules. This leads to stiffer collagen membranes and slows down the enzymatic degradation. There are various cross-linking techniques, such as ultraviolet light,[77] hexamethylene diisocyanate (HMDIC),[78] glutaraldehyde plus irradiation,[79] diphenyl phosphorylazide,[80] and glycation sugar-derived cross-links.[81,82] The glutaraldehyde technique was reported to leave cytotoxic residue during the process and those residues caused inflammation at the site of surgery.[61,83] Although CLM degradation time is usually longer than NCLM, there are membranes that show decreased membrane thickness, 8 weeks postop, while others did not result in reduction of thickness even after 6 months (Table 2A,B).[60,61,68,69] In general, CLM membranes were found to be more resistant to degradation than NCLM. In this regard, it was reported that, in cases of submerged healing, sugar-based CLM exhibited bone apposition and ossification within the membrane.[82,84] Brunel et al. evaluated the effect of different degrees of cross-linking on GBR. Their results confirm earlier studies demonstrating a positive correlation between the degree of cross-linking and the resorption rate. However, no statistically significant difference in bone fill was observed between membranes with different cross-linking degrees.[80] Moreover, a higher degree of cross-linking may lead to membrane exposure and compromised healing.[85] Other ways to prolong the degradation time or to increase the stability of the collagen membrane have been suggested, namely, application of a double layer of membrane[73] or systemic administration of tetracycline.[86]

In some cases, collagen membranes may be unintentionally exposed to the oral cavity. In such cases, bacterial proteases and collagenases increase the degradation rate,[87] concomitantly with an increased inflammatory reaction in the adjacent tissues, that promotes the enzymatic activity of macrophages and neutrophils recruited to the area. This, in turn, affects the structural integrity of the membrane, causing decreased barrier function and less bone regeneration or bone fill.[88] Sela et al. demonstrated that both CLM and NCLM membranes were degraded in a dose-dependent manner by *Porphyromonas gingivalis* and *Treponema denticola*. Moreover, both types of collagen membranes were cleaved by *Porphyromonas gingivalis*-associated proteases. *Porphyromonas gingivalis* produces large amounts of Arg-gingipain (Rgp) and Lys-gingipain (Kgp), which were both shown to have the ability to degrade extracellular matrix proteins like collagen (type I and IV), fibronectin, and laminin. In addition, *Porphyromonas gingivalis* peptidases, capable of hydrolyzing peptide bonds containing proline residues, have been described. These peptidases have the potential to hydrolyze collagen-derived oligopeptides rich in proline residues generated by collagenases.[89] To date, the data regarding the degradation rate of exposed CLM and NCLM are controversial; while several studies show that some CLM are more resistant to resorption than NCLM when left exposed to the oral environment,[84,90] Klinger et al.[91] showed no difference. Paul et al.[92] found that collagen membranes which were exposed to the oral environment were resorbed after 1 week. Therapeutic concentrations of antibacterial and antibiotics such as chlorhexidine, cetylpyridinium chloride, minocycline, and doxycycline were found to partially inhibit the enzymatic breakdown of the membranes.[93] However, in order to try delaying the degradation process of membranes by using these agents during GBR, further studies should be performed.

4.1.2 | Dehydrated human amnion chorion membrane (dHACM)

HAC is a tissue derived from the placenta, an organ that develops in the uterus during pregnancy. This structure provides oxygen and nutrients to the growing fetus. It consists of two fetal sheets: the outer chorionic sheet, and the inner amnion membrane.[94] Each layer harbors

TABLE 2A Commercially available natural resorbable membranes.

Classification	Commercial name	Main component (provided by manufacturer)	Structure and layers (provided by the manufacturer)	Pros	Cons	Additional information provided by the manufacturer
Noncross-linked collagen	Bio-Gide®, Geistlich Pharma AG, Switzerland	Type I, III collagen. Porcine pericard	Bilayer collagen membrane, comprised of a smooth and rough, open-pored layer. 0.4 mm thickness	Rapid vascularization[a], elasticity which improves the ability of handling as well as the adaptation to more irregular surfaces		The membrane may be sutured or attached with pins, but this is unnecessary in most cases due to its marked hydrophilic and adhesive properties
	Bio-Gide Compressed®, Geistlich Pharma AG, Switzerland	Type I, III collagen. Porcine pericardium	Bilayer collagen membrane, comprised of a smooth and rough, open-pored layer			Geistlich Bio-Gide® Compressed has a smoother surface, is firmer in touch and easier to cut than Geistlich Bio-Gide®
	Evolution®, OsteoBiol®, Italy	Heterologous mesenchymal tissue. Equine or porcine pericardium	Structured like an interconnected porous system. Thickness availability: 0.2 mm, 0.3 mm, 0.4 mm			
	Collprotect®, Botiss, Germany	Porcine dermis	Dense network collagen bundles with pores for vascularization. 0.4 mm thickness			
	Jason®, Botiss, Germany	Type III collagen. Porcine pericardium	Multi-oriented collagen fibers, strong tear-resistance. 0.15 mm thickness			
Cross-linked collagen	Ossix Plus®, Datum Dental Ltd., Israel	Ribose cross-linked (GLYMATRIX®). Type I collagen, bovine	0.2 mm thickness, highly condensed	Ossifying collagen barrier membrane[a], capable of supporting gingival healing when prematurely exposed[a]	Increased fragility and brittleness, a highly dense membrane, thus should not be attempted to suture through, requires practice[b]	
	Biomend®, Zimvie (Zimmer) USA	Glutharaldehyde cross-linked. Type I collagen, bovine	0.25 mm thickness	Enhanced early osteoblast attachment		
	Biomend Extended®, Zimvie (Zimmer) USA	Glutharaldehyde cross-linked. Type I collagen, bovine	0.3 mm thickness			
Amnion-chorion	BioXclude®, Snoasis Medical, USA	Deepithelialized amnion-chorion membrane. Rich in type I, III, IV, V, VI collagens	0.3 mm thickness	Bioactive properties, antimicrobial activity[98]		

[a]According to the manufacturer.
[b]According to the authors personal experience.

TABLE 2B Natural resorbable membranes. Biological and mechanical characteristics.

	Biological characteristics				Mechanical characteristics	
Commercial name	**Degradation time**	**Vascularization**	**Immunogenicity**	**Resistance in exposure**	**Fixation[a]**	**Handling/tissue adaptation**
Bio-Gide®, Geistlich Pharma AG, Switzerland	4–16 weeks	After 2 weeks	No signs of pronounced inflammatory reaction	3–10 days	Sutures, pins and screws	Easy handling, good tissue adaptation
Bio-Gide Compressed®, Geistlich Pharma AG, Switzerland	Possesses the same biological properties as Bio-Gide®[a]				Sutures, pins and screws	Easy handling, tear-resistant
Evolution®, OsteoBiol®, Italy	8–16 weeks (depends on membrane thickness)					
Collprotect®, Botiss, Germany	4–8 weeks					
Jason®, Botiss, Germany	8–12 weeks				Sutures, pins and screws	Tear-resistant, good tissue adaptation
Ossix Plus®, Datum Dental Ltd., Israel	16–24 weeks	After 24 weeks	No signs of pronounced inflammatory reaction	3–5 weeks[a]	Nonsuturable. Periosteal sutures possible. Fixation with screws or pins is not recommended	Not tear-resistant
Biomend®, Zimvie (Zimmer) USA	8 weeks	After 4 weeks	Infiltration of inflammatory cells in the adjacent tissue	3–10 days	Suturable	Easy handling, tear-resistant
Biomend Extended®, Zimvie (Zimmer) USA	18 weeks	After 4 weeks	Infiltration of inflammatory cells in the adjacent tissue	3–10 days	Suturable	Easy handling, tear-resistant
BioXclude®, Snoasis Medical, USA	8–12 weeks[a]		Nonimmunogenic		Nonsuturable. Periosteal sutures possible. No need to tack or suture	Good tissue adaptation

[a]According to the manufacturer.

different cell populations and variable plasticity. Amnion tissue is rich in collagen types III, IV, and VI, while the chorionic layer is abundant in collagen types I, III, IV, V and VI,[95] glycoproteins, and proteoglycan. It contains angiogenic growth factors and induces endothelial cell proliferation and migration.[96] The human amniotic membrane expresses growth factors such as epidermal growth factor (EGF), keratinocyte growth factor (KGF), hepatocyte growth factor (HGF), and β-fibroblast growth factor (β-FGF) that may benefit the epithelialization process.[97] In vitro experiments showed bactericidal properties of the dHACM, in which this membrane inhibited oral bacterial growth within 24 h after placement, similar to tetracycline administration, while a collagen membrane failed to do so.[98] Kobb et al.[99] showed that dehydrated HACM has quantifiable levels of growth factors (PDGF, TGFβ, FGF, and GCSF) and cytokines (Interleukin-4, -6, -8, and -10). They also pointed out that, in an in vivo model of skin flap, dHACM promoted migration and recruitment of mesenchymal stem cells to the wound site, 7 days after injury. This group also demonstrated that dHACM promotes amplification of angiogenic cues by inducing endothelial cell proliferation, that are likely to be responsible for neovascularization and healing of chronic wounds.[96] In periodontal defects created in rats, dHACM enhanced healing times due to the promotion of cell proliferation and migration, and induced angiogenesis.[100]

In the medical field, amnion, chorion, and amnion-chorion membranes have been successfully used to treat ulcers[101,102] burns[103,104] and chronic wounds in the oral mucosa[105] due to their efficacy in wound healing and epithelialization.[106] dHACM is also available for dental applications. According to the manufacturer, this membrane resorbs between 8 and 12 weeks. Clinical reports and case studies successfully used dHACM for peri-implantitis treatment,[107] alveolar ridge preservation[108-110] maxillary sinus membrane repair,[111] periodontal regeneration (reviewed in [112]),[113,114] root coverage,[114,115] and GBR. A case series of three cases of lateral ridge augmentation was reported by Yu.[116] In this study, the dHACM membrane was left exposed intentionally (2–3 mm gap) and, after 1 week, the membrane could be observed between the flaps, healing was uneventful, and bone gain was reached as expected.

In another study by Hassan et al., a dHACM was left intentionally exposed during ridge preservation and compared to a d-PTFE membrane. After 3 months, no difference was found between the two groups, as measured by clinical and radiographic ridge dimension. However, postoperative visual analog scale (VAS) scores were significantly lower in the dHACM cohort.[110] Miller et al. reported uneventful healing after intentionally leaving dHACM exposed in one case of alveolar ridge preservation and in one case of GBR. Both cases resulted in good clinical outcome without the need for further augmentation, 4 months posttreatment, and culminating in stable implants, 5 years after placement.[117]

4.1.3 | Safety issues

The risk of disease transmission using a natural origin material (either allogeneic or xenogeneic) is a matter of concern. In order to make these materials safe for use, the membranes may undergo a myriad of sterilization processes. Different protocols are used: heat treatment, irradiation (Gamma, E-beam, and UV), plasma and chemical sterilization (EtO, peracetic acid, ethanol, and iodine). These protocols are able to inactivate bacteria, bacteria spores, fungi and even prions (all but the irradiation protocols).[118,119] It is important to mention that some commonly used collagen membranes undergo sterilization through irradiation protocols only. Kim et al.[120] reported in a systematic review that bovine-derived graft biomaterials may carry a risk of bovine spongiform encephalopathy prion transmission to patients, although the risk cannot be quantified. Despite that, to the best of the authors knowledge, there is no evidence in the literature of prions transmission disease by autogenous and or xenogenous collagen and or bone substitutes in the dental field.

The use of membranes (or grafts) from natural origin may impact the relationship with some social groups and blood donor patients. Several health regulators (Food and Drug Administration – USA, European Commission Public Health - Europe, World Health Organization (WHO)) unanimously state that patients who received xenografts for alveolar reconstructions are categorized as definitively ineligible for blood donation. These regulations are based on the risk of prionic disease transmission to the host. Moreover, the WHO recommend that patients that received allogeneic graft since 1980 are ineligible to donate blood.[121] Additionally, patients with certain religious and behavioral beliefs (like vegans or vegetarians) may exclude, partially or totally, the use of animal-based products. In these cases, the use of synthetic materials may be considered.

4.2 | Synthetic membranes

4.2.1 | Polylactic acid (PLA)

PLA, a semicrystalline and aliphatic polyester which is obtained from lactic acid, is one of the most common and widely used polymers in GBR applications. While PLA is highly biocompatible, its mechanical properties have been improved by homogenous bending of poly-D,L-lactic acid and poly-L-lactic acid. Owing to its good processability, the latter modification is also used to manufacture bone screws for membrane fixation.[122] PLA can also form a copolymer with poly glycolic acid (PGA) to form polylactic-co-glycolic acid (PLGA).[123] Interestingly, while PLA requires a longer time (>4 years) to degrade than PGA, copolymerization with PGA decreases the resorption time of PLA to less than 1 year.[124]

The stiffness of PLA and PLGA membranes limit their manipulation abilities during surgical procedures. This limitation was minimized by application of various softeners, including N-methyl-2-pyrrolidone (NMP) or lauric acid.[125] Finally, their ability to trigger a foreign body response due to their acidic degradation by-products has been suppressed by blending these membranes with hydroxyapatite.[126]

Earlier studies show clinical advantages of PLA membranes in terms of new tissue attachment and bone gain around intrabony defects; however, these results were similar to the clinical outcomes of

e-PTFE membranes,[127,128] and notably, e-PTFE membranes demonstrated higher amounts of bone regeneration.[127] Interestingly, Schliephake et al. found that the vertical extension of the regenerated bone observed 3 months post-surgery, which occurred when using PLA and e-PTFE membranes, disappeared in the PLA group after 6 months. The success rate in PLA/PGA membranes depends on the time of resorption; when completion of resorption occurs too early, the repopulation of bone progenitor cells may not take place, which usually requires 3–4 weeks. Accordingly, Donos et al.[129] found in an animal model that early exposure of a PLA/PRA copolymer resorbable membranes led to extensive graft resorption. Immediate postsurgical exposures are common in both resorbable and non-resorbable membranes, yet membrane exposure rates were conflicting; some studies observed membrane exposure less frequently in PLA groups (six out of 10 cases) than in e-PTFE membranes (nine out of 10 cases),[130] while opposite results, less frequent exposures in the e-PTFE group than in the PLA group were also reported.[131] According to Zybutz et al.[128] rates of marginal membrane exposure in guided tissue regeneration (GTR) treatment using either PLA and e-PTFE membranes are approximately 30%, 2 weeks post-therapy. One advantage of PLA/PGA membranes is their complete resorption within 3–4 weeks, thereby avoiding membrane removal surgery and resulting in no disruption of the healing process.[132]

4.2.2 | Polycaprolactone (PCL)

PCL contains an aliphatic semicrystalline polyester structure. As compared to PLA or PLGA membranes, its main advantages are the lack of an acidic environment during its degradation and its cytocompatibility. Owing to these properties, PCL has been used successfully as surgical sutures and root canal fillings in dental medicine.[133] However, its long degradation time, (usually more than 24 months)[134] and high hydrophobicity, which suppresses cellular adhesion, are its main limitations. The preferred method to overcome these limitations is plasma treatment, which does not alter its advantageous mechanical properties.[135] While it is generally accepted that PCL has good mechanical properties, it does have limitations in its ability to withstand mechanical loads.[136] An emulsion templating method has been proposed as a new manufacturing technique to promote cell migration and growth.[137] Finally, the biological properties of PCL have been continuously developed by implementing gelatin microparticles,[138] β-tricalcium phosphate,[139] or magnesium oxide.[140] Data on utilization of PCL for GBR, especially information on membrane exposure and bacterial contamination, are limited.[141]

4.2.3 | Polyethylene glycol (PEG)

Polyethylene glycol is a non-ionic, mucoadhesive, and biocompatible material, and has high cell-occlusive and biodegradable properties. PEG membranes are composed of two liquid PEG compound that react upon mixing and form a hydrogel, that with time polymerize and become rigid. Studies comparing PEG to collagen membranes for the treatment of bone dehiscence defects in bone level implants produced similar results.[142] Equal amounts of new bone was observed in both groups, 4 weeks post-surgery.[143] PEG membranes were as effective as e-PTFE membranes in their ability to maintain space as the membrane collapses, which is a common shortcoming of GBR membranes.[143,144] Finally, prevention of soft tissue collapses and ingrowth of epithelial cells and fibroblasts were found to be similar in defects that were covered with either PGE or PLA membranes.[144] Nevertheless, there are various cross-linking techniques in the production of PEG and each method can affect the biological and mechanical properties of the resulting material.[145] Zambon et al.[146] demonstrated in a mini-pig bone dehiscence model, that PEG hydrogel membrane may fracture after polymerization, impairing wound healing and leading to lack of implant osseointegration. Moreover, use of PEG membranes together with freeze-dried bone xenograft failed to support new bone formation, indicating that not all graft and PEG membrane combinations may be clinically functional.[147] Clinical implant studies did not only demonstrate PEG membrane exposure induced bacterial contamination,[148] but also buccal dehiscence defects with implant shoulder exposures were noticed in three of the nine cases (33%) in the PEG hydrogel membrane group.[149]

4.3 | Other resorbable membranes

4.3.1 | Chitosan

Chitosan is a chitin-derivative polysaccharide with antimicrobial, biodegradable, and biocompatible properties. Its chemical structure allows it to be processed into membranes and gels. Human studies using chitosan membranes did not show any toxic or allergic reactions for the length of the 12-week study.[150] When grafted into rat subcutaneous tissue, chitosan maintained its shape until postoperative week 6.[151] However, chitosan may have unsatisfactory rigidity and strength, which could eventually cause membrane collapse.[152] The explanation behind these conflicting results might be associated with the preparation methods that have significant effects on biological properties of chitosan, including its degradation rate. A study on beagle dogs described insignificant differences between standard collagen membranes and chitosan in terms of their bone regeneration enhancement abilities.[153] Results of membrane exposure were not described in this study.

4.3.2 | Cellulose

Alkali-cellulose membranes were first described and developed by Novaes et al.[154] in 1995. Subsequently, various studies have described equal bone formation-supporting ability of these membranes to the gold standard e-PTFE membranes.[155,156] Yet, e-PTFE membranes are still first choice for GBR due to their superior manipulation and degradation characteristics.[156] Bacterial cellulose, or

its oxidized form, has been used in production of commercial resorbable membranes.[157] Notably, bacterial cellulose can be combined with various other compounds, including collagen, gelatin, fibroin, or chitosan.[158] During degradation, however, cellulose may present itself as an indigestible foreign material, which may activate a more extensive and severe inflammatory response.[159]

4.3.3 | Alginate

Alginate is a salt derivative of alginic acid. Due to its poor mechanical strength, alginate membranes are not produced from pure alginate.[160] Rather, commercial alginate membranes are mainly formed of sodium alginate (Na-Alg) or calcium alginate (Ca-Alg), and have been extensively used in the field of medicine, mainly due to their abundance, low price, low toxicity, and scaffold-forming ability.[161] Self-setting alginate membranes were initially introduced by a Japanese group.[162] The principle behind the self-setting alginate membrane is to fill the bone defect with aqueous Na-Alg solution, followed by drops of aqueous $CaCl_2$ solution. This chemical reaction forms an alginate membrane on top of the bone defect, while the defect continues to be filled with aqueous Na-Alg solution. The authors demonstrated successful outcomes, especially when they compared their results to ready-made membranes.[163,164] Successful results were also produced upon application of Na-Alg and chitosan/tricalcium phosphate microparticles to bone defects in the form of a self-setting composite.[165] Oxidized Na-Alg also has favorable properties for bone engineering, including improved biodegradability, structural stability, thermostability, and hydrophilic character.[161]

4.3.4 | Agarose

Agarose is a biodegradable natural polymer. Its ability to form a three-dimensional network has been advantageous in bone regeneration studies. Moreover, its mechanical properties can be improved in conjunction with other materials, such as hydroxyapatite, to increase osteogenic behavior of mesenchymal stem cells.[166] Membranes formed of agarose acetate and Poly(D, L-lactide) have been used for femur defect regeneration in rabbits.[167] Yet, information on the use of agarose membranes on GBR applications is very limited.

5 | EFFECTS OF THE TYPE OF MEMBRANE ON CLINICAL RESULTS

5.1 | Survival rate of implants with different membranes

There is a high level of evidence that survival rate of dental implants placed simultaneously with or as a second stage after bone augmentation with resorbable or non-resorbable membranes is similar to the survival rate of implants placed into pristine bone.[168,169] Jung et al.[10] evaluated the performance of implants placed simultaneously with GBR using NCLM or non-resorbable membranes compared to implants placed in pristine bone. With a follow-up of 22–24 years, the survival rate was 89.3% in the resorbable membrane group, 90.2% in the non-resorbable membrane group and 93.8% in the pristine bone group, resulting in no significant difference between the three groups. Implant placement with GBR procedures, either with resorbable or non-resorbable membranes, provides treatment outcomes with favorable implant survival rates of 89%–94% after 23.5 years.[10] Zitzmann et al. conducted a prospective study regarding implants placed with GBR using NCLM and non-resorbable membrane and implants placed in pristine bone. One hundred and twelve implants were treated with collagen membranes, 41 implants were augmented by applying e-PTFE membranes, and 112 implants were inserted without bone regeneration. The survival rates in the three groups were as follows: collagen membrane 95.4%, e-PTFE membrane 92.6%, and controls lacking bone regeneration 97.3%. There was no significant difference between the groups.[6] Overall, the data show that the type of membrane used in GBR, whether resorbable or not resorbable, did not affect the survival rate of implants.

5.2 | Bone gain with different membranes

Collagen membranes are being successfully used to increase both lateral and vertical bone volume.[19,170,171] Mordenfeld et al.[172] evaluated volumetric changes after lateral augmentation with a bone graft and an NCLM in edentulous sites. Bone gain was 3.5 mm, when measured 3 mm from the top of the bone crest, following a healing period of 7.5 months. Hammerle et al.[173] reported a mean bone gain of 3.6 mm after lateral augmentation with a bone graft and an NCLM and Urban et al.[174] reported a mean bone gain of 5.6 mm after horizontal bone augmentation with an NCLM and a particulated bone graft. Thoma et al. evaluated the efficacy of lateral bone augmentation performed simultaneously with implant placement in a meta-analysis. The results show that the mean defect resolution was 81%, with a range of 56.4%–97.1%, and that the defect height reduction was significant in favor of CLM and NCLM as compared to an e-PTFE membrane (Table 3).[175] Beitlitum et al.[176] evaluated the clinical outcomes of vertical bone augmentation with the use of bone substitute covered by a CLM membrane applied in a bilayered technique and found a mean vertical bone gain of 3.5 mm. Llambes et al. performed vertical ridge augmentation simultaneously with implant placement in a tenting technique. The implants were covered with autogenous bone and a CLM membrane. The mean height of the exposed implant was 3.5 mm at stage 1 surgery and 0.5 mm at 2 stage surgery. The mean bone gain was 3 mm, which represented 83% of the exposed implant at stage 1. One year after loading, the implants showed a mean bone loss of 1.4 mm. Histology from one successful case showed new trabecular bone development with large cellular marrow spaces in the regenerated area.[177] Cardaropoli et al.

TABLE 3 Compilation of meta-analysis centered on the effect of different membrane materials in different treatments and approaches.

Treatments	Simultaneous with implants/ staged approach	Outcome	Complications	Comments	Reference (Author, Year)
Vertical GBR	Simultaneous and staged approach	GBR was the most frequently reported procedure (13 studies with non-resorbable and 7 with resorbable membranes). The average vertical bone gain was 5.0 mm and 4.3 mm for dPTFE and ePTFE, respectively, 4.2 mm and 2.7 mm for cross-linked and non-cross-linked collagen membranes, respectively. The type of bone graft used influenced the outcome.	The most common complications were membrane and graft exposures with or without infection. The GBR complication rate was 12.1%, 6.9% for non-resorbable membranes (dPTFE were less prone to complications than ePTFE), and 22.7% for resorbable membranes.	All non-resorbable membranes included were titanium reinforced.	Urban et al. 2019[171]
Lateral bone augmentation	Simultaneous and staged approach		The type of membrane had no statistically significant influence on any postsurgical complications. Minor complication rate 11.4% of sites. Major complication rate was 1.6% at a patient level. Seventeen studies with resorbable membranes, two studies with ePTFE membranes. Staged or simultaneous approach did not significantly affect complication incidence, however, there is a trend toward more complications with the staged approach.	Resorbable collagen or PLA and non-resorbable ePTFE membranes included. This study included lateral bone augmentation using bone block or GBR. Results were not categorized by treatment.	Tay et al. 2020[185]
Lateral bone augmentation	Simultaneous and staged approach	The intervention combining bone graft with barrier membranes was associated with superior outcomes.	The most frequent complication was membrane/ graft exposure. Nonexposed sites gained significantly more bone in the simultaneous and staged approach.		Sanz-Sanchez et al. 2018[179]
Lateral GBR	Simultaneous and staged approach		Seven studies included. The overall RR for exposure was 1.43 without significant difference between the cross-linked and the non-cross-linked membranes. Although with a marginal tendency toward higher exposures in cross-linked membranes.	The NCLM membranes were Bio-Gide, the CLM membranes were Ossix, Ossix Plus, VN and Ossguide	Jimenez Garcia et al. 2017[181]
Lateral GBR	Simultaneous and staged approach	Percentage of horizontal bone width gain after GBR at edentulous ridges was 76.2% more bone gain without exposure compared to exposed membranes. Six studies were included. Peri-implant bone dehiscence after GBR. A total of 27.2% more defect reduction without exposure versus with exposure. Two studies were included.	Not reported	Resorbable and non-resorbable membranes were included. Peri-implant bone dehiscence reduction after GBR with non-resorbable membrane was not affected whether there was a membrane exposure or not. Two studies were included.	Garcia et al. 2018[184]

(Continues)

TABLE 3 (Continued)

Treatments	Simultaneous with implants/ staged approach	Outcome	Complications	Comments	Reference (Author, Year)
Lateral GBR	Simultaneous approach	The mean defect resolution was 81%. Twenty studies were included. The only significant difference at reentry was calculated between CM+XE and ePTFE+BS, in favor of the collagen membrane, two studies were included.	The overall membrane exposure rate was 23%. There was no significant difference between the membranes. Twenty studies were included.	GBR performed with a membrane was significantly more favorable than bone substitute alone. Two studies were included. In five studies, the necessity of regrafting upon reentry was described.	Thoma et al. 2019[175]
Lateral + Vertical GBR (mainly lateral)	Simultaneous and staged approach		Overall membrane exposure rate: 23%. The membrane exposure rate for cross-linked membranes was approximately 50% higher than non-cross-linked membranes. Fourteen studies were included. Membrane fixation was weakly associated with increased vertical bone gain.		Wessing et al. 2018[180]
Vertical + Lateral GBR	Simultaneous and staged approach		The weighted complication rate of the overall soft tissue complications, including membrane exposure, soft tissue dehiscence, and infection/ abscess was 16.8% without significant difference between resorbable and non-resorbable membranes. Fifteen studies were included.	Included resorbable and non-resorbable membranes.	Lim et al. 2018[182]
Vertical GBR	Simultaneous and staged approach	The RoM of vertical bone gained was 0.65 and 0.62 when membrane exposure without suppuration (four studies) and abscess formation without membrane exposure occurred (three studies), respectively, versus uneventful healing.	The overall incidence of healing complications occurring at the augmented site at a site and patient level was 11% and 10.8%, respectively. Twenty-eight studies were included. At patient level, there were no significant difference between simultaneous or staged approach, or with the regenerative device used.	Included resorbable and non-resorbable membranes.	Tay et al. 2022[186]
Lateral GBR	Staged approach	Barrier membrane did not yield a significant difference in terms of bone width gain and graft resorption. Two studies were included.			Naenni et al. 2019[196]

evaluated the treatment of alveolar bone deficiencies combined with dental implant placement. The bone regeneration procedures were performed using a combination of bovine bone-derived mineral stabilized with a fibrin-fibronectin sealing system and covered with a bilayer NCLM, resulting in a mean bone gain of 3.95 mm.[178] Sanz-Sanchez et al.[179] evaluated the effect of lateral ridge augmentation (both simultaneously with implant placement or as a staged procedure) on peri-implant health or disease, the results showed that when lateral GBR with bone substitute and a collagen membrane was compared to spontaneous healing in the treatment of dehiscence defects, the spontaneous healing resulted in a greater amount of bone loss (Table 3). Thoma et al.[175] evaluated the effect of lateral bone augmentation procedures in relation to defect resolution in cases of horizontal ridge deficiencies after implant placement, and found that GBR performed in the presence of a membrane had a significantly more favorable outcome than bone substitute alone (Table 3).

5.3 | Membrane exposure and its impact on bone gain

In the clinical practice, despite a perfect surgical technique, dehiscence in the soft tissue may appear, leaving the membrane exposed to the oral cavity. Membrane exposure and its subsequent bacterial contamination may hamper the regenerative outcome. When a membrane is combined with biomaterials, the incidence of bacterial infection may increase.[15] Membrane exposure in GBR procedures occurs when using either resorbable or non-resorbable membranes. Wessing et al.[180] found an overall exposure rate of 23%, while the exposure rate for CLM was 50% higher than NCLM. On the other hand, Garcia et al.[181] found that after horizontal GBR, the relative risk for membrane exposure was 1.43 without significant difference between NCLM and CLM. Other studies investigated the difference of membrane exposure and other complications between resorbable and non-resorbable membranes. Thoma et al.[175] found an overall membrane exposure rate of 23% and Lim et al.[182] reported that the overall soft tissue complications, including membrane exposure, soft tissue dehiscence, and infection/abscess was 16.8%, and were not significantly different between resorbable and non-resorbable membranes. In a systematic review, Donos et al.[183] concluded that the most common complication was flap dehiscence/membrane exposure, which was present in 16.3% of the implants treated with a collagen membrane and varied from 11.1% to 24.4% of the implants treated with an e-PTFE membrane. Garcia et al. performed a meta-analysis, evaluating the effect of membrane exposure on lateral GBR with resorbable or non-resorbable membranes. The authors concluded that there was 76.2% more bone gain at edentulous ridges without exposure. At peri-implant bone dehiscence, there was 27.2% more defect reduction when the membrane was not exposed. It was found that, while exposures of resorbable membranes decrease bone gain, exposures of non-resorbable membranes did not affect the results significantly, probably due to the large variance in the results of the studies that used non-resorbable membranes and were included in the meta-analysis (Table 3). The data suggest that there is no significant difference in the outcome of GBR following exposure of resorbable membranes compared to exposure of non-resorbable membranes.[184] Tay et al. investigated healing complications and their detrimental effects on bone gain in horizontal[185] and vertical[186] GBR with resorbable and non-resorbable membranes. During lateral GBR, the type of membrane had no statistically significant influence on any postsurgical complications. Staged or simultaneous approach did not significantly affect the complication incidence, however, there was a trend toward more complications with the staged approach.[185] In vertical GBR, the results show that the RoM (ratio of means) of vertical bone gain was 0.65 when membrane exposure without suppuration occurred, versus uneventful healing, regardless of the type of membrane used.[186] This systematic review also found that resorbable collagen membranes resulted in a significantly greater incidence of membrane exposures without suppuration than non-resorbable membranes (Table 3).[186]

6 | DISCUSSION

In 1993, Lindhe stated the indications for GBR: treatment of dehiscence and fenestration defects at implant installation, immediate installation of implants in fresh extraction sockets and augmentation of bone volume prior to implant placement.[187] These indications for GBR are still relevant today, with the use of membranes expanding into other indications, such as GTR after mandibular third molar extraction, endodontic surgeries, and surgical treatment of peri-implantitis.[188]

Successful osseous regeneration by GBR depends on the migration of pluripotential and osteogenic cells into an empty space (bone defect), and on the exclusion of epithelial cells and fibroblasts.[14,189,190] The rate of regeneration must exceed the fibrogenesis rates of the surrounding tissues.[191] Without intervention, this process is unpredictable. Hence, the role of an occlusive membrane seems to be critical in order to ensure successful bone formation. The first membranes used in dentistry by Nyman et al. were cellulose acetate filters manufactured by Millipore.[13] Since then, a wide range of membranes have been developed. In 1984, the same research group introduced the Gore-Tex® e-PTFE membrane to the dental field.[192] e-PTFE membranes were considered the gold standard for GBR during the 1990s[19] due to their high biocompatibility, inertness, and resistance to breakdown.[16,23] At present, e-PTFE dental membranes are rarely used,[88] although d-PTFE membranes were shown to be as effective, or perhaps better in particular clinical indications. The main advantage of d-PTFE is that bacteria are not able to penetrate this membrane, thus it may be left intentionally exposed. The main disadvantage of PTFE non-resorbable membranes is the need for a second surgery, increasing patient morbidity, chair time, and decreasing cost-effectiveness. Although PTFE and titanium are non-resorbable and require a second surgery, surgeons continue their use due to its surgical

handling properties, malleability, structural rigidity in preventing collapse, and space maintenance for large ridge defects.[193] The timing of membrane removal is also important, because premature removal can lead to resorption of regenerated bone, whereas late removal can increase the risks of bacterial contamination and infection.[193]

Resorbable (natural or synthetic) membranes were introduced at a later stage, eliminating the need for a second surgery. The use of either cross-linked or non-cross-linked collagen, membranes, is well-documented. They are composed mostly of porcine- or bovine-derived collagen type I and/or III. The available membranes used for GBR have wide range of porosity, allowing selective cell migration, and the passage of chemicals, biomolecules, and viruses. Collagen membranes are highly biocompatible in vitro and in vivo; however, the degradation process may initiate some inflammatory response. The unpredictable degree and time of resorption of all resorbable membrane is still a matter of concern. CLM degradation time is usually longer than NCLM.[60,61,68,69] In some cases, the collagen membrane may be unintentionally exposed to the oral cavity. In such cases, the presence of bacterial proteases and collagenases increases the degradation rate.[87] It was shown that augmentation at implant dehiscence defects using bioresorbable membranes enhances bone regeneration, mostly, in conjunction with the use of supporting graft material.[194,195]

dHACM seems to have promising biological properties. This membrane, composed mainly by different collagen types that resemble the basement membrane of oral mucosa, provide an efficient barrier function. Additionally, it contains growth factors and cytokines, converting this membrane into a biologically active component that promotes epithelialization, angiogenesis, and wound healing.[99] Lastly, it was shown to contain antimicrobial factors, reducing the risk of infection.[98] dHACM is a most promising material. This membrane is commercialized only in USA and Canada (internal communication with the company). dHACM has been successfully used in dentistry for a variety of purposes including peri-implantitis treatment,[107] alveolar ridge preservation[108-110] maxillary sinus membrane repair,[111] periodontal regeneration,[113,114] root coverage,[114,115] and GBR.[116] More clinical research is needed to thoroughly validate its indications. The main disadvantage of these resorbable membranes is their relatively low mechanical strength, hence, they are susceptible to tearing and collapsing into the defect.[196,197]

GBR is a well-established and predictable technique to augment deficient ridges.[198] There is much evidence showing that survival rate of dental implants placed simultaneously with or at a second stage following bone augmentation with resorbable or non-resorbable membranes is similar to the survival rate of implants placed into pristine bone.[168,169] Regarding bone gain, we can conclude that either non-resorbable or resorbable membranes are able to reach high amount of new bone formation, without significant differences between the membranes. Despite the good results, sometimes healing complications may occur. According to recent systematic reviews, membrane exposure is a common event with a reported mean incidence that ranges from 11% to 23%.[180,183,186] It is clear from these studies that membrane exposure, with or without infection, dampens the overall bone gain. Resorbable and non-resorbable membranes seem to have the same overall incidence of exposure. Yet, in vertical augmentation procedures, surprisingly, collagen membranes have higher exposure rate than PTFE devices.[171,186] Among collagen membranes, cross-linked membranes have higher exposure rates compared to non-cross-linked membranes.[171] Those differences may be related to the specific structure of each membrane. Non-cross-linked membranes are more affordable for premature transmembranous formation of blood vessels than cross-linked membranes,[61,90] hence improving early blood supply of the soft tissues.[68,199] Other possible explanations for the higher exposure rate with cross-linking membranes include inflammation induction by several types of cross-linked membranes, lack of cell adhesion, and interference in the inflammatory reaction and soft tissue healing.[61,200] Additionally, cross-link membranes are more resistant to degradation than the non-cross-link membranes, so they are more likely to be exposed to oral environments over the same follow-up period.[181] Regarding the differences in exposure rate of PTFE and collagen membrane, in which the last has significantly higher exposure rate, while collagen membranes allow blood supply from the regenerated area to the soft tissues, PTFE membranes are completely hermetic. We can hypothesize that the degradation process of resorbable membranes may hamper the epithelization process above them leading, in some cases, to unintentional exposure in higher rates when comparing to PTFE membrane Despite the increasing amount of research on GBR, there is no clear superiority of one membrane above the others. In addition, upon membrane exposure, there is no study comparing bone gain among different membranes.

We now clearly understand that barrier membranes are more than a mere occlusive foil. Rather, they play an active role in hosting and modulating bone regeneration during GBR.[201] Along with the native bioactivity of GBR membranes, incorporating growth factors and specific cell types in membranes or in conjunction with graft materials may augment the regenerative processes in underlying defects. New trends in membrane research aim to improve the biological characteristics. For example, the addition of antimicrobial substances such as antibiotics or silver ions may improve healing and potentially avoid bacterial-related complications. Yet, bacterial resistance is still a matter of concern if antibiotics will be incorporated into the membrane material.[202] Another strategy for membrane improvement is adding growth factors that favor bone formation. Growth factors have received much attention due to their multiple functions during bone healing, including cell recruitment, proliferation, and differentiation. Positive results have been derived from in vivo animal experiments using bone morphogenetic proteins (BMP), fibroblast growth factors (FGF), or platelet-derived growth factor (PDGF) with resorbable membranes.[201] Other efforts are being made to improve membranes' properties, such as enhanced biocompatibility and controlled degradation. Future research and perspectives in the field includes nanotechnology-based membranes. These membranes are designed to be made of nanofibers and microparticles as a way to create improved strength, porosity, antibacterial

activity, and biocompatibility.[203,204] Stem cell-based membranes, or cell-bearing scaffold membranes can also improve bone regeneration and enhance healing as they provide a source for bone-forming cells.[205-207] Smart membranes can also be designed to adjust their properties to changes in the local environment such as pH or temperature. These membranes can improve the efficiency and effectiveness of GBR by delivering drugs or growth factors to the desired location.[208]

Clinical and scientific evidence strongly suggests that the use of barrier membranes is mandatory to reach optimal results in GBR. To date, each available membrane bears inherent advantages and disadvantages that were discussed in this review. The choice of membrane is still being dictated by the defect configuration, the need for augmentation in horizontal or vertical directions, the use of a predictable clinical protocol,[183] the clinician's personal experience and dexterity, considering patient religious and behavioral beliefs. The "ideal membrane" is yet to be developed; however, it should be biocompatible, semipermeable (should prevent epithelial and bacterial proliferation, without dampening neovascularization and nutrients passage), mechanically stable and easy to handle and adapt, "tissue friendly" slowly resorbable (without exerting toxic effects on its surroundings during the process), and actively promote on one side bone regeneration and on the other side soft tissue proliferation. Future research should embrace the paradigm shift toward the idea that the membrane is an active component in GBR rather than a mere physical barrier.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

G. Mizraji https://orcid.org/0000-0003-2692-1732

REFERENCES

1. Tonelli P, Duvina M, Barbato L, et al. Bone regeneration in dentistry. *Clin Cases Miner Bone Metab*. 2011;8(3):24-28.
2. Cho JY. The periodontist and the edentulous area–localised ridge augmentation. *Int Dent J*. 1998;48(3 Suppl 1):326-329.
3. Bornstein MM, Halbritter S, Harnisch H, Weber HP, Buser D. A retrospective analysis of patients referred for implant placement to a specialty clinic: indications, surgical procedures, and early failures. *Int J Oral Maxillofac Implants*. 2008;23(6):1109-1116.
4. Retzepi M, Donos N. Guided bone regeneration: biological principle and therapeutic applications. *Clin Oral Implants Res*. 2010;21(6):567-576.
5. Wang HL, Boyapati L. "PASS" principles for predictable bone regeneration. *Implant Dent*. 2006;15(1):8-17.
6. Zitzmann NU, Scharer P, Marinello CP. Long-term results of implants treated with guided bone regeneration: a 5-year prospective study. *Int J Oral Maxillofac Implants*. 2001;16(3):355-366.
7. Buser D, Dula K, Lang NP, Nyman S. Long-term stability of osseointegrated implants in bone regenerated with the membrane technique. 5-year results of a prospective study with 12 implants. *Clin Oral Implants Res*. 1996;7(2):175-183.
8. Fugazzotto PA, Shanaman R, Manos T, Shectman R. Guided bone regeneration around titanium implants: report of the treatment of 1,503 sites with clinical reentries. *Int J Periodontics Restorative Dent*. 1997;17(3):292, 3–9.
9. Blanco J, Alonso A, Sanz M. Long-term results and survival rate of implants treated with guided bone regeneration: a 5-year case series prospective study. *Clin Oral Implants Res*. 2005;16(3):294-301.
10. Jung RE, Brugger LV, Bienz SP, Husler J, Hammerle CHF, Zitzmann NU. Clinical and radiographical performance of implants placed with simultaneous guided bone regeneration using resorbable and nonresorbable membranes after 22-24 years, a prospective, controlled clinical trial. *Clin Oral Implants Res*. 2021;32(12):1455-1465.
11. Collins English Dictionary: Collins; 2023. https://www.collinsdictionary.com/dictionary/english/membrane
12. Hurley LA, Stinchfield FE, Bassett AL, Lyon WH. The role of soft tissues in osteogenesis. An experimental study of canine spine fusions. *J Bone Joint Surg Am*. 1959;41-A:1243-1254.
13. Nyman S, Lindhe J, Karring T, Rylander H. New attachment following surgical treatment of human periodontal disease. *J Clin Periodontol*. 1982;9(4):290-296.
14. Dahlin C, Linde A, Gottlow J, Nyman S. Healing of bone defects by guided tissue regeneration. *Plast Reconstr Surg*. 1988;81(5):672-676.
15. Sanz M, Dahlin C, Apatzidou D, et al. Biomaterials and regenerative technologies used in bone regeneration in the craniomaxillofacial region: consensus report of group 2 of the 15th European workshop on periodontology on bone regeneration. *J Clin Periodontol*. 2019;46(Suppl 21):82-91.
16. Elgali I, Omar O, Dahlin C, Thomsen P. Guided bone regeneration: materials and biological mechanisms revisited. *Eur J Oral Sci*. 2017;125(5):315-337.
17. Dimitriou R, Mataliotakis GI, Calori GM, Giannoudis PV. The role of barrier membranes for guided bone regeneration and restoration of large bone defects: current experimental and clinical evidence. *BMC Med*. 2012;10:81.
18. Caballe-Serrano J, Abdeslam-Mohamed Y, Munar-Frau A, Fujioka-Kobayashi M, Hernandez-Alfaro F, Miron R. Adsorption and release kinetics of growth factors on barrier membranes for guided tissue/bone regeneration: a systematic review. *Arch Oral Biol*. 2019;100:57-68.
19. Hammerle CH, Jung RE. Bone augmentation by means of barrier membranes. *Periodontol 2000*. 2003;33:36-53.
20. Sheikh Z, Qureshi J, Alshahrani AM, et al. Collagen based barrier membranes for periodontal guided bone regeneration applications. *Odontology*. 2017;105(1):1-12.
21. Liu J, Kerns DG. Mechanisms of guided bone regeneration: a review. *Open Dent J*. 2014;8:56-65.
22. Ebnesajjad S, ed. 3 – Discovery and history of fluoropolymers. *Introduction to Fluoropolymers*. William Andrew Publishing; 2013:17-35.
23. Roina Y, Auber F, Hocquet D, Herlem G. ePTFE-based biomedical devices: An overview of surgical efficiency. *J Biomed Mater Res B Appl Biomater*. 2022;110(2):302-320.
24. Haney JM, Nilveus RE, McMillan PJ, Wikesjo UM. Periodontal repair in dogs: expanded polytetrafluoroethylene barrier membranes support wound stabilization and enhance bone regeneration. *J Periodontol*. 1993;64(9):883-890.
25. Gutta R, Baker RA, Bartolucci AA, Louis PJ. Barrier membranes used for ridge augmentation: is there an optimal pore size? *J Oral Maxillofac Surg*. 2009;67(6):1218-1225.
26. Trobos M, Juhlin A, Shah FA, Hoffman M, Sahlin H, Dahlin C. In vitro evaluation of barrier function against oral bacteria of dense and expanded polytetrafluoroethylene (PTFE) membranes for guided bone regeneration. *Clin Implant Dent Relat Res*. 2018;20(5):738-748.
27. Simion M, Baldoni M, Rossi P, Zaffe D. A comparative study of the effectiveness of e-PTFE membranes with and without early

exposure during the healing period. *Int J Periodontics Restorative Dent*. 1994;14(2):166-180.
28. Marouf HA, El-Guindi HM. Efficacy of high-density versus semipermeable PTFE membranes in an elderly experimental model. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2000;89(2):164-170.
29. Carbonell JM, Martin IS, Santos A, Pujol A, Sanz-Moliner JD, Nart J. High-density polytetrafluoroethylene membranes in guided bone and tissue regeneration procedures: a literature review. *Int J Oral Maxillofac Surg*. 2014;43(1):75-84.
30. Crump TB, Rivera-Hidalgo F, Harrison JW, Williams FE, Guo IY. Influence of three membrane types on healing of bone defects. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 1996;82(4):365-374.
31. Zellin G, Linde A. Effects of different osteopromotive membrane porosities on experimental bone neogenesis in rats. *Biomaterials*. 1996;17(7):695-702.
32. Lamb JW 3rd, Greenwell H, Drisko C, Henderson RD, Scheetz JP, Rebitski G. A comparison of porous and non-porous teflon membranes plus demineralized freeze-dried bone allograft in the treatment of class II buccal/lingual furcation defects: a clinical reentry study. *J Periodontol*. 2001;72(11):1580-1587.
33. Barber HD, Lignelli J, Smith BM, Bartee BK. Using a dense PTFE membrane without primary closure to achieve bone and tissue regeneration. *J Oral Maxillofac Surg*. 2007;65(4):748-752.
34. Bartee BK. The use of high-density polytetrafluoroethylene membrane to treat osseous defects: clinical reports. *Implant Dent*. 1995;4(1):21-26.
35. Bartee BK, Carr JA. Evaluation of a high-density polytetrafluoroethylene (n-PTFE) membrane as a barrier material to facilitate guided bone regeneration in the rat mandible. *J Oral Implantol*. 1995;21(2):88-95.
36. Alauddin MS, Abdul Hayei NA, Sabarudin MA, Mat Baharin NH. Barrier membrane in regenerative therapy: a narrative review. *Membranes (Basel)*. 2022;12(5):444.
37. Lundgren A, Lundgren D, Taylor A. Influence of barrier occlusiveness on guided bone augmentation. An experimental study in the rat. *Clin Oral Implants Res*. 1998;9(4):251-260.
38. Ronda M, Rebaudi A, Torelli L, Stacchi C. Expanded vs. dense polytetrafluoroethylene membranes in vertical ridge augmentation around dental implants: a prospective randomized controlled clinical trial. *Clin Oral Implants Res*. 2014;25(7):859-866.
39. Cucchi A, Ghensi P. Vertical guided bone regeneration using titanium-reinforced d-PTFE membrane and Prehydrated Corticocancellous bone graft. *Open Dent J*. 2014;8:194-200.
40. Matumoto EK, Correa MG, Couso-Queiruga E, et al. Influence of partially exposed nonabsorbable membrane for alveolar ridge preservation: a randomized controlled trial. *Clin Implant Dent Relat Res*. 2023;25:447-457.
41. Buser D, Dula K, Belser U, Hirt HP, Berthold H. Localized ridge augmentation using guided bone regeneration. 1. Surgical procedure in the maxilla. *Int J Periodontics Restorative Dent*. 1993;13(1):29-45.
42. Dahlin C, Andersson L, Linde A. Bone augmentation at fenestrated implants by an osteopromotive membrane technique. A controlled clinical study. *Clin Oral Implants Res*. 1991;2(4):159-165.
43. Buser D, Bragger U, Lang NP, Nyman S. Regeneration and enlargement of jaw bone using guided tissue regeneration. *Clin Oral Implants Res*. 1990;1(1):22-32.
44. Schenk RK, Buser D, Hardwick WR, Dahlin C. Healing pattern of bone regeneration in membrane-protected defects: a histologic study in the canine mandible. *Int J Oral Maxillofac Implants*. 1994;9(1):13-29.
45. Jovanovic SA, Nevins M. Bone formation utilizing titanium-reinforced barrier membranes. *Int J Periodontics Restorative Dent*. 1995;15(1):56-69.
46. Jovanovic SA, Schenk RK, Orsini M, Kenney EB. Supracrestal bone formation around dental implants: an experimental dog study. *Int J Oral Maxillofac Implants*. 1995;10(1):23-31.
47. Machtei EE. The effect of membrane exposure on the outcome of regenerative procedures in humans: a meta-analysis. *J Periodontol*. 2001;72(4):512-516.
48. Sela MN, Steinberg D, Klinger A, Krausz AA, Kohavi D. Adherence of periodontopathic bacteria to bioabsorbable and non-absorbable barrier membranes in vitro. *Clin Oral Implants Res*. 1999;10(6):445-452.
49. De Sanctis M, Zucchelli G, Clauser C. Bacterial colonization of barrier material and periodontal regeneration. *J Clin Periodontol*. 1996;23(11):1039-1046.
50. Donos N, Kostopoulos L, Karring T. Alveolar ridge augmentation by combining autogenous mandibular bone grafts and non-resorbable membranes. *Clin Oral Implants Res*. 2002;13(2):185-191.
51. Krauser JT. High-density PTFE membranes: uses with root-form implants. *Dent Implantol Update*. 1996;7(9):65-69.
52. Turri A, Cirgic E, Shah FA, et al. Early plaque formation on PTFE membranes with expanded or dense surface structures applied in the oral cavity of human volunteers. *Clin Exp Dent Res*. 2021;7(2):137-146.
53. Zelikman H, Slutzkey G, Rosner O, Levartovsky S, Matalon S, Beitlitum I. Bacterial growth on three non-resorbable polytetrafluoroethylene (PTFE) membranes-An In vitro study. *Materials (Basel)*. 2022;15(16):5705.
54. Cooperman L, Michaeli D. The immunogenicity of injectable collagen. I. a 1-year prospective study. *J Am Acad Dermatol*. 1984;10(4):638-646.
55. Locci P, Calvitti M, Belcastro S, et al. Phenotype expression of gingival fibroblasts cultured on membranes used in guided tissue regeneration. *J Periodontol*. 1997;68(9):857-863.
56. Postlethwaite AE, Seyer JM, Kang AH. Chemotactic attraction of human fibroblasts to type I, II, and III collagens and collagen-derived peptides. *Proc Natl Acad Sci U S A*. 1978;75(2):871-875.
57. Bubalo M, Lazic Z, Matic S, et al. The impact of thickness of resorbable membrane of human origin on the ossification of bone defects: a pathohistologic study. *Vojnosanit Pregl*. 2012;69(12):1076-1083.
58. Takata T, Wang HL, Miyauchi M. Attachment, proliferation and differentiation of periodontal ligament cells on various guided tissue regeneration membranes. *J Periodontal Res*. 2001;36(5):322-327.
59. Rothamel D, Schwarz F, Sculean A, Herten M, Scherbaum W, Becker J. Biocompatibility of various collagen membranes in cultures of human PDL fibroblasts and human osteoblast-like cells. *Clin Oral Implants Res*. 2004;15(4):443-449.
60. Alpar B, Leyhausen G, Gunay H, Geurtsen W. Compatibility of resorbable and nonresorbable guided tissue regeneration membranes in cultures of primary human periodontal ligament fibroblasts and human osteoblast-like cells. *Clin Oral Investig*. 2000;4(4):219-225.
61. Schwarz F, Rothamel D, Herten M, et al. Immunohistochemical characterization of guided bone regeneration at a dehiscence-type defect using different barrier membranes: an experimental study in dogs. *Clin Oral Implants Res*. 2008;19(4):402-415.
62. Rothamel D, Schwarz F, Sager M, Herten M, Sculean A, Becker J. Biodegradation of differently cross-linked collagen membranes: an experimental study in the rat. *Clin Oral Implants Res*. 2005;16(3):369-378.
63. von Arx T, Broggini N, Jensen SS, Bornstein MM, Schenk RK, Buser D. Membrane durability and tissue response of different bioresorbable barrier membranes: a histologic study in the rabbit calvarium. *Int J Oral Maxillofac Implants*. 2005;20(6):843-853.
64. Sell SA, McClure MJ, Garg K, Wolfe PS, Bowlin GL. Electrospinning of collagen/biopolymers for regenerative

medicine and cardiovascular tissue engineering. *Adv Drug Deliv Rev*. 2009;61(12):1007-1019.
65. Ferreira AM, Gentile P, Chiono V, Ciardelli G. Collagen for bone tissue regeneration. *Acta Biomater*. 2012;8(9):3191-3200.
66. Schmid J, Hammerle CH, Olah AJ, Lang NP. Membrane permeability is unnecessary for guided generation of new bone. An experimental study in the rabbit. *Clin Oral Implants Res*. 1994;5(3):125-130.
67. Gugala Z, Gogolewski S. Regeneration of segmental diaphyseal defects in sheep tibiae using resorbable polymeric membranes: a preliminary study. *J Orthop Trauma*. 1999;13(3):187-195.
68. Schwarz F, Rothamel D, Herten M, Sager M, Becker J. Angiogenesis pattern of native and cross-linked collagen membranes: an immunohistochemical study in the rat. *Clin Oral Implants Res*. 2006;17(4):403-409.
69. Owens KW, Yukna RA. Collagen membrane resorption in dogs: a comparative study. *Implant Dent*. 2001;10(1):49-58.
70. Zhao S, Pinholt EM, Madsen JE, Donath K. Histological evaluation of different biodegradable and non-biodegradable membranes implanted subcutaneously in rats. *J Craniomaxillofac Surg*. 2000;28(2):116-122.
71. An YZ, Kim YK, Lim SM, et al. Physiochemical properties and resorption progress of porcine skin-derived collagen membranes: In vitro and in vivo analysis. *Dent Mater J*. 2018;37(2):332-340.
72. Zhang Y, Zhang X, Shi B, Miron RJ. Membranes for guided tissue and bone regeneration. *Ann Oral Maxillofac Surg*. 2013;1(1):10.
73. Kozlovsky A, Aboodi G, Moses O, et al. Bio-degradation of a resorbable collagen membrane (bio-Gide) applied in a double-layer technique in rats. *Clin Oral Implants Res*. 2009;20(10):1116-1123.
74. Calciolari E, Ravanetti F, Strange A, et al. Degradation pattern of a porcine collagen membrane in an in vivo model of guided bone regeneration. *J Periodontal Res*. 2018;53(3):430-439.
75. Ghanaati S. Non-cross-linked porcine-based collagen I-III membranes do not require high vascularization rates for their integration within the implantation bed: a paradigm shift. *Acta Biomater*. 2012;8(8):3061-3072.
76. Hoornaert A, d'Arros C, Heymann MF, Layrolle P. Biocompatibility, resorption and biofunctionality of a new synthetic biodegradable membrane for guided bone regeneration. *Biomed Mater*. 2016;11(4):045012.
77. Park JY, Jung IH, Kim YK, et al. Guided bone regeneration using 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide (EDC)-cross-linked type-I collagen membrane with biphasic calcium phosphate at rabbit calvarial defects. *Biomater Res*. 2015;19:15.
78. Minabe M, Kodama T, Kogou T, et al. Different cross-linked types of collagen implanted in rat palatal gingiva. *J Periodontol*. 1989;60(1):35-43.
79. Quteish D, Dolby AE. The use of irradiated-crosslinked human collagen membrane in guided tissue regeneration. *J Clin Periodontol*. 1992;19(7):476-484.
80. Brunel G, Piantoni P, Elharar F, Benque E, Marin P, Zahedi S. Regeneration of rat calvarial defects using a bioabsorbable membrane technique: influence of collagen cross-linking. *J Periodontol*. 1996;67(12):1342-1348.
81. Tanaka S, Avigad G, Eikenberry EF, Brodsky B. Isolation and partial characterization of collagen chains dimerized by sugar-derived cross-links. *J Biol Chem*. 1988;263(33):17650-17657.
82. Zubery Y, Nir E, Goldlust A. Ossification of a collagen membrane cross-linked by sugar: a human case series. *J Periodontol*. 2008;79(6):1101-1107.
83. Speer DP, Chvapil M, Eskelson CD, Ulreich J. Biological effects of residual glutaraldehyde in glutaraldehyde-tanned collagen biomaterials. *J Biomed Mater Res*. 1980;14(6):753-764.
84. Tal H, Kozlovsky A, Artzi Z, Nemcovsky CE, Moses O. Long-term bio-degradation of cross-linked and non-cross-linked collagen barriers in human guided bone regeneration. *Clin Oral Implants Res*. 2008;19(3):295-302.
85. Crigger M, Bogle GC, Garrett S, Gantes BG. Repair following treatment of circumferential periodontal defects in dogs with collagen and expanded polytetrafluoroethylene barrier membranes. *J Periodontol*. 1996;67(4):403-413.
86. Moses O, Shemesh A, Aboodi G, Tal H, Weinreb M, Nemcovsky CE. Systemic tetracycline delays degradation of three different collagen membranes in rat calvaria. *Clin Oral Implants Res*. 2009;20(2):189-195.
87. Mayrand D, Grenier D. Detection of collagenase activity in oral bacteria. *Can J Microbiol*. 1985;31(2):134-138.
88. Rakhmatia YD, Ayukawa Y, Furuhashi A, Koyano K. Current barrier membranes: titanium mesh and other membranes for guided bone regeneration in dental applications. *J Prosthodont Res*. 2013;57(1):3-14.
89. Sela MN, Kohavi D, Krausz E, Steinberg D, Rosen G. Enzymatic degradation of collagen-guided tissue regeneration membranes by periodontal bacteria. *Clin Oral Implants Res*. 2003;14(3):263-268.
90. Tal H, Kozlovsky A, Artzi Z, Nemcovsky CE, Moses O. Cross-linked and non-cross-linked collagen barrier membranes disintegrate following surgical exposure to the oral environment: a histological study in the cat. *Clin Oral Implants Res*. 2008;19(8):760-766.
91. Klinger A, Asad R, Shapira L, Zubery Y. In vivo degradation of collagen barrier membranes exposed to the oral cavity. *Clin Oral Implants Res*. 2010;21(8):873-876.
92. Paul BF, Mellonig JT, Towle HJ 3rd, Gray JL. Use of a collagen barrier to enhance healing in human periodontal furcation defects. *Int J Periodontics Restorative Dent*. 1992;12(2):123-131.
93. Sela MN, Babitski E, Steinberg D, Kohavi D, Rosen G. Degradation of collagen-guided tissue regeneration membranes by proteolytic enzymes of Porphyromonas gingivalis and its inhibition by antibacterial agents. *Clin Oral Implants Res*. 2009;20(5):496-502.
94. Parolini O, Alviano F, Bagnara GP, et al. Concise review: isolation and characterization of cells from human term placenta: outcome of the first international workshop on placenta derived stem cells. *Stem Cells*. 2008;26(2):300-311.
95. Chua WK, Oyen ML. Do we know the strength of the chorioamnion? A critical review and analysis. *Eur J Obstet Gynecol Reprod Biol*. 2009;144(Suppl 1):S128-S133.
96. Koob TJ, Lim JJ, Massee M, et al. Angiogenic properties of dehydrated human amnion/chorion allografts: therapeutic potential for soft tissue repair and regeneration. *Vasc Cell*. 2014;6:10.
97. Koizumi NJ, Inatomi TJ, Sotozono CJ, Fullwood NJ, Quantock AJ, Kinoshita S. Growth factor mRNA and protein in preserved human amniotic membrane. *Curr Eye Res*. 2000;20(3):173-177.
98. Ashraf H, Font K, Powell C, Schurr M. Antimicrobial activity of an amnion-chorion membrane to Oral microbes. *Int J Dent*. 2019;2019:1269534.
99. Koob TJ, Rennert R, Zabek N, et al. Biological properties of dehydrated human amnion/chorion composite graft: implications for chronic wound healing. *Int Wound J*. 2013;10(5):493-500.
100. Imamura K, Hamada Y, Yoshida W, et al. Investigating the effects of dehydrated human amnion-chorion membrane on periodontal healing. *Biomolecules*. 2022;12(6):857.
101. Tettelbach WH, Armstrong DG, Chang TJ, et al. Cost-effectiveness of dehydrated human amnion/chorion membrane allografts in lower extremity diabetic ulcer treatment. *J Wound Care*. 2022;31(Sup2):S10-S31.
102. Oropallo A, Goodwin A, Morrissey M, Del Pin C, Rao A. Human amnion chorion membrane allografts in the treatment of chronic diabetic foot ulcers: a literature review. *Adv Skin Wound Care*. 2021;34(4):1-7.
103. Sawhney CP. Amniotic membrane as a biological dressing in the management of burns. *Burns*. 1989;15(5):339-342.

104. Tenenhaus M. The use of dehydrated human amnion/chorion membranes in the treatment of burns and complex wounds: current and future applications. *Ann Plast Surg*. 2017;78(2 Suppl 1):S11-S13.
105. Kar IB, Singh AK, Mohapatra PC, Mohanty PK, Misra S. Repair of oral mucosal defects with cryopreserved human amniotic membrane grafts: prospective clinical study. *Int J Oral Maxillofac Surg*. 2014;43(11):1339-1344.
106. Kogan S, Sood A, Granick MS. Amniotic membrane adjuncts and clinical applications in wound healing: a review of the literature. *Wounds*. 2018;30(6):168-173.
107. Bhide VM, Goldberg MB, Tenenbaum HC. Surgical treatment of peri-implantitis with guided bone regeneration using dehydrated amnion-chorion membranes: a case report with a 2-year follow-up. *Int J Periodontics Restorative Dent*. 2022;42(3):e59-e66.
108. Holtzclaw D. Extraction site preservation using new graft material that combines mineralized and demineralized allograft bone: a case series report with histology. *Compend Contin Educ Dent*. 2014;35(2):107-112; quiz 12.
109. Faraj SA, Kutkut A, Taylor RC, et al. Comparison of dehydrated human amnion-chorion and type 1 bovine collagen membranes in alveolar ridge preservation: a clinical and histological study. *J Oral Implantol*. 2021;47(5):385-393.
110. Hassan M, Prakasam S, Bain C, Ghoneima A, Liu SS. A randomized Split-mouth clinical trial on effectiveness of amnion-chorion membranes in alveolar ridge preservation: a clinical, radiologic, and morphometric study. *Int J Oral Maxillofac Implants*. 2017;32(6):1389-1398.
111. Holtzclaw D. Maxillary sinus membrane repair with amnion-chorion barriers: a retrospective case series. *J Periodontol*. 2015;86(8):936-940.
112. Devarampati LJ, Koduganti RR, Savant S, Gullapelli P, Manchala S, Mydukuru A. Role of placental extracts in periodontal regeneration: a literature review. *Cureus*. 2022;14(6):e26042.
113. Kothiwale S, Bhimani R, Kaderi M, Ajbani J. Comparative study of DFDBA and FDBA block grafts in combination with chorion membrane for the treatment of periodontal intra-bony defects at 12 months post surgery. *Cell Tissue Bank*. 2019.
114. Kaur J, Bathla SC. Regenerative potential of autologous platelet-rich fibrin with and without amnion membrane in the treatment of grade-II furcation defects: a clinicoradiographic study. *J Indian Soc Periodontol*. 2018;22(3):235-242.
115. Rehan M, Khatri M, Bansal M, Puri K, Kumar A. Comparative evaluation of coronally advanced flap using amniotic membrane and platelet-rich fibrin membrane in gingival recession: An 18-month clinical study. *Contemp Clin Dent*. 2018;9(2):188-194.
116. Yu SH, Oh TJ, Wang HL, Chan HL. Amnion-chorion membrane in open-wound approach for localized horizontal ridge augmentation: a case series report. *Clin Adv Periodontics*. 2022;12(2):101-105.
117. Miller RJ, Korn RJ, Miller RJ. The use of a dehydrated, deepithelialized amnion-chorion membrane in guided bone regeneration involving staged implant placement: case series with a 5-year follow-up. *Int J Periodontics Restorative Dent*. 2021;41(5):657-662.
118. Aprile P, Letourneur D, Simon-Yarza T. Membranes for guided bone regeneration: a road from bench to bedside. *Adv Healthc Mater*. 2020;9(19):e2000707.
119. Dai Z, Ronholm J, Tian Y, Sethi B, Cao X. Sterilization techniques for biodegradable scaffolds in tissue engineering applications. *J Tissue Eng*. 2016;7:2041731416648810.
120. Kim Y, Nowzari H, Rich SK. Risk of prion disease transmission through bovine-derived bone substitutes: a systematic review. *Clin Implant Dent Relat Res*. 2013;15(5):645-653.
121. Zenobio EG, Resende DF, de Albuquerque VN, Mendes PA, de Abreu FAM, Cosso MG. How the use of xenogeneic grafts can impact the relationship with some social groups and blood donor patients. *Clin Implant Dent Relat Res*. 2023.
122. Chang WJ, Pan YH, Tzeng JJ, et al. Development and testing of X-ray imaging-enhanced poly-L-lactide bone screws. *PLoS One*. 2015;10(10):e0140354.
123. Hutmacher DW. Scaffolds in tissue engineering bone and cartilage. *Biomaterials*. 2000;21(24):2529-2543.
124. Gentile P, Chiono V, Tonda-Turo C, Ferreira AM, Ciardelli G. Polymeric membranes for guided bone regeneration. *Biotechnol J*. 2011;6(10):1187-1197.
125. Karfeld-Sulzer LS, Ghayor C, Siegenthaler B, Gjoksi B, Pohjonen TH, Weber FE. Comparative study of NMP-preloaded and dip-loaded membranes for guided bone regeneration of rabbit cranial defects. *J Tissue Eng Regen Med*. 2017;11(2):425-433.
126. Qasim SB, Delaine-Smith RM, Fey T, Rawlinson A, Rehman IU. Freeze gelated porous membranes for periodontal tissue regeneration. *Acta Biomater*. 2015;23:317-328.
127. Simion M, Scarano A, Gionso L, Piattelli A. Guided bone regeneration using resorbable and nonresorbable membranes: a comparative histologic study in humans. *Int J Oral Maxillofac Implants*. 1996;11(6):735-742.
128. Zybutz MD, Laurell L, Rapoport DA, Persson GR. Treatment of intrabony defects with resorbable materials, non-resorbable materials and flap debridement. *J Clin Periodontol*. 2000;27(3):169-178.
129. Donos N, Kostopoulos L, Karring T. Alveolar ridge augmentation using a resorbable copolymer membrane and autogenous bone grafts. An experimental study in the rat. *Clin Oral Implants Res*. 2002;13(2):203-213.
130. Teparat T, Solt CW, Claman LJ, Beck FM. Clinical comparison of bioabsorbable barriers with non-resorbable barriers in guided tissue regeneration in the treatment of human intrabony defects. *J Periodontol*. 1998;69(6):632-641.
131. Karapataki S, Hugoson A, Falk H, Laurell L, Kugelberg CF. Healing following GTR treatment of intrabony defects distal to mandibular 2nd molars using resorbable and non-resorbable barriers. *J Clin Periodontol*. 2000;27(5):333-340.
132. Simion M, Maglione M, Iamoni F, Scarano A, Piattelli A, Salvato A. Bacterial penetration through Resolut resorbable membrane in vitro. An histological and scanning electron microscopic study. *Clin Oral Implants Res*. 1997;8(1):23-31.
133. Miner MR, Berzins DW, Bahcall JK. A comparison of thermal properties between gutta-percha and a synthetic polymer based root canal filling material (Resilon). *J Endod*. 2006;32(7):683-686.
134. Thuaksuban N, Nuntanaranont T, Suttapreyasri S, Pattanachot W, Sutin K, Cheung LK. Biomechanical properties of novel biodegradable poly epsilon-caprolactone-chitosan scaffolds. *J Investig Clin Dent*. 2013;4(1):26-33.
135. Jokinen V, Suvanto P, Franssila S. Oxygen and nitrogen plasma hydrophilization and hydrophobic recovery of polymers. *Biomicrofluidics*. 2012;6(1):16501-1650110.
136. Osathanon T, Chuenjitkuntaworn B, Nowwarote N, et al. The responses of human adipose-derived mesenchymal stem cells on polycaprolactone-based scaffolds: an in vitro study. *Tissue Eng Regen Med*. 2014;11(3):239-246.
137. Aldemir Dikici B, Dikici S, Reilly GC, MacNeil S, Claeyssens F. A novel bilayer polycaprolactone membrane for guided bone regeneration: combining electrospinning and emulsion templating. *Materials (Basel)*. 2019;12(16):1-24.
138. Al-Namnam NM, Kutty MG, Chai WL, et al. An injectable poly(-caprolactone trifumarate-gelatin microparticles) (PCLTF-GMPs) scaffold for irregular bone defects: physical and mechanical characteristics. *Korean J Couns Psychother*. 2017;72:332-340.
139. Ku JK, Kim YK, Yun PY. Influence of biodegradable polymer membrane on new bone formation and biodegradation of biphasic bone

substitutes: an animal mandibular defect model study. *Maxillofac Plast Reconstr Surg*. 2020;42(1):34.
140. Peng W, Ren S, Zhang Y, et al. MgO nanoparticles-incorporated PCL/gelatin-derived coaxial electrospinning nanocellulose membranes for periodontal tissue regeneration. *Front Bioeng Biotechnol*. 2021;9:668428.
141. Shim JH, Won JY, Park JH, et al. Effects of 3D-printed polycaprolactone/beta-tricalcium phosphate membranes on guided bone regeneration. *Int J Mol Sci*. 2017;18(5):1-16.
142. Jung RE, Mihatovic I, Cordaro L, et al. Comparison of a polyethylene glycol membrane and a collagen membrane for the treatment of bone dehiscence defects at bone level implants-a prospective, randomized, controlled, multicenter clinical trial. *Clin Oral Implants Res*. 2020;31(11):1105-1115.
143. Jung RE, Zwahlen R, Weber FE, Molenberg A, van Lenthe GH, Hammerle CH. Evaluation of an in situ formed synthetic hydrogel as a biodegradable membrane for guided bone regeneration. *Clin Oral Implants Res*. 2006;17(4):426-433.
144. Thoma DS, Halg GA, Dard MM, Seibl R, Hammerle CH, Jung RE. Evaluation of a new biodegradable membrane to prevent gingival ingrowth into mandibular bone defects in minipigs. *Clin Oral Implants Res*. 2009;20(1):7-16.
145. Reddy MSB, Ponnamma D, Choudhary R, Sadasivuni KK. A comparative review of natural and synthetic biopolymer composite scaffolds. *Polymers (Basel)*. 2021;13(7):1105.
146. Zambon R, Mardas N, Horvath A, Petrie A, Dard M, Donos N. The effect of loading in regenerated bone in dehiscence defects following a combined approach of bone grafting and GBR. *Clin Oral Implants Res*. 2012;23(5):591-601.
147. Vierra M, Mau LP, Huynh-Ba G, Schoolfield J, Cochran DL. A lateral ridge augmentation study to evaluate a synthetic membrane for guided bone regeneration: an experiment in the canine mandible. *Clin Oral Implants Res*. 2016;27(1):73-82.
148. Mihatovic I, Golubovic V, Becker J, Schwarz F. Immunohistochemical analysis of staged guided bone regeneration and osseointegration of titanium implants using a polyethylene glycol membrane. *Clin Oral Investig*. 2014;18(2):429-435.
149. Jung RE, Halg GA, Thoma DS, Hammerle CH. A randomized, controlled clinical trial to evaluate a new membrane for guided bone regeneration around dental implants. *Clin Oral Implants Res*. 2009;20(2):162-168.
150. Ylitalo R, Lehtinen S, Wuolijoki E, Ylitalo P, Lehtimaki T. Cholesterol-lowering properties and safety of chitosan. *Arzneimittelforschung*. 2002;52(1):1-7.
151. Shin SY, Park HN, Kim KH, et al. Biological evaluation of chitosan nanofiber membrane for guided bone regeneration. *J Periodontol*. 2005;76(10):1778-1784.
152. Xu C, Lei C, Meng L, Wang C, Song Y. Chitosan as a barrier membrane material in periodontal tissue regeneration. *J Biomed Mater Res B Appl Biomater*. 2012;100(5):1435-1443.
153. Li X, Wang X, Zhao T, et al. Guided bone regeneration using chitosan-collagen membranes in dog dehiscence-type defect model. *J Oral Maxillofac Surg*. 2014;72(2):304.
154. Novaes AB Jr, Gutierrez FG, Francischetto IF, Novaes AB. Bacterial colonization of the external and internal sulci and of cellulose membranes at time of retrieval. *J Periodontol*. 1995;66(10):864-869.
155. dos Anjos B, Novaes AB Jr, Meffert R, Barboza EP. Clinical comparison of cellulose and expanded polytetrafluoroethylene membranes in the treatment of class II furcations in mandibular molars with 6-month re-entry. *J Periodontol*. 1998;69(4):454-459.
156. Salata LA, Hatton PV, Devlin AJ, Craig GT, Brook IM. In vitro and in vivo evaluation of e-PTFE and alkali-cellulose membranes for guided bone regeneration. *Clin Oral Implants Res*. 2001;12(1):62-68.
157. Luz E, Das Chagas BS, De Almeida NT, et al. Resorbable bacterial cellulose membranes with strontium release for guided bone regeneration. *Korean J Couns Psychother*. 2020;116:111175.
158. de Oliveira Barud HG, da Silva RR, Borges MAC, Castro GR, Ribeiro SJL, da Silva BH. Bacterial nanocellulose in dentistry: perspectives and challenges. *Molecules*. 2020;26(1):49.
159. Farnezi Bassi AP, Bizelli VF, Brasil LFdM, et al. Is the bacterial cellulose membrane feasible for Osteopromotive property? *Membranes (Basel)*. 2020;10(9):230.
160. Yang Z, Wu C, Shi H, et al. Advances in barrier membranes for guided bone regeneration techniques. *Front Bioeng Biotechnol*. 2022;10:921576.
161. He Y, Tian Y, Zhang W, et al. Fabrication of oxidized sodium alginate-collagen heterogeneous bilayer barrier membrane with osteogenesis-promoting ability. *Int J Biol Macromol*. 2022;202:55-67.
162. Ishikawa K, Ueyama Y, Mano T, Koyama T, Suzuki K, Matsumura T. Self-setting barrier membrane for guided tissue regeneration method: initial evaluation of alginate membrane made with sodium alginate and calcium chloride aqueous solutions. *J Biomed Mater Res*. 1999;47(2):111-115.
163. Ueyama Y, Ishikawa K, Mano T, et al. Usefulness as guided bone regeneration membrane of the alginate membrane. *Biomaterials*. 2002;23(9):2027-2033.
164. Ueyama Y, Koyama T, Ishikawa K, et al. Comparison of ready-made and self-setting alginate membranes used as a barrier membrane for guided bone regeneration. *J Mater Sci Mater Med*. 2006;17(3):281-288.
165. Bojar W, Kucharska M, Bubak G, et al. Formation and preclinical evaluation of a new alloplastic injectable bone substitute material. *Acta Bioeng Biomech*. 2012;14(1):39-44.
166. He Z, Zhou X, Wang Y, et al. Asymmetric barrier membranes based on polysaccharide micro-nanocomposite hydrogel: synthesis, characterization, and their antibacterial and osteogenic activities. *Carbohydr Polym*. 2021;273:118525.
167. Zhao R, Xu Z, Li B, et al. A comparative study on agarose acetate and PDLLA scaffold for rabbit femur defect regeneration. *Biomed Mater*. 2019;14(6):065007.
168. Hammerle CH, Jung RE, Feloutzis A. A systematic review of the survival of implants in bone sites augmented with barrier membranes (guided bone regeneration) in partially edentulous patients. *J Clin Periodontol*. 2002;29(Suppl 3):226-231; discussion 32–3.
169. Benic GI, Bernasconi M, Jung RE, Hammerle CH. Clinical and radiographic intra-subject comparison of implants placed with or without guided bone regeneration: 15-year results. *J Clin Periodontol*. 2017;44(3):315-325.
170. Benic GI, Hammerle CH. Horizontal bone augmentation by means of guided bone regeneration. *Periodontol 2000*. 2014;66(1):13-40.
171. Urban IA, Montero E, Monje A, Sanz-Sanchez I. Effectiveness of vertical ridge augmentation interventions: a systematic review and meta-analysis. *J Clin Periodontol*. 2019;46(Suppl 21):319-339.
172. Mordenfeld A, Johansson CB, Albrektsson T, Hallman M. A randomized and controlled clinical trial of two different compositions of deproteinized bovine bone and autogenous bone used for lateral ridge augmentation. *Clin Oral Implants Res*. 2014;25(3):310-320.
173. Hammerle CH, Jung RE, Yaman D, Lang NP. Ridge augmentation by applying bioresorbable membranes and deproteinized bovine bone mineral: a report of twelve consecutive cases. *Clin Oral Implants Res*. 2008;19(1):19-25.
174. Urban IA, Nagursky H, Lozada JL, Nagy K. Horizontal ridge augmentation with a collagen membrane and a combination of particulated autogenous bone and anorganic bovine bone-derived mineral: a prospective case series in 25 patients. *Int J Periodontics Restorative Dent*. 2013;33(3):299-307.
175. Thoma DS, Bienz SP, Figuero E, Jung RE, Sanz-Martin I. Efficacy of lateral bone augmentation performed simultaneously with dental implant placement: a systematic review and meta-analysis. *J Clin Periodontol*. 2019;46(Suppl 21):257-276.

176. Beitlitum I, Artzi Z, Nemcovsky CE. Clinical evaluation of particulate allogeneic with and without autogenous bone grafts and resorbable collagen membranes for bone augmentation of atrophic alveolar ridges. *Clin Oral Implants Res*. 2010;21(11):1242-1250.
177. Llambes F, Silvestre FJ, Caffesse R. Vertical guided bone regeneration with bioabsorbable barriers. *J Periodontol*. 2007;78(10):2036-2042.
178. Cardaropoli D, Gaveglio L, Cardaropoli G. Vertical ridge augmentation with a collagen membrane, bovine bone mineral and fibrin sealer: clinical and histologic findings. *Int J Periodontics Restorative Dent*. 2013;33(5):583-589.
179. Sanz-Sanchez I, Carrillo de Albornoz A, Figuero E, et al. Effects of lateral bone augmentation procedures on peri-implant health or disease: a systematic review and meta-analysis. *Clin Oral Implants Res*. 2018;29(Suppl 15):18-31.
180. Wessing B, Lettner S, Zechner W. Guided bone regeneration with collagen membranes and particulate graft materials: a systematic review and meta-analysis. *Int J Oral Maxillofac Implants*. 2018;33(1):87-100.
181. Jimenez Garcia J, Berghezan S, Carames JMM, Dard MM, Marques DNS. Effect of cross-linked vs non-cross-linked collagen membranes on bone: a systematic review. *J Periodontal Res*. 2017;52(6):955-964.
182. Lim G, Lin GH, Monje A, Chan HL, Wang HL. Wound healing complications following guided bone regeneration for ridge augmentation: a systematic review and meta-analysis. *Int J Oral Maxillofac Implants*. 2018;33(1):41-50.
183. Donos N, Mardas N, Chadha V. Clinical outcomes of implants following lateral bone augmentation: systematic assessment of available options (barrier membranes, bone grafts, split osteotomy). *J Clin Periodontol*. 2008;35(8 Suppl):173-202.
184. Garcia J, Dodge A, Luepke P, Wang HL, Kapila Y, Lin GH. Effect of membrane exposure on guided bone regeneration: a systematic review and meta-analysis. *Clin Oral Implants Res*. 2018;29(3):328-338.
185. Tay JRH, Lu XJ, Lai WMC, Fu JH. Clinical and histological sequelae of surgical complications in horizontal guided bone regeneration: a systematic review and proposal for management. *Int J Implant Dent*. 2020;6(1):76.
186. Tay JRH, Ng E, Lu XJ, Lai WMC. Healing complications and their detrimental effects on bone gain in vertical-guided bone regeneration: a systematic review and meta-analysis. *Clin Implant Dent Relat Res*. 2022;24(1):43-71.
187. Linde A, Thoren C, Dahlin C, Sandberg E. Creation of new bone by an osteopromotive membrane technique: an experimental study in rats. *J Oral Maxillofac Surg*. 1993;51(8):892-897.
188. Lee SW, Kim SG. Membranes for the guided bone regeneration. *Maxillofac Plast Reconstr Surg*. 2014;36(6):239-246.
189. Becker W, Becker BE. Guided tissue regeneration for implants placed into extraction sockets and for implant dehiscences: surgical techniques and case report. *Int J Periodontics Restorative Dent*. 1990;10(5):376-391.
190. Becker W, Becker BE, Handlesman M, et al. Bone formation at dehisced dental implant sites treated with implant augmentation material: a pilot study in dogs. *Int J Periodontics Restorative Dent*. 1990;10(2):92-101.
191. Gher ME, Quintero G, Assad D, Monaco E, Richardson AC. Bone grafting and guided bone regeneration for immediate dental implants in humans. *J Periodontol*. 1994;65(9):881-891.
192. Gottlow J, Nyman S, Karring T, Lindhe J. New attachment formation as the result of controlled tissue regeneration. *J Clin Periodontol*. 1984;11(8):494-503.
193. Rodriguez I, Selders G, Fetz A, et al. Barrier membranes for dental applications: a review and sweet advancement in membrane developments. *Mouth Teeth*. 2018;2(1):1-9.
194. Hockers T, Abensur D, Valentini P, Legrand R, Hammerle CH. The combined use of bioresorbable membranes and xenografts or autografts in the treatment of bone defects around implants. A study in beagle dogs. *Clin Oral Implants Res*. 1999;10(6):487-498.
195. Sevor JJ, Meffert RM, Cassingham RJ. Regeneration of dehisced alveolar bone adjacent to endosseous dental implants utilizing a resorbable collagen membrane: clinical and histologic results. *Int J Periodontics Restorative Dent*. 1993;13(1):71-83.
196. Naenni N, Lim H-C, Papageorgiou SN, Hämmerle CHF. Efficacy of lateral bone augmentation prior to implant placement: A systematic review and meta-analysis. *Journal of Clinical Periodontology*. 2019;46:287-306.
197. Mir-Mari J, Wui H, Jung RE, Hammerle CH, Benic GI. Influence of blinded wound closure on the volume stability of different GBR materials: an in vitro cone-beam computed tomographic examination. *Clin Oral Implants Res*. 2016;27(2):258-265.
198. Fu JH, Wang HL. Horizontal bone augmentation: the decision tree. *Int J Periodontics Restorative Dent*. 2011;31(4):429-436.
199. Cha JK, Joo MJ, Yoon S, Lee JS, Choi SH, Jung UW. Sequential healing of onlay bone grafts using combining biomaterials with cross-linked collagen in dogs. *Clin Oral Implants Res*. 2017;28(1):76-85.
200. Rothamel D, Benner M, Fienitz T, et al. Biodegradation pattern and tissue integration of native and cross-linked porcine collagen soft tissue augmentation matrices – an experimental study in the rat. *Head Face Med*. 2014;10:10.
201. Omar O, Elgali I, Dahlin C, Thomsen P. Barrier membranes: more than the barrier effect? *J Clin Periodontol*. 2019;46(Suppl 21):103-123.
202. Solomon S-M, Sufaru I-G, Teslaru S, Ghiciuc CM, Stafie CS. Finding the perfect membrane: current knowledge on barrier membranes in regenerative procedures: a descriptive review. *Appl Sci*. 2022;12(3):1042.
203. Berton F, Porrelli D, Di Lenarda R, Turco G. A critical review on the production of electrospun Nanofibres for guided bone regeneration in oral surgery. *Nanomaterials (Basel)*. 2020;10(1):16.
204. Abdelaziz D, Hefnawy A, Al-Wakeel E, El-Fallal A, El-Sherbiny IM. New biodegradable nanoparticles-in-nanofibers based membranes for guided periodontal tissue and bone regeneration with enhanced antibacterial activity. *J Adv Res*. 2021;28:51-62.
205. Egusa H, Sonoyama W, Nishimura M, Atsuta I, Akiyama K. Stem cells in dentistry–part II: clinical applications. *J Prosthodont Res*. 2012;56(4):229-248.
206. Egusa H, Sonoyama W, Nishimura M, Atsuta I, Akiyama K. Stem cells in dentistry–part I: stem cell sources. *J Prosthodont Res*. 2012;56(3):151-165.
207. Berahim Z, Moharamzadeh K, Rawlinson A, Jowett AK. Biologic interaction of three-dimensional periodontal fibroblast spheroids with collagen-based and synthetic membranes. *J Periodontol*. 2011;82(5):790-797.
208. Zakaria O, Madi M, Kasugai S. Introduction of a novel guided bone regeneration memory shape based device. *J Biomed Mater Res B Appl Biomater*. 2020;108(2):460-467.

How to cite this article: Mizraji G, Davidzohn A, Gursoy M, Gursoy UK, Shapira L, Wilensky A. Membrane barriers for guided bone regeneration: An overview of available biomaterials. *Periodontol 2000*. 2023;93:56-76. doi:10.1111/prd.12502