Clinical Applications and Outcomes of non-resorbable Polytetrafluoroethylene (PTFE) Membranes in Guided Bone Regeneration: Review

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Abstract
Developments in bone regenerative techniques have increased implant placement success in mandible sites previously considered unsuitable for implants. Guided bone regeneration (GBR) procedures preserve tooth sockets immediately after teeth are extracted. GBR can also be applied to regenerate lost bone in defective alveolar ridges before or in conjunction with implant emplacements. Resorbable and non-resorbable membranes have been used in GBR.

Non-resorbable membranes can be used alone or in combination with bone grafts. Titanium reinforced, non-resorbable membranes have the advantage of being molded and shaped for tenting and preserving space between teeth. Expanded polytetrafluoroethylene (e-PTFE) membranes are associated with an inherent risk of infection upon exposure to the oral environment due to its highly porous surface. However, a dense polytetrafluoroethylene (d-PTFE) membrane does not require primary flap closure because bacteria cannot penetrate its surface.

This review article summarizes the utilization of non-resorbable barrier membranes alone and together with various bone graft materials, relevant clinical studies, case reports, and the advantages and limitations of various combinations of procedures.

Keywords: Guided bone regeneration, GBR, Augmentation, Non-resorbable membranes, PTFE.

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Introduction
Guided bone regeneration (GBR) is similar to guided tissue regeneration (GTR), except that the latter includes all periodontal components, whereas GBR includes only bone and connective tissues.¹-⁴ Bone regeneration is promoted by protecting bone against invasion by competing, non-osteogenic tissues. Connective tissue can be excluded in GBR by applying a barrier membrane that allows only bone regeneration to occur. The advent of GBR membranes has provided clinicians with a method for enhancing extraction socket healing and augmenting other bone defects.⁵,⁶ Studies in which direct measurements between the alveolar ridge crest and fixed reference points were taken have shown that the use of membrane alone or with grafting materials can reduce bone loss significantly.³,⁵ Both non-resorbable and resorbable membranes were evaluated in these studies, with and without grafting materials. Ridge resorption can be prevented in GBR by applying particulate autografts, allografts, alloplasts, xenografts, and membranes that are manufactured from a wide variety of materials, including combinations of resorbable or non-resorbable membranes and naturally derived or synthetic membranes.²-⁴ Each of these combinations of biomaterials has characteristic advantages and disadvantages.

GBR arose from early periodontal research focused on tissue regeneration following tooth implants and normally relies on surgical procedures that prevent undesirable proliferation of epithelial cells.² Such disruptive cell proliferation occurs when a semipermeable membrane is interposed between the bones, flap, and tooth root long enough for periodontal tissue cells to multiply and heal the wound.
GBR surgery, originally performed in the 1950s, has been applied in spinal fusion and maxillofacial reconstruction. The original hypothesis underlying GBR was that because cells and tissue components (i.e., fibroblasts and other substances) migrate to a wound at different rates during healing, perhaps healing could be guided mechanically with barrier membranes in a manner that would allow regeneration to occur between membrane barriers. This guided process also entails angiogenesis and osteogenic cell migration, which proceeds from the periphery towards the center area of a wound, resulting in the creation of well-vascularized, granulated tissue upon healing. Although membranes are typically used to prevent invasion by soft tissues, soft-tissue ingrowth is still possible. Because such soft-tissue ingrowth has a tendency to occur in tissues that are less than 1 mm thick and located under the barrier membrane, typically, they overly bone that is being regenerated. Ingrowth can occur secondarily to the shrinking of blood clots that formed under the membrane in response to air entrapment or micro-movements in the membrane. Research has not yet established whether the layer of soft tissue under the membrane becomes mineralized if it is left unattended for a long period of time.

Use of bioresorbable and porous synthetic materials in GBR surgery requires a primary closure over the extraction socket, a requirement that increases surgical complexity, reduces the amount of available keratinized gingiva, and disrupts the natural architecture of local soft tissues. Membranes made of polytetrafluoroethylene (PTFE) have been designed specifically for use in both for periodontal and ridge grafting surgeries. The main clinical advantage of non-resorbable PTFE membranes is that they simplify surgical procedures at bone regeneration sites by minimizing flap reflection, while providing exceptional biocompatibility, allowing for removal of the membrane, providing mechanical stability of the graft and wound, creating stiffness for space maintenance, and preserving and regenerating keratinized tissues. Because PTFE membranes can improve the success of GBR treatments appreciably, they are now widely used in bone and periodontal regeneration applications.

The aim of this report is to review and summarize the periodontal literature that compares the potential effectiveness of the various types of PTFE membranes currently used for facilitating regeneration in alveolar bone defect sites.

**Types of PTFE membranes, their roles, and basic characteristics**

Several types of non-resorbable and bioresorbable barrier membranes have been developed and their various uses have been investigated thoroughly in the literature. Although the ideal membranes for particular clinical applications have not yet been identified, much research is underway in this regard.

All GBR membranes are similar in their basic characteristics, including their biocompatibility, cell-occlusiveness, and space-making functions. In addition, they can all be easily integrated into tissues. However, degradable membranes have a tendency to collapse (more so when the magnitude of the bone defect is severe). In contrast, PTFE membranes retain their structural integrity during implantation. In addition, PTFE membranes are superior to degradable membranes in their ability to maintain space needed for cell occlusion. In fact, PTFE membranes developed for use in both periodontal and ridge grafting surgeries because they are resistant to collapse.

Non-resorbable, expanded polytetrafluoroethylene (e-PTFE) and dense polytetrafluoroethylene (d-PTFE) are the most common, non-resorbable membranes used today in GBR surgery. Although both membrane types are made of polytetrafluoroethylene, the larger pore size of e-PTFE (5–30 µm) enables it to be stretched more than d-PTFE (pore size, 0.2 µm). Owing to its superior stretchability, the e-PTFE membrane was considered to be the best type of non-resorbable membrane for use in GBR surgery.

**Attributes of e-PTFE membranes**

An e-PTFE membrane is composed of a chemically stable, biologically inert polymer, but its structure is both porous and flexible. These combinations of characteristics enable e-PTFE membranes to resist degradation produced by microbiological or enzymatic reactions (i.e., the membrane does not stimulate immunological reactions). The structure of e-PTFE
membranes consists of two distinct parts, an open microstructure (100–300 µm porosity) and an occlusive structure (<8 µm porosity). The porous microstructure promotes ingrowth of collagen fibrils, thus enhancing membrane stability and allowing nutrient diffusion through its pores, which together stimulate more new bone formation during the initial healing period than do nonporous devices. In contrast, the occlusive portion is relatively impermeable to fluids and completely blocks the migration of soft tissue cells into the area of bone growth. For this reason, the presence of a porous portion in barrier materials is regarded as important for achieving satisfactory results in regenerative therapy. On the other hand, Ronda et al. concluded that although the presence of a porous portion in a membrane seems to play a role in stabilizing the membrane and favors its integration with soft tissues, it does not appear to be essential for bone regeneration to occur.

The e-PTFE microstructure is comprised of two different parts: a coronal border and an occlusive layer. The coronal border possesses an open microstructure collar that facilitates early blood clot formation and collagen fiber attachment, which together stabilizes the membrane until it becomes fixed in place. The occlusive layer is comprised of numerous small pores that encourage tissue cell attachment (which helps stabilize the host-tissue interface) and allows nutrient inflow, but prevents the infiltration of other tissue cell types. These smaller pores also restrict epithelial cell migration.

It is well established that the porous portion of the membrane favors bacterial biofilm accumulation. Specifically, a surface roughness from 10–100 µm promotes adhesion of bacteria because air entrapped in rough areas initiates protein and cell adhesion. Consequently, bacterial penetration from the outer to the inner surface of an e-PTFE membrane is unavoidable in an oral environment and occurs within four weeks.

Previous research performed using histologic techniques and scanning electron microscopy indicate that e-PTFE membranes become contaminated on both their internal and external surfaces and along the thick portion of the membrane that is partially occlusive. However, the degree of membrane permeability should be regarded with caution because bacterial penetration is augmented when the edges of the membrane’s open microstructure are exposed to the oral cavity. In addition, a bacterium’s ability to penetrate the closed occlusive portion of the e-PTFE membrane has not been fully investigated and competing explanations for bacterial contamination are possible. Simon et al. determined that although oral bacteria contaminated e-PTFE membranes exposed to the oral cavity, the partially occlusive porosity of the membranes delayed bacterial penetration by 3–4 weeks, thus suggesting that after this amount of time, prematurely exposed e-PTFE membranes should be removed to prevent bacterial infection of the underlying regenerating tissues.

**Attributes of d-PTFE membranes**

Bacterial infiltration into a bone augmentation site is eliminated with use of a d-PTFE membrane due to its high density and small pore size (0.2 µm), which protects the underlying graft material and/or implant from exposure. In addition, closure of primary soft tissue is not required when d-PTFE is used with implants.

Exposed d-PTFE membranes can prevent epithelial migration in healing sockets without consequences to periodontal health when post-extraction sockets are filled with nanocrystalline hydroxyapatite and covered partially with d-PTFE membranes. Histologic samples have shown a dense connective tissue devoid of epithelial cells and no signs of a reaction to foreign bodies. Barboza et al. observed similar alveolar ridge preservation results in two groups of patients provided with d-PTFE membranes in 420 cases.

Because the small pore size of d-PTFE membranes reduces bacterial penetration, they can be left in the oral cavity without subsequent infection. In addition, because d-PTFE membranes maintain space and stabilize wound areas more than e-PTFE membranes, they allow sufficient time for tissue regeneration to occur without disturbing the healing of mucosal tissue. The removal of d-PTFE membranes through the mucosa, without raising a flap, is possible because this membrane does not attach to tissue. Although a d-PTFE membrane does not have a porous structure and its cohesion is weak, its textured surface enhances its stability.
during tissue formation. However, this membrane still requires special care and attention during its positioning and stabilization. Successful bone regeneration with d-PTFE is achieved when adequate blood supply is obtained from the surrounding cortical perforations. However, the low porosity of d-PTFE membranes can restrict blood supply in the surgical area. This low porosity underscores the importance of inserting multiple perforations into the cortical bone to enhance blood supply to the augmented area. The low porosity (<0.3 μm) of the d-PTFE membrane also prevents cell adhesion, meaning that implants are less prone to bacterial infection. Human studies on socket preservation with d-PTFE membranes left intentionally exposed showed improved clinical and histological outcomes without signs of infection during regeneration.

Some studies have suggested that d-PTFE membranes should block penetration of food and bacteria completely and thus should provide an exceptional membrane barrier even in the oral cavity. In fact, when exposed to the oral cavity under artificial conditions, the partially occlusive porosity of the inner portion of e-PTFE membranes helps prevent bacteria from penetrating the membrane for 3–4 weeks. The inflammatory tissue responses to a novel dPTFE membrane (permamem®) have preclinically been evaluated using a collagen membrane as control and the subcutaneous implantation model in BALB/c mice by means of histopathological and histomorphometrical analyses and immunohistochemical detection of M1- and M2-macrophages. The obtained results demonstrated that the tissue response to the dPTFE membrane involves inflammatory macrophages; however, similar cell numbers were found for the control collagen membrane. Although these data indicated that dPTFE membrane is not fully bioinert, its biocompatibility is comparable to collagen-based membranes.

The role of membrane stability and preparation of surgical sites

Membrane stability is important because bone formation is prevented by micro-movements that occur between bone and implanted material. Micro-movements provide conditions that favor the development of fibrous tissues at the implant site. Therefore, stability and minimal stress are imperative for facilitating early differentiation of tissues that infiltrate bone or are derived from bone. If the site of bone formation is highly vascularized, bone formation can occur within porous materials even when the initial substrate mobility is limited. In addition, local inflammatory reactions must be suppressed for bone tissue to form properly. Formation of new vascular networks is also required for successful bone generation.

Proper bone formation is affected by mechanical conditions such that delays in mechanical loading enhance bone formation and stimulate vascular remodeling, which is achieved by expansion of the number of large blood vessels and with a reduction in the number of small vessels Therefore, the membrane is attached firmly to bone to optimize membrane stability.

Efficacy of e-PTFE membranes

When implants are grafted with titanium-reinforced e-PTFE membranes and allogeneic bone matrix, patients exhibit various degrees of trabecular bone growth after six months of maturation and mineralization in the augmented area. In the apical portion of an implant, native lamellar bone is in direct contact with overlying regenerated bone and osteoblastic activity can be identified adjacent to newly formed bone, demonstrating ongoing deposition of osteoid matrix in augmented areas.

Dahlin et al. provided the first evidence supporting the effectiveness of e-PTFE membranes in promoting peri-implant bone formation in rabbit tibiae. Where a porous PTFE membrane was placed around exposed parts of the implant, to create a secluded space for osteogenesis and prevent soft-tissue ingrowth, the threads of the implant became enveloped with new bone. Schmid et al. tested bone growth in rabbit calvaria for eight months on e-PTFE membranes with titanium cylinders. The results showed that membrane permeability is not necessary for GBR to be successful on titanium. When Zellin and Linde compared new bone formation among e-PTFE membranes with three different porosities over 26 weeks of healing, they found that the greatest amount of new bone was obtained after 6 weeks using the two more permeable membranes (20–25 μm and 100 μm), but there were no group differences in
new bone growth after 12 weeks.

A clinical and radiographic study of titanium implants in bone regenerated in submerged e-PTFE-protected bone defects demonstrated that implants can achieve ankylosis within three months following the placement of implants. After some implants were restored with fixed partial dentures and others were not, and after both were functionally loaded for six months, osseointegration was observed with direct bone-to-implant contact for all implants. This result suggests that bone regenerated in membrane-protected defects and non-regenerated bone respond similarly to implant placement and that such bone is capable of bearing and sustaining a functional load. A histological comparison of restored and unrestored sites demonstrated no apparent differences in relation to bone-remodeling activities. In addition, control sites (without an implant) demonstrated bone atrophy, with a thin cortical layer and sparse bone trabeculae underneath the membranes. This result suggests that placement of an implant into regenerated bone stimulates bone maturation and remodeling, whereas implant loading does not influence bone remodeling, at least under the study conditions employed.

Schenk et al. evaluated the pattern of bone regeneration in membrane-protected bone-defects (in the mandibles of dogs) using reinforced e-PTFE membranes. Control sites without membranes exhibited incomplete osseous healing with a persistent defect after 2–4 months of healing, whereas reinforced e-PTFE membrane defect sites demonstrated significantly better bone healing, although bone regeneration was not complete after four months. Histological evaluations showed that once bone regeneration is activated, it progresses in a programmed sequence through a series of maturation steps that resembles bone growth patterns during development.

Warrer et al. explored whether covering recipient implant sites with e-PTFE membranes can improve implant osseointegration. On one side of the jaw, membranes were adjusted to cover the implants, whereas implants on the other side of the jaw were only covered by tissue flaps (control). Microscopic analysis after three months of healing revealed that soft tissue on the control side faced the coronal portion of the implants to varying degrees, whereas osseointegration was consistently observed on top of the membrane-covered immediately placed implants. These results suggest that e-PTFE membranes protect osseointegration of immediately placed implants well. These results were supported by a similar study in which e-PTFE membranes were used 32 titanium implants inserted immediately into the extraction sockets in dogs. When soft tissue dehiscence occurred and the membranes were left exposed without proper oral hygiene during healing, there was significantly less bone integration in sites with e-PTFE membranes than in sites without the membranes.

When assessing the potential of GBR to treat exposed threads of implants using submerged e-PTFE membranes in dog mandibles, Becker and Becker reported a mean increase in bone height of 1.37 mm for the GBR-treated sites compared to a 0.23mm bone height increase in control threads. Likewise, in a recent literature review, Retzepi and Donos reported that vertical augmentation of the mandibular growth process (in dogs) with application of e-PTFE membranes around implants exhibited new subcortical bone growth.

Simion et al. evaluated the efficacy of a 1:1 mixture of bovine bone graft and autogenous bone graft associated with a submerged e-PTFE membrane applied for vertical ridge augmentation in humans with a healing period six months. They recorded new bone formation, ongoing autogenous bone growth, and remodeling of graft particles. In a similar study, Simion et al. provided clinical evidence for the effectiveness of the GBR technique in promoting bone augmentation in non-space-maintaining vertical defects with simultaneous implant emplacement. Using titanium-reinforced submerged e-PTFE membranes, they obtained a mean gain in bone height of 4 mm, whereas the direct contact between regenerated bones and implant surfaces averaged 45% after nine months of healing. Laurito et al. evaluated the efficacy of an exposed d-PTFE membrane in preventing epithelial migration in post-extraction sockets filled with nanocrystalline hydroxyapatite (nc-HA) and covered partially with d-PTFE membranes. After 28 days, there was growth of dense connective tissue and no epithelial cells or no signs of a foreign body reaction, indicating that exposed d-PTFE membranes can prevent epithelial migration in healing sockets without
negative impacts on periodontal health. In another study, Laurito et al.\textsuperscript{23} analyzed post-extraction bone changes in sockets treated with nanocrystalline nc-HA and exposed d-PTFE membranes. Clinical, histological, and histomorphometric measurements taken after tooth extraction and six months later showed an overall reduction in newly formed bone: bone formed in 25.92% (± 18.78%) of cases, soft tissue formed in 28.55% (± 9.73%) of cases, and residual graft particles occurred in 15.43% (± 11.08%) of cases.

In a large-scale regeneration study (409 extraction sockets in 276 patients), Hoffmann et al.\textsuperscript{23} found that, after 12 months, sockets preserved with d-PTFE membranes exposed in the oral cavity without graft material formed new bone tissue with a regular trabecular structure. Active bone formation was evidenced by the presence of osteocytes and osteoblasts. Localized areas of bone marrow with lymphocytes and (more rarely) granulocytes were also observed.

Bartee and Carr\textsuperscript{11} evaluated the use of d-PTFE membranes to facilitate GTR by creating bilateral through-and-through defects in the mandibles of rats. The experimental sides were covered with d-PTFE membranes, while the opposite sides served as within-subject controls. Within two weeks, osteogenic tissue had bridged the defects and after six weeks of healing, osteogenic repair was evident at defect margins with islands of woven bone in central areas. Complete ossification occurred on the d-PTFE-treated side after 10 weeks with very little osseous regeneration, whereas only a rounding of the defective margins occurred in the control side.

**Clinical application: Submerged versus exposed membranes**

Ronda et al.\textsuperscript{8} compared the performance of titanium-reinforced d-PTFE membranes with titanium-reinforced e-PTFE membranes (both relative to controls). All membranes were submerged with a graft material comprised of 50% autologous bone and 50% mineralized bone allograft. After 6 months, the mean fill defect was 5.49 mm for the e-PTFE group and 4.91 mm for the d-PTFE group. The percent change did not differ significantly between the two membrane types and the controls. However, membrane removal was easier with the d-PTFE membrane than with the e-PTFE membrane.

When Urban et al.\textsuperscript{41} evaluated success and survival rates of vertical GBR over a 72-month period using submerged e-PTFE membranes and autographs, they determined that the growth rates of vertically augmented bone were similar to that seen with implants placed in native bone. Lekovic et al.\textsuperscript{26} covered extraction sockets with submerged e-PTFE membranes without additional grafting material. They observed better ridge dimensions (p ≤ 0.05) for the experimental grafts than controls after six months. In addition, membrane exposure occurred in only 3/82 implants (3.7%) during the healing period. Dimensional changes in exposed membranes were also similar to those seen with conventional implants (controls).

In a study comparing submerged e-PTFE membranes with resorbable poly(lactic acid) and poly(glycolic acid) (PLA/PGA) membranes placed around implants in post-extraction sockets, Simion et al.\textsuperscript{42} found that the implants were osseointegrated in new bone. Furthermore, non-resorbable e-PTFE membranes were more effective in regenerating bone and producing denser bone than resorbable PLA/PGA membranes. In another study, Simion et al.\textsuperscript{17} compared healing outcomes in patients treated with submerged e-PTFE membranes that had been placed in fresh extraction sockets, with a focus on microbial morphology and the ability of microbes to penetrate membrane pores. They concluded that e-PTFE membranes are effective for treating fresh extraction sockets with osseointegrated implants. In addition, they found that the membranes were highly biocompatible with gingival tissues, but that early exposure of the membranes to peri-implant tissues during the healing process can hinder the effectiveness of GTR.\textsuperscript{17}

Ronda and Stacchi\textsuperscript{27} reported a mean bone gain of 5.2 mm after 6–7 months of healing following implant placement with simultaneous vertical augmentation using submerged e-PTFE membranes and mineralized allograft and autogenous bone (1:1). Complications occurred in 4/69 patients (5.8%), all of whom were smokers with signs of infection in the augmented areas, swelling, and purulent exudate during the first two weeks after surgery (despite primary flap closure being perfectly maintained). In another study, Ronda and Stacchi\textsuperscript{28} examined implant
placement and vertical augmentation using submerged d-PTFE membranes with mineralized allografts, and reported a success rate of 96.1% after a healing period of 6–7 months. The complications affecting the remaining 3.9% included partial membrane exposure in one patient (treated by regular application of 0.2% chlorhexidine gel), membrane exposure and purulent exudate in one patient, and an abscess that had not been exposed to the membrane in one patient.

Simion et al. reported that a composite bone graft (1:1, bovine bone graft: autogenous bone) covered with a submerged, titanium-reinforced e-PTFE membrane provided a stable implant with hard regenerated tissue similar to bone. Becker et al. found that immediately placed implants covered with submerged e-PTFE barrier membranes had substantial amounts of bone formation adjacent to the implant sites. The greater bone formation and fewer exposed membrane threads were retained six months after fixture installation in sites with early membrane removal. Fontana et al. determined that after six months, the performance of allogeneic bone matrix was similar to that of autogenous bone graft when covered with titanium-reinforced e-PTFE membranes for vertical ridge augmentation.

Merli et al. compared vertical bone augmentation obtained following autogenous bone grafts covered with either non-resorbable, submerged titanium-reinforced e-PTFE barriers (N = 18) or resorbable collagen barriers (N = 11). No implants failed and all resorbable barriers attained 100% regeneration, whereas more than 50% regeneration was achieved for the six implants with non-resorbable barriers that had not attained complete regeneration. One patient had a dehiscence with suppuration that required an additional surgical intervention to remove the barrier. Barboza et al. found that similar results could be obtained with and without additional grafting material when alveolar ridges were preserved with d-PTFE membranes exposed for two days.

Zafiropoulos and Hoffman reported a case study of a 41-year-old man who received overdenture restorations, wherein 11 implants were emplaced eight months after the sockets were preserved with exposed d-PTFE membranes (without additional grafts) and loaded four months later. Over the 5-year evaluation period, all 11 implants survived with stable bone levels. In another study of immediate loading in regenerated bone in which exposed d-PTFE membranes were used (without additional grafts), authors showed a minimal attachment loss of only 1.5 mm in the first three years with no further loss after two more years. Using resonance frequency analysis, Deli et al. determined that implants placed in regenerated bone (using exposed d-PTFE membranes without additional grafts) were more stable (p = 0.03) than implants in naturally healing bone after 12 months.

A non-randomized post hoc study comparing tapered versus cylindrical implants across different times of implant placement and loading (immediate placement and loading using bovine bone graft and resorbable membrane vs. delayed placement and loading 8 months post-augmentation with a partially exposed d-PTFE membrane without additional use of grafting material) showed an attachment loss of 1.5 mm during the first three years, without significant effects of implant type or time of implant placement and loading on survival rate. In another non-randomized post-hoc study, the use of partially exposed d-PTFE membranes without additional graft material was associated with enlargement of keratinized gingiva and vertical regeneration of missing buccal bone walls approximately one year postoperatively. Hard tissue biopsies taken during implant emplacement 12 months after surgery confirmed that the newly formed tissue was mature bone.

In a recent report, Zafiropoulos et al. described regeneration of peri-implant defects after implant removal and coverage of the defects with only exposed d-PTFE membranes. The same team of clinical investigators described bone regeneration with the use of exposed d-PTFE membranes without any graft material following immediate implant placement into a mandibular molar socket. In the latter study, an attachment loss of 1.5 mm was observed during the first three years after loading, and there were no additional changes between the 3-year and 8-year follow-up examinations.

In a recent study of 34 patients with sockets exhibiting ≥3 mm hard-tissue loss in at least one wall, the patients were randomized into two groups: a test group in which alveolar ridge preservation was performed with a d-PTFE
membrane; and a natural socket healing control group. After four months, significantly less change in ridge width was observed in the test group than in the control group, with no significant differences between the two groups with respect to vertical or horizontal ridge changes. Requirements for bone augmentation at implant placement were significantly lower for the test group than the control group. The authors concluded that alveolar ridge preservation with a d-PTFE membrane and an allogenic bone graft reduced horizontal bone resorption in bone-deficient sockets.

**Medication, postoperative care, and management of clinical complications**

Many clinical studies have examined the effects of using analgesics 0.2% chlorhexidine digluconate solution rinses and prophylactic systemic antibiotics (mostly amoxicillin/clavulanate potassium) in patients with standard postoperative care (cold pack applied to the wound, avoidance of hot drinks and food, avoidance of physical exertion, and no placement of dentures onto the treated area) with suture removal occurring 15 days after surgery in almost all cases. 

Note that the minimum time that a membrane needs to be retained to facilitate optimal bone maturation is not known. Most surgeons leave submerged membranes for GBR in place for six months and leave partially exposed membranes in place for 4–5 weeks. Recently, Fontana et al. classified complications during healing, including associations with e-PTFE membranes, based on treatment modalities in clinical publications. The four classes of exposure and associated recommendations that they described were as follows:

**Class I:** Small membrane exposure (≤3 mm) without purulent exudate. The membrane should not be removed because bacteria can traverse the e-PTFE barrier and infiltrate the treated area in 3–4 weeks. During healing, 0.2% chlorhexidine gel should be applied regularly in the exposed area and weekly follow-up exams should be scheduled.

**Class II:** Large membrane exposure (≥3 mm) without purulent exudate. Fontana et al. suggested immediate membrane removal and flap closure to allow submerged healing of the augmented area. We believe that the dimensions of exposure should be evaluated to determine if the membrane should be removed or treated as in Class I exposure.

**Class III:** Membrane exposure and presence of purulent exudate. Postoperative treatment consists of membrane removal and curetting of the augmented area. Any implant placed at the time of augmentation should be removed.

**Class IV:** Abscess in the treated area without membrane exposure. This exposure is associated with bacterial contamination of the grafted area. It should be treated the same as a Class III exposure but with additional systemic antibiotics.

Although there have been previous classifications of complications during healing, the above summarized scheme is the first to include evidence-based consequent clinical treatments. Thus, prior classifications should be considered to be recommendations based on the authors’ clinical experiences. Because complications requiring membrane and graft removal have led to implant loss have specifically in smokers, smoking should be considered a counterindication for GBR.

**Conclusions**

PTFE membranes are chemically stable, biologically inert polymers featuring a porous structure and flexible form. They are resistant to enzymatic degradation and do not stimulate immunological reactions. The open microstructure of e-PTFE membranes promotes an ingrowth of collagen fibrils on its surface, which enhances membrane stability and allows for the diffusion of nutrients through its pores. The occlusive portion blocks the migration of soft tissue cells into the area of bone growth. However, when e-PTFE is exposed to the oral environment, the porous portion promotes bacterial adhesion and enables bacterial penetration. e-PTFE membranes should be submerged and their removal is not easy. They can not be placed partially exposed to facilitate removal.

The low porosity of d-PTFE membranes prevents cell adhesion and bacterial penetration. However, because d-PTFE integration is weak, they require fixation. d-PTFE membranes can be placed partially exposed and their removal is easy.

Both PTFE membrane types are used for vertical bone regeneration with comparable outcomes.
Declaration of Interest
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