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Review

Current barrier membranes: Titanium mesh and other membranes for guided bone regeneration in dental applications

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Research on guided bone regeneration (GBR) is still ongoing, with evidence mainly from preclinical studies. Various current barrier membranes should fulfill the main design criteria for GBR, such as biocompatibility, occlusivity, spaciousness, clinical manageability and the appropriate integration with the surrounding tissue. These GBR characteristics are required to provide the maximum membrane function and mechanical support to the tissue during bone formation. In this review, various commercially available, resorbable and non-resorbable membranes with different characteristics are discussed and summarized for their usefulness in preclinical studies. Membranes offer promising solutions in animal models; however, an ideal membrane has not been established yet for clinical applications. Every membrane type presents both advantages and disadvantages. Titanium mesh membranes offer superb mechanical properties for GBR treatment and its current efficacy in trials will be a focus in this review. A thorough understanding of the benefits and limitations inherent to various materials in specific clinical applications will be of great value and aid in the selection of an optimal membrane for GBR.

Keywords: Titanium mesh; Guided bone regeneration; Resorbable; Non resorbable; Membrane

Contents

1. Introduction . . . 4
2. Principles of guided bone regeneration . . . 4
3. Design criteria for GBR membrane . . . 4
   3.1. Biocompatibility . . . 4
   3.2. Create a space for ingrowth . . . 4
   3.3. Occlusivity . . . 4
   3.4. Tissue integration . . . 5
   3.5. Clinical manageability . . . 5
4. Barrier membranes for GBR . . . 8
   4.1. Resorbable membranes . . . 8
   4.2. Non-resorbable membranes . . . 9
      4.2.1. e-PTFE membrane . . . 9
      4.2.2. d-PTFE membrane . . . 9
      4.2.3. Titanium mesh . . . 9

Abbreviations: GBR, guided bone regeneration; GTR, guided tissue regeneration; Ti, titanium; e-PTFE, expanded polytetrafluoroethylene; d-PTFE, dense polytetrafluoroethylene; Max, maxilla; Mand, mandibular; CTM, configured titanium mesh; M-TAM, micro titanium augmentation material; GT, Gore-Tex®; GTRM, Gore-Tex® regenerative membrane; GTAM, Gore-Tex® augmentation material; RIF, rigid internal fixation; MI, microporous membrane; MIP, microporous laser-perforated membrane; BG, bone grafts; MAR, mineral apposition rate; PRP, protein rich plasma; DBM, demineralized bone matrix; w, weeks; m, months; y, years; Ant, anterior; Post, posterior; ND, no data.

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5. Focus on titanium mesh and its role in GBR . . . 9
6. Conclusion . . . 11
References . . . 11

1. Introduction

Adequate bone volume is an important prerequisite for a predictable, long-term prognosis in implant dentistry. However, some patients present with insufficient horizontal or vertical bone, which frequently precludes the successful outcome of an ideal implant placement (Fig. 1). Various methods have been developed to increase bone volume and augment new tissue growth: (1) Distraction osteogenesis, which describes the surgical induction of a fracture and the subsequent gradual separation of the two bone ends to create spontaneous bone regeneration between the two fragments [1]; (2) Osteoinduction, which employs appropriate growth factors and/or stem/osteoprogenitor cells to encourage new bone formation [2–4]; (3) Osteoconduction, in which a grafting material serves as a scaffold for new bone formation [5]; and (4) Guided bone regeneration (GBR), which provides spaces using barrier membranes that are to be subsequently filled with new bone [6,7].

Most biochemical osteoinductive approaches still have an extremely limited clinical application, such as the use of bone morphogenetic proteins (BMPs) [8]. In addition, in certain locations, such as in the jaw, distraction osteogenesis is still in its development phase and often leaves undesirable tissue scarring [9]. This leaves GBR and the use of bone grafting materials or combinations of these methods as the only ones commonly applied in clinical practice. GBR is reported as providing the best and the most predictable results when employed to fill peri-implant bone defects with new bone [6,7,10]. Furthermore, GBR improves the predictability of bone augmentation and provides long-term stability to the newly augmented site [11,12].

2. Principles of guided bone regeneration

The underlying concept of GBR was first introduced more than 50 years ago, when cellulose acetate filters were experimentally used for the regeneration of nerves and tendons [13]. Subsequently, cellulose acetate (Millipore™ membrane filter) enhanced osseous healing of rib, radial bone and femoral bone defects [14]. Later, a series of animal studies provided evidence to show that GBR can predictably facilitate bone regeneration in critical-sized osseous defects [15–20], as well as the healing of bone defects around dental implants by augmenting the height and the width of atrophic alveolar ridges prior to implant insertion [21–26].

The basic principle of GBR (Fig. 2) involves the placement of mechanical barriers to protect blood clots and to isolate the bone defect from the surrounding connective tissue, thus providing bone-forming cells with access to a secluded space intended for bone regeneration [27]. According to this principle, the use of a barrier membrane is advantageous to facilitate augmentation of alveolar ridge defects, induce bone regeneration, improve bone-grafting results, and treat failing implants [28].

3. Design criteria for GBR membrane

In addition to the surgical technique used, there are many factors that contribute to a successful GBR outcome, including barrier occlusion and stability, the size of the barrier perforations, peripheral sealing between the barrier and the host bone, an adequate blood supply, and access to bone-forming cells [29–35]. Moreover, in the last few years, several membrane designs have been studied that not only enhance new bone formation, but also stabilize the bone graft below the membrane and minimize the risk of collapse and/or soft tissue ingrowth (Table 1) [19,25,31,32,36–48].

For use as a medical device, barrier membranes must fulfill five main design criteria, as described by Scantlebury [49]: biocompatibility, space-making, cell-occlusiveness, tissue integration and clinical manageability.

3.1. Biocompatibility

The membrane must provide an acceptable level of biocompatibility. The interaction between the material and tissue should not adversely affect the surrounding tissue, the intended healing result, or the overall safety of the patient.

3.2. Create a space for ingrowth

The membrane should have an adequate stiffness to create and maintain a suitable space for the intended osseous regeneration. This quality is predominantly related to the membrane thickness. In addition, a membrane should provide an optimal space that can be maintained for tissue ingrowth but also still provide adequate support to the tissue, even in large defects. The material should also be appropriately malleable to provide the specific geometry required for functional reconstruction, but be sufficiently stiff to withstand the pressures exerted by external forces, such as mastication in jaw reconstructions [50]. If the membrane were to collapse into the defect space, the volume for regeneration is reduced and an optimal clinical outcome would not be achieved.

3.3. Occlusivity

An optimal barrier should be sufficiently occlusive to avoid fibrous tissue formation, which may prevent or delay bone formation. Occlusivity is therefore closely linked to membrane porosity; this factor has a major influence on the potential for cell invasion [46]. Indeed, barrier occlusivity of a membrane

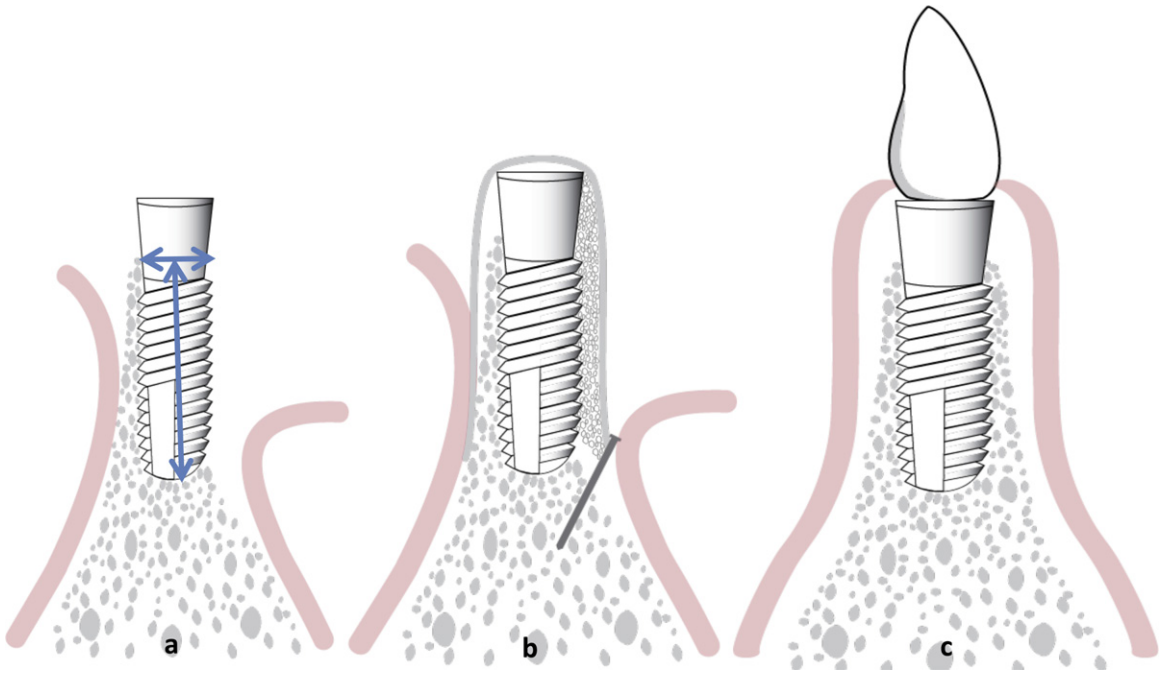

Fig. 1. (a) An adequate bone volume (height and width) is a prerequisite for successful implant treatment. (b) Barrier membrane and bone graft as bone substitute materials are placed to accelerate bone formation. (c) After new bone is formed final prosthesis is fabricated.

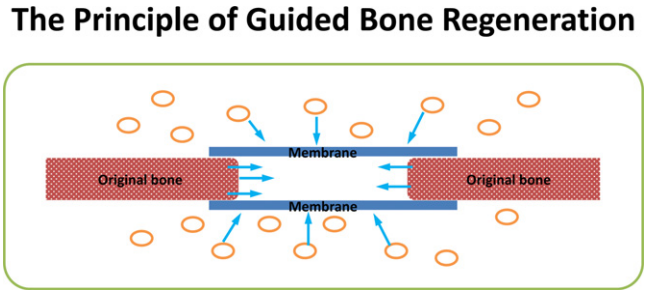

Fig. 2. The principle of guided bone regeneration using mechanical barriers (membranes) to seal off the bone defect from the surrounding soft connective tissue into a secluded space by which cells only from the surrounding bone can migrate.

may be at least as important as its space-maintaining properties when regenerating bone defects [51].

The architecture of the porous structures in general, and not the type of material used, has been suggested to confer the biological activity of a material [52]. Membrane pores facilitate the diffusion of fluids, oxygen, nutrients and bioactive substances for cell growth, which is vital for bone and soft tissue regeneration. However, these pores must also be impermeable to epithelial cells or gingival fibroblasts (in the case of dental implants); a larger pore size will allow these faster-growing cells to overpopulate the defect space and inhibit the infiltration and activity of bone-forming cells [50]. A larger pore size also acts an easy pathway for bacterial contamination, and surgical removal of these contaminated membranes becomes complicated because of the excess soft tissue ingrowth [53,54]. If pores are too small, on the other hand, cell migration of all cells is limited, which leads to enhanced collagen deposition, the formation of avascular tissue, and an absence of capillary growth and infiltration [55]. Pore size will also affect the capacity of the material to support the tissue. A large pore size will inevitably decrease the resulting surface area of the material, which could limit the important initial steps of cell adhesion onto the membrane [56] and subsequent decrease of blood vessel ingrowth [53].

3.4. Tissue integration

Tissue integration is the key aspect of all tissue regeneration techniques as it is essential that the host tissue integrates with the membrane. It is well established that the structural integrity of the barrier membrane and the sufficient adaptability of its borders to the adjacent original bone constitute prerequisites for predictable new bone formation [29]. Tissue integration stabilizes the healing wound process, and helps to create a seal between the bone and the material to prevent fibrous connective tissue integration into the defect site. Tissue integration between the membrane and the contours of the adjacent bone is reliant on the membrane space-making capacity of the material; a material that is too stiff would not be able to mold to the shape of the defect site.

3.5. Clinical manageability

A membrane should be practical for clinical use, particularly for dental work. A membrane that is difficult to use, such as one that is too malleable, can be frustrating and will often lead to complications if it cannot be reproducibly used in a clinical setting, particularly the usually small setting inherent with dental implants [50]. On

Table 1
Summary of studies using GBR membranes with different membrane structures and designs.

Year [Ref] Author	Animal model	Type of membrane	Study design	Assessment	Outcome
2012 [36] Rothamel	Dog maxilla	Remotis (multilayered with interconnected system of pores); BioGide (bilayer structure, smooth upper surface and coarser bottom surface)	Histological evaluation at 4, 8, 12 and 24 weeks	Biodegradation and bone formation	Remotis: an interconnective pore system, Bio-Gide: more fibrous structure. Both membranes integrated into the surrounding tissue without any inflammatory infection, allowed early vascularization and supported underlying bone formation. Biodegradation: Remotis (8–12 weeks); Bio-Gide: 4–8 weeks.
2010 [37] de Santana	Mouse calvaria	Synthetic polylactide	SEM; histological and morphometric evaluation at 14 and 28 days	Topographic (porosity of membrane); bone formation	Interconnecting pores and channels (Φ: 6–60 μm), with smooth internal walls. Different sides of the barrier promote differential soft tissue responses; however, similar amounts of enhanced bone formation.
2009 [38] Gutta	Dog mandible	Ti meshes (macro: 1.2 mm; micro: 6 mm porous); polylactic acid (1 mm porous)	Histological and morphometric evaluation at 1, 2, and 4 months	Bone growth and soft tissue ingrowth area; MAR	Macroporous membrane: greater bone regeneration, prevented significant soft tissue ingrowth, the lowest MAR compared with microporous and Polylactic acid.
2008 [39] Sverzut	Dog mandible	RIF, BG, MI, MI + BG, MIP, MIP + BG	Histological and morphometric evaluation at 6 months	Bone area	MI + BG: larger amounts of bone compared with other groups. MIP alone and BG alone: no difference. MI: the least bone area and reduced the amount of grafted bone.
2004 [40] Polimeni	Dog mandible	e-PTFE (15–25 μm pore size and reinforced with polyprophylene mesh) and the 300 μm porous devices	Histological and morphometric evaluation at 8 weeks	Bone regeneration (height); wound area; bone width	Occlusive and porous GTR; both space-provision and device occlusivity; occlusive and space-provision compared to sites with porous GTR device or more limited space-provision: significant bone regeneration.
2004 [41] Polimeni	Dog mandible	e-PTFE membranes (15–25 μm pore size); calcium carbonate CI (resorbable, porous)	Histological and morphometric evaluation at 4 weeks	Bone regeneration (height); wound area	Space-provision: significant effect on bone regeneration following GTR. Coral biomaterial: enhances space-provision and supports bone regeneration.
2003 [42] Van Steenberghe	Rabbit skull	Titanium barriers dome shaped (φ: 12 mm; height: 6 mm; thickness: 0.2 mm)	Microradiograph; histological evaluation at 3, 6 and 12 months	Area of tissue; area of trabeculae; mean trabeculae in dome	The bone grew systematically along the titanium surface. After removal of the barrier, on average 75.3% and 59.4% of the newly created tissue volume was maintained after 3 and 9 months, respectively.
2003 [43] Mardas	Rat mand. ramus	Hemisperical teflon packed with DBM. Test capsules: 9 perforations; φ: 0.3 mm. Contralateral side: non perforated (cell occlusive)	Histological evaluation; planimetric measurement at 30, 60 and 120 days	The space in the capsule; newly formed bone; DBM particles; loose connective tissue	In cell-permeable and cell-occlusive capsules grafted with DBM: similar amounts of bone formed. Invasion of undifferentiated mesenchymal cells from the surrounding soft tissues into the barrier-protected area is unnecessary for bone formation with GTR.
2003 [44] Yamada	Rabbit calvaria	Hemispherical cap of titanium. One cap had small holes (13 holes, φ holes: 1.5 mm) and the other had no holes	Histological evaluation at 1 and 3 months	Areas of newly generated tissue (%) and mineralized bone in the newly generated tissue under the Ti cap	Statistically significant difference: the amount of tissue generated between 1 and 3 months; the amount of mineralized bone generated at 3 months under the cap without holes. Total occlusiveness, sufficient stiffness and passage of time allow predictable mineralized bone augmentation.
2000 [19] Marouf	Rabbit calvaria	High density PTFE (TefGen-FD); semipermeable e-PTFE (Gore-Tex)	Histological and morphologic evaluation at 4, 8 and 16 weeks	Pattern of bone healing by morphological classification	TefGen: easier to detach from the underlying bone than GT. GBR: GT is more effective than TefGen-FD. GT membrane lamellae were infiltrated by fibro-osseous tissue.

Table 1 (*Continued*)

Year [Ref] Author	Animal model	Type of membrane	Study design	Assessment	Outcome
1999 [45] Simion	Dog mandible	Ti reinforced e-PTFE: GTRM 1; GTRM 2; GTRM 3	Histological and morphometric evaluation	Regenerated tissue, membrane contact with regenerated bone or with bone	An extremely open porous microstructure + a totally occlusive barrier: significant regenerative outcomes. However, these design may be applied only to resorbable devices. Do not require removal.
1998 [32] Lundgren	Rat calvaria	Prefabricated silicone frames + 7 barriers with different occlusiveness (a stiff plastic plate and 6 polyester meshes, perforation: 10, 25, 50, 75, 100 and 300 μm)	Histological and morphometric evaluation at 4, 8 and 12 weeks	Total area of tissue and total area of mineralized bone	Totally occlusive barriers: the slowest rate of bone tissue augmentation. Barriers with perforations >10 μm: faster rate of bone augmentation. The amount of augmented mineralized bone related to perforation sizes >10 μm: no differences.
1998 [31] Lundgren	Rabbit; edent. area of the maxilla	Gore-Tex augmentation material (GTAM); non perforated titanium foil; perforated titanium foil	Histological and morphometric evaluation at 4 weeks	Total of original bone area; remaining bone area; mineralized bone; cortical and trabeculae bone; bone marrow	The highest degree of regeneration: in defects underneath the titanium foils, particularly if perforated (covered/not by GTAM-barriers). The space maintaining properties of a barrier may be at least as important as barrier occlusiveness when regenerating bone defects.
1997 [46] Salzmann	Rat subcut. tissue and epididymal fat pads	e-PTFE of 30, 60, 100 μm structural differences	Histological and immunohistochemical examination at 5 weeks	Fibrous capsule formation, endothelialization and activated monocytes and macrophages	30 μm subcutaneous implants: dense fibrous capsule formation. 60 μm: the greatest endothelialization. 100 μm: the largest values for the Monocyte/Macrophage Index. Material structure and implant site influence the healing of ePTFE. Activated monocytes/macrophages may inhibit endothelialization of e-PTFE.
1996 [47] Zellin	Rat calvaria	Dome-shaped e-PTFE membranes with different membrane porosity: <8, 20–25 and 100 μm	Histological and morphometric evaluation at 6, 12, 18 weeks and 6 months	Percentage bone fill of domes	The amount of new bone: at 6 weeks essentially obtained with the two most porous membranes compared to the least porous; at 12 weeks: no difference. The smallest internodal distance: lack of membrane stabilization and more soft tissue ingrowth from the side.
1995 [25] Zellin	Rat mand. ramus	Resorbable: Guidor, Periogen, Resolut LT, Resolut ST, Vicryl C, Vicryl PM; non resorbable: GTAM, Millipore (pore size:0.22 μm), NYT, Ti-foil (50 μm gauge)	Histological evaluation	Numerical score of blood clot, bone union, compact bone, bone marrow, inflammatory response	GTAM, Millipore and Resolut 'long term': good osteopromotive effect compared to others membranes. Inflammatory reaction was displayed in the surrounding soft tissue. Different membranes differ strongly in osteopromotive efficacy. Membranes developed primarily for periodontal regeneration purposes may not be adequate to promote bone healing.
1994 [48] Schmid	Rabbit calvaria	Titanium cast gold device (2 tubes). 1 tube: closed by the cast metal, 1 tube: covered by an e-PTFE with 4 different structures (GT Periodontal; GTAM center part; GTAM outer part; GT RC-10	Histological evaluation at 8 months	Bone formation area in the cylinders irrespective of whether the chamber was sealed off by cast titanium or the e-PTFE membrane	After 8 months of healing, new bone had formed in all cylinders in all animals irrespective of whether the chamber for bone formation was sealed off by cast titanium or the ePTFE membrane. It is concluded that permeability of the membrane is not necessary in the guided generation of new bone.

Table 2
Typical commercially available membranes.

Commercial name	Properties (pores; thick)	Comments
Non resorbable expanded polytetrafluoroethylene (e-PTFE)		
Gore-Tex®	0.5–30 μm. Discontinued	Longest studies [59–63]
Non resorbable high dense polytetrafluoroethylene (d-PTFE)		
Cytoplast™ (GBR; TXT)	Less than 0.3 μm	Primary closure unnecessary [64,65]
Cytoplast® Non Resorb	Less than 1.36 μm	Favorable bone regeneration [61]
TefGen FD™	0.2–0.3 μm	Easy to detach [19,54]
Nonresorbable ACE	<0.2 μm; 0.2 mm	Limited cell proliferation [66]
Non resorbable titanium mesh		
Frios® BoneShields	0.03 mm; 0.1 mm	Sufficient bone and graft maturity [67,68]
Tocksystem Mesh™	0.1–6.5 mm; 0.1 mm	No sign of inflammation/resorption [68]
M-TAM™	1700 μm; 0.1–0.3 mm	Excellent tissue compatibility [69]
Ti-Micromesh ACE	1700 μm; 0.1 mm	Long term survival and success rate [70]
Resorbable collagen (origin type of collagen; resorption time)		
BioGide®	Porcine (I and III); 24 weeks	Useful alternative to e-PTFE [71]
BioMend®	Bovine (I); 8 weeks	Bone growth, modulate cell behaviors [72,73]
Biosorb® Membrane	Bovine (I); 26–38 weeks	Provided stable fixation [74]
Neomem™	Bovine (I); 26–38 weeks	Two layers, used in severe case [75]
OsseoGuard®	Bovine (I); 24–32 weeks	Improves aesthetic outcome [76]
Ossix	Porcine (I); 16–24 weeks	Increased the woven bone [77]
Resorbable synthetic (origin; resorption time)		
Atrisorb®	Poly-DL-lactide; 36–48 weeks	Custom fabricated membrane [78]
Biofix®	Polyglycolic acid; 24–48 weeks	Act as barrier to gingival cells and bacteria [79]
Epiguide®	Poly-DL-lactic acid; 24–48 weeks	Support developed blood clot [73]
Resolut XT	Poly-DL-lactide/Co-glycolide; 8 weeks	Porous structure influence the cells attached [73]
OsseoQuest®	Hydrolyzable Polyester; 16–24 weeks	Good tissue integration [80]
Vicryl	Polyglactin 910 mesh; 8 weeks	Most reliable results compared with non-resorbable [72]

the other hand, a membrane that is too stiff cannot be contoured easily, and the sharp edges could perforate the gingival tissue and subsequent exposure of the membrane [57]. One study showed that non-resorbable barriers provided a suitable stiffness over resorbable membranes for optimal bone width and height in GBR [58].

4. Barrier membranes for GBR

Numerous barrier membranes have been developed to serve a variety of functions in clinical applications, which can be grouped as resorbable or non-resorbable membranes. The biomaterial and physical properties of membranes ultimately influence their function, and selection of a specific material is based on the biological properties of the membrane as well as the treatment requirements [59], with each material bearing inherent advantages and disadvantages. Several of the commercially available membranes are summarized in Table 2 [19,54,59–80].

4.1. Resorbable membranes

Resorbable materials that are used as membranes all belong to the groups of natural or synthetic polymers. Of these, collagen and aliphatic polyesters, such as polyglycolide or polylactide, are best known for their medical applicability [81]. Collagen is derived from a number of sources and is treated in various ways for membrane fabrication. Polyglycolide or polylactide can be made in large quantities, and the wide range of available materials allows for the creation of a wide spectrum of membranes with different physical, chemical, and mechanical properties [82].

As the name suggests, resorbable materials offer the advantage of being resorbed by the body, thus eliminating the need for second-stage removal surgery. For this reason, resorbable membranes appeal to both clinician and patients, in reducing the risk of morbidity, the risk of tissue damage, and from a cost-benefit point of view. In principle, stiff resorbable membranes promote a similar degree of bone regeneration and bone formation as non-resorbable membranes [83,84]. Moreover, in situations where the bone defect margins are appropriately maintained by the membrane, favorable results have been reported [85,86].

The disadvantages of resorbable materials, however, are their unpredictable degree of resorption, which can significantly alter the amount of bone formation [72]. If they are resorbed too fast, the consequential lack of rigidity means that additional support is required [38,87]. They also have shortcomings when trying to protect large particulate grafts [60]. When the membranes are exposed and/or associated with inflammatory reactions in the adjacent tissue, the enzymatic activity of macrophages and neutrophils causes the membrane to rapidly degree, thereby affecting the structural integrity of the membrane and causing decreased barrier function and less bone regeneration or bone fill; this is particularly problematic when grafting in conjunction with implant placement, as the implant becomes unstable [88]. When

the bone defect is not supported by a physical barrier, bone regeneration fails. Even if the membranes are initially able to keep the space, they generally lose strength, collapse into the space and lead to a failed reconstruction [25]; for example, when treating periodontal defects, resorbable membrane may have a tendency to collapse [89].

4.2. Non-resorbable membranes

Non-resorbable membranes include polytetrafluoroethylene (PTFE) and titanium mesh. One drawback in the use of this type of membrane is the necessity for its removal with a second-stage surgical procedure. However, this disadvantage may be overshadowed by the advantages offered. These membranes provide an effective barrier function in terms of biocompatibility [86], they can maintain the space beneath the membrane for a sufficient period, they are more predictable in their performance, they have a reduced risk of long-term complications, and they are simple to manage clinically [90]. Non-resorbable membranes also offer a unique characteristic. Their structure can be varied with changes in porosity if a more adaptable and tissue-compatible alternative, and multiple designs are commercially available and can be further developed on demand [59]. We will discuss three predominant non-resorbable membranes: the expanded and dense forms of PTFE (e- and d-PTFE) and titanium mesh.

4.2.1. e-PTFE membrane

According to its structure, PTFE can be divided into two types: expanded-PTFE (e-PTFE) and high density-PTFE (d-PTFE). The Gore-Tex® membrane (W.L. Gore & Associates, Flagstaff, AZ, USA), which is composed of e-PTFE, has been widely used in clinical treatment and had become a first choice material for tissue/bone regeneration. It is also used extensively for digestive, cerebral and cardio-vascular surgeries, and basic research has indicated its effectiveness in tissue-guided repair [61]. Indeed, in a recent controlled study [63], it was shown that a combination of an e-PTFE membrane and autogenous bone graft at edentulous sites may limit graft resorption, thus enhancing bone repair.

e-PTFE membrane has two different microstructures: a coronal border and an occlusive portion. The coronal border, with internodal distance of 25 μm, has an open microstructure collar that facilitates early clot formation and collagen fiber attachment to stabilize the membrane until it becomes fixed [59,61]. The occlusive portion has an internodal distance of less than 8 μm to allow nutrient inflow while preventing the infiltration of other tissue cell types [59]. e-PTFE comprises numerous small pores, which encourage tissue cell attachment that stabilizes the host-tissue interface. These smaller pores also act to restrict the migration of epithelial cells [62]. However, this material requires second-stage surgical extraction, which may expose the membrane to bacteria [60]. Furthermore, e-PTFE must be removed immediately in the case of inflammation. At present, e-PTFE membrane has been discontinued and is not available for dental use; however, possible alternatives are available.

4.2.2. d-PTFE membrane

High density PTFE (d-PTFE) membrane (ex. Cytoplast™ Regentex GBR-200 or TXT-200; Osteogenics Biomedical Inc., Lubbock, Texas, USA) is one alternative to e-PTFE. This membrane was originally developed in 1993, and its success in bone and tissue regeneration is well documented [64,65]. This membrane is made of a high-density PTFE, with a submicron (0.2 μm) pore size. Because of this high density and small pore size, bacterial infiltration into the bone augmentation site is eliminated, which protects the underlying graft material and/or implant. Furthermore, primary soft tissue closure is not required [54,65]. Previous authors have reported that d-PTFE completely blocks the penetration of food and bacteria, and thus, even if it is exposed to the oral cavity, it is still acts as an appropriate membrane barrier [91,92]. Interestingly, one of the materials, Cytoplast™, does not have porous structure and its attachment to tissues is weak. Thus, it can be removed easily by pulling on the membrane without lifting the mucosal flap. In addition, even if it is exposed, the risk of infection is less than that of e-PTFE [61].

4.2.3. Titanium mesh

Besides PTFE membranes, titanium is another non-resorbable material applicable for dental bone repair. In 1969, Boyne et al. inaugurated a mesh from titanium for the reconstruction of large discontinuity osseous defects [96]. Titanium has been used extensively in numerous surgical applications because of its high strength and rigidity, its low density and corresponding low weight, its ability to withstand high temperatures and its resistance to corrosion [87,93,94]. This metal is highly reactive, and can be readily passivated to form a protective oxide layer, which accounts for its high corrosion resistance [95]. The low density of titanium provides both high-strength and lightweight dental materials [95].

5. Focus on titanium mesh and its role in GBR

Research into GBR is still ongoing and evidence for the use of titanium in dental applications is expanding, particularly for alveolar ridge reconstruction prior to implant placement. We searched the PubMed Medline databases from 1991 to 2011 and retrieved all relevant articles (in English only) reporting the use of titanium mesh for bone regeneration in the clinic, using various search terms (membrane/gbr/bone regeneration/titanium mesh/titanium membrane). The study summaries are shown in Table 3 [35,60,68–70,94,97–107].

Titanium mesh (Ti-mesh) has excellent mechanical properties for the stabilization of bone grafts beneath the membrane. Its rigidity provides extensive space maintenance and prevents contour collapse; its elasticity prevents mucosal compression; its stability prevents graft displacement; and its plasticity permits bending, contouring, and adaptation to any unique bony defect [60,97]. Various studies have shown that Ti-mesh maintains space with a higher degree of predictably, even in cases with a large bony cavity [57,71,108,109]. In addition, it is believed that the smooth surface of Ti-mesh makes it less susceptible to bacterial contamination than resorbable materials

Table 3
Summary of clinical studies with titanium mesh membranes prior to implant placement.

Study	Titanium mesh	No. of patients	Defect type	Bone Grafts	Bone (%)	Infection, Exposures, or Removal	Implant placement (months)	No. of implants	Implant survival (follow-up)
2012 [97] Her	MTAM 0.1-mm-thick; φ pores: 1.7 mm	27	Alveolar ridge max and mand	Bone Graft Material	85.18	Exposure: 26%	5.7	69	100% (2 years)
2010 [98] Torres	Ti-mesh	15: mesh only; 15: mesh + PRP	Edentulous ridge max and mand	Anorganic bovine bone	100	Exposure: 28.5% (Ti mesh only)	6	97	Mesh only: 97.3%; Mesh + PRP: 100% (2 years)
2009 [70] Corinaldesi	ACE	24	Alveolar ridge	Mand ramus	85	Exposure and removal: 14.8%	8–9	56	100% (3–8 years)
2008 [99] Louis	Ridge Form Mesh	44	Alveolar ridge max and mand	Illiac crest/tibia/mand. + hydroxyapatite	97.72	Exposure: 52.7% Removal: 7 Failed placement: 1	6.9	174	ND
2007 [100] Roccuzzo	Micro Dynamic Mesh	23	Edentulous ridge max and mand	Mand ramus or mental symphysis	83.33	Exposure: 33.33% (4 from 12 sites) Removal: 8.33%	4–6	24	ND
2006 [101] Molly	Custom fit	11	Max	Hip onlay grafts	54	Exposure: 5 (bone was formed enough)	9–17	Ant: 30 Post: 16	Ant: 82.6% (9 years); Post: 76.6% (6 years)
2006 [68] Proussaefs	Frios	17	Alveolar ridge max and mand	Chin, ramus, extra socket, Max tuber + Bio-Oss	73	Exposure: 35.3%	8.47	41	71% (6 months)
2004 [35] Roccuzzo	Micro Dynamic and Modus 1, 5	18	Edentulous ridge max and mand	Mand ramus or mental symphysis	83.33	Exposure: 22.22% Temporary paresthesia: 27.77%	4–6	37	100% (2 months)
2003 [102] Artzi	CTM	10	Alveolar ridge	Bovine bone mineral	81.2	Exposure: 20%	9	10	ND
2003 [94] Degidi	Cortical Mesh	18	Alveolar ridge	No	100	No	4–6	50	100% (7 years)
2002 [103] Lozada	Sofamor Danek	1	Edentulous ridge	Iliac crest	100	No	7	Max (10), Mand (6)	ND
2001 [104] Assenza	Bonesheet + e-PTFE	22	Alveolar ridge	No	81.8	Exposure: 4 sites Removal: 2 sites	Max (6), Mand (4)	22	ND
2001 [105] Maiorana	0.2-mm-thick Ti-mesh	14	Edentulous	Illiac and anorganic bovine bone	100	Exposure: 14.28%	4–5	59	98.3% (4 years)
1999 [106] von Arx	M-TAM	15	Alveolar ridge	Cancellous bone	93.5	Exposure and removal: 1 sites	5–10	20	ND
1998 [69] Malchiodi	Tocksystem 80 μm microhole	25	Edentulous ridge max	Retromolar mand	96	Dehiscence: 3 implants (1 patient)	8	120	ND
1998 [107] von Arx	M-TAM	18	Alveolar ridges	Retromolar area and chin	100	No	5.2	27	100% (1–3 years)
1996 [60] von Arx	M-TAM	20	Alveolar ridge	Retromolar area, impacted canine, chin	90	Exposure: 50% Removal: 1 patient	6–8	28	ND

[67]. Studies indicate that, because of their spongy architecture, resorbable membranes are a possible nidus for infection, and microbial colonization within superficial and deep portions of membrane is favored [110,111].

However, the stiffness of the Ti-mesh also lends itself to causing an increased number of exposures, such as mechanical irritation to the mucosal flaps [112]. In addition, the sharp edges, caused by cutting, trimming, and bending of titanium mesh, might be responsible for exposure of titanium barriers [57]. Despite the exposure, von Arx et al. noticed no infection in any of their patients [60]. This offers an advantage as compared with e-PTFE barriers, which result in infection when exposed [113,114].

The superb properties of Ti-mesh make it optimal for successful GBR [35,70,94,98,105,107]. However, many problems still remain and need to be resolved to increase the predictable nature of these materials. Most problems with Ti-mesh arise from their exposure and from soft tissue ingrowth. The stiffness of Ti-mesh can maintain space better than other membrane, but may result in mucosal irritation that leads to exposure of the membrane. This space maintenance and resistance to collapse is influenced by the thickness of the Ti-mesh, and as such, an appropriate thickness must be balanced with the likelihood of irritation when using Ti-mesh for GBR.

Another common feature of commercially available Ti-mesh membranes is its macroporosity (in the millimeter range). This is thought to play a critical role in maintaining blood supply and is believed to enhance regeneration by improving wound stability through tissue integration and allowing diffusion of extracellular nutrients across the membrane [54,115,116]. Another advantage of this macroporosity is related to the attachment of soft tissues, which may stabilize and restrict the migration of epithelial cells [61,117,118]. However, this makes the material difficult to remove at the second surgery. These macro- and multi-porous characteristics also create sharp spots when the material is cut or bent, and may provide an easy pathway for microbial contamination into the healing site [94]. Thus, the development of less porous and micropore-sized Ti-mesh membrane could alleviate some of the current difficulties associated with Ti-mesh in dental applications.

6. Conclusion

The concept of GBR for the reconstruction of the alveolar ridge defect prior to implant placement has been developed in an effort to optimize treatment strategies. Research from animal and clinical studies in this field is still ongoing in order to establish an ideal membrane for treatment. Since every membrane offers both advantages and disadvantages, a membrane should be selected based on a thorough understanding of the benefits and limitations inherent to the materials in relation to the functional requirements in the specific clinical application.

Titanium mesh offers an excellent solution for GBR in dental applications over other membrane types. Preliminary clinical studies have also shown its predictable nature in both lateral and vertical bone augmentation. However, necessary adjustments to the pore size and frequency in titanium mesh biomaterials should improve their efficacy in dental applications.

Conflict of interest statement

All authors state that they have no conflicts of interest.

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