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Membranes for guided bone regeneration in dentistry: a review of human randomized blinded clinical trials

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• Conflicts of interest: none declared.

Abstract

Objective: to review the literature currently available on membranes for guided bone regeneration in clinical dental practice. **Material and Methods:** a literature search was performed on PubMed, Web of Science and Scopus. The Jadad Scale was used for data collection and selection. The quality of the studies was evaluated through Cochrane Center Guidelines. Randomized and blinded clinical trials published in Portuguese, Spanish and English were included. Literature reviews of studies without randomization and blinding or when a percentage equal to or greater than 20% of the sample did not proceed with the study follow-up were excluded. We selected 27 studies that were categorized according to the findings. **Results:** the number of publications found limited the conclusions on the success of GBR in dentistry. **Conclusion:** the variety of techniques and membranes applied, as well as the small number of studies found are in need of well-designed studies in order to better evaluate the potential of GBR in patients submitted to these treatment approaches, as well as to determine accurate treatment protocols.

Keywords: Biocompatible materials; Artificial membranes; Guided tissue regeneration; Dentistry.

Introduction

Diseases, injuries or trauma may cause tissue loss or degeneration in the human body leading to the need for treatments that facilitate its repair, replacement or regeneration.[1] The history of tissue repair goes back to prehistory and, over a long period of time, has occurred empirically, aiming the inertia, non-toxicity and tolerance of the biomaterial.[2]

Tissue engineering aims at regenerating injured tissue through the development and use of biological substitutes,[3] which act as a scaffold to regenerate, maintain, improve, or stimulate the formation of new tissues.[1] The area is of interest to most dental specialties including periodontics, orthodontics, surgery, endodontics and dental implantology[1,4,5] with the need for materials capable of effective and rapid bone formation.[6]

Several methods have been developed to increase bone volume as well as to stimulate the formation of this tissue such as distraction osteogenesis,[7] osteoinduction,[8] osteoconduction[9] and guided bone regeneration (GBR).[10] The concept of Guided Bone Regeneration (GBR) is attributed to the combination of bone substitutes and membranes commonly used to restore lost or defective bone.[11]

Literature shows that membranes would exclude non-osteogenic tissues from interfering with the healing process or bone repair.[12] However, this hypothesis remains speculative given that the mechanisms of bone regeneration through the use of membranes were not accurately described,[11] having a need of better understanding of its chemical and biological processes.[13]

In order to be used for medical and dental purposes, membranes must follow certain criteria such as: biocompatibility, space creation, tissue integration and adequate handling,[14] biodegradability, architecture and satisfactory mechanical properties as well as the technology for its manufacture[1]. Although, promising solutions in animal models, an ideal membrane has not been established for clinical applications. Its selection should be based on a thorough understanding of its benefits and limitations in view of its specific clinical application.[15]

According to biodegradability, the membranes used for GBR are classified into two groups: non-absorbable and resorbable.[5] In the last decades, the research focused on the development of resorbable membranes once they overcome the limitations of the non-resorbable membranes[16] such as the non-need for additional surgical procedures for its removal and a lower risk of developing infections.[17-19]

The literature accounts for a variety of studies aimed at evaluating the properties and clinical perspectives of the use of biomaterials in combination with resorbable and non-resorbable membranes for guided tissue and bone regeneration in different areas of dentistry.[20-31] However, there is no

evidence of systematic reviews aimed on the use of membranes for guided bone regeneration in humans. The present work aimed to analytically review the literature currently available on membranes for guided bone regeneration in dental practice.

Material and Methods

Identification and Selection of Relevant Studies

In order to answer the question, "What are the evidence and perspectives currently available on membranes for guided bone regeneration in dental practice?", we followed the instructions provided by Moher *et al*.[32] Thus, An exploratory bibliographic search was performed through the electronic databases: Public Medline (PubMed), ISI Web of Science and Scopus. The databases were accessed from 07/07/2017 to 10/12/2017. Two authors (P-MS and L-LDS) performed the search using the search terms described in Table 1.

Table 1. Search strategy

Search Terms Combination	Databases
1. "biocompatible materials" OR "biocompatible" AND "materials OR "biocompatible materials" OR "biomaterials AND "guided" AND "bone regeneration" OR "bone" AND "regeneration" OR "bone regeneration" AND "barrier" AND "membranes" OR "membranes" OR "membrane". Stipulated time: ┤10/12/2017.	PubMed
2. "biocompatible materials" OR "biocompatible" AND "materials OR "biocompatible materials" OR "biomaterials AND "guided" AND "bone regeneration" OR "bone" AND "regeneration" OR "bone regeneration" AND "barrier" AND "membranes" OR "membranes" OR "membrane". Stipulated time: ┤10/12/2017. Indexers: SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI, CCR-EXPANDED, IC.	Web of Science
3. TITLE-ABS-KEY ("biocompatible materials" OR "biocompatible" AND "materials OR "biocompatible materials" OR "biomaterials AND "guided" AND "bone regeneration" OR "bone" AND "regeneration" OR "bone regeneration" AND "barrier" AND "membranes" OR "membranes" OR "membrane"). Stipulated time: ┤10/12/2017.	Scopus

Eligibility Criteria

The articles were selected and evaluated by two reviewers through the Jadad Scale selection method, also known as Oxford Quality Scale Scoring System[33] and were based on the inclusion and exclusion criteria. Any disagreements were resolved by further discussion with a third reviewer.

Inclusion criteria was randomized and blinded clinical trials in humans were published in Portuguese, Spanish and English. No limits were applied on the date of publication (┤10/12/2017). Systematic reviews with or without meta-analysis were also included in order to help to discuss the results. We excluded literature reviews of another nature, comparative studies without randomization and blinding, animal studies or in which a percentage equal to or greater than 20% of the sample did not proceed with the study.

Articles with less than 6 months follow-up period were also excluded, due to the fact that the alveolar bone presents the peak of bone reduction during the period of the first six months.[34] Moreover, the lack of knowledge of the minimum time for regeneration with barrier membranes, in order to guarantee a safe period for bone formation and maturation, a minimum period of six months for evaluation of results was adopted.

Data Collection and Analysis

Data was extracted by two authors independently. Disagreements were resolved by discussion after a thorough review of the studies. The articles were identified and imported into Mendeley Desktop software version 1.17.11 (Glyph & Cog, Petaluma, CA, USA) in which the duplicates were removed. Subsequently, titles and abstracts were selected by relevance, using the inclusion and exclusion criteria.

The articles were obtained in full text, and the eligible studies were included in this review. Review articles, clinical case reports, manuscripts in other languages, articles not available in full text, non-relevant publications, non-randomized and blinded or follow-up period of less than six months were removed. Eligible studies had their reference lists screened as well.

Selected Studies

The 27 studies found in the bibliographic search were categorized as evidence related to: preservation of alveolar bone in surgical procedures (n=6); application of barrier membranes in endodontics (n=2); application of membranes in dental implants (n=5); use of membranes in furcation and intraosseous lesions (n=14).

Based on these findings, we determined the following features for critical analysis: synthesis of the results and characteristics of the studies according to the categories. Limitations of the study as well as its implications for clinical practice are presented in order to have a better understanding of its findings considering the design of this review.

Risk Assessment of Bias

The criteria used to assess the quality of the selected Randomized Clinical Trials (RCTs) were modified from the Cochrane Center ECR checklist.[35] Two reviewers evaluated all included articles independently, and the final evaluation was reached with the discussion (Table 2).

Table 2. Quality assessment of the included clinical articles

Study	Sequence generation	Allocation concealment	Blinding of the participants, personnel and outcomes assessors	Incomplete outcome data	Selective outcome reporting	Other sources of bias
Cortellini, Prato e Tonetti, 1996	Yes	Not Clear	Yes	No	No	No
Christgau *et al*., 1998	Yes	Not Clear	Yes	No	No	No
Kim *et al*., 1998	Yes	Not Clear	Yes	No	No	No
Lekovic *et al*. 1998	Yes	Not Clear	Yes	No	No	No
Eickholz *et al*., 2000	Yes	Not Clear	Yes	No	No	No
Garret *et al*., 2002	Yes	Not Clear	Yes	No	No	No
Joly *et al*., 2002	Yes	Not Clear	Yes	No	No	No
Vouros, Aristodimou e Konstantinidis, 2004	Yes	Not Clear	Yes	No	No	No
Aimet, Pigella e Romano, 2007	Yes	Not Clear	Yes	No	No	No
Dori *et al*., 2007	Yes	Not Clear	Yes	No	No	No
Yassibag-Berkman *et al*., 2007	Yes	Not Clear	Yes	No	No	No
Merli, Migani e Esposito, 2007	Yes	Not Clear	Yes	No	No	No
Jung *et a*l., 2008	Yes	Not Clear	Yes	No	No	No
Paolantonio *et al*., 2008	Yes	Not Clear	Yes	No	No	No
Sammartino *et al*., 2009	Yes	Not Clear	Yes	No	No	No
Santana, Matos, Dyke, 2009	Yes	Not Clear	Yes	No	No	No
Mardas, Chadha e Donos, 2010	Yes	Not Clear	Yes	No	No	No
Nygaard-Østby *et al*., 2010	Yes	Not Clear	Yes	No	No	No
Agelis *et al*., 2011	Yes	Not Clear	Yes	No	No	No
Friedmann *et al*., 2011	Yes	Not Clear	Yes	No	No	No
Goyal *et al*., 2011	Yes	Not Clear	Yes	No	No	No
Siciliano *et al*., 2011	Yes	Not Clear	Yes	No	No	No
Ramel *et al*., 2012	Yes	Not Clear	Yes	No	No	No
Gassling *et al*., 2013	Yes	Not Clear	Yes	No	No	No
Cortell-Ballester *et al*., 2015	Yes	Not Clear	Yes	No	No	No
Esposito *et al*., 2015	Yes	Not Clear	Yes	No	No	No

Synthesis of Results

For this literature review, the initial search resulted in a total of 919 records found in the electronic databases: PubMed (n = 319), Web of Science (n = 88) and Scopus (n = 512). 363 studies were excluded for duplication and the remaining 556 studies were selected as potentially relevant. 393 publications were excluded after reading their titles and abstracts according to the Oxford Quality Scale Scoring System.[33] The remaining 163 studies were then obtained in full text and evaluated for eligibility, taking into account the inclusion and exclusion criteria as well as the quality assessment of the studies through the recommendations of the Cochrane Center.[35] Finally, 27 manuscripts were selected, no study from the reference lists was added (Figure 1).

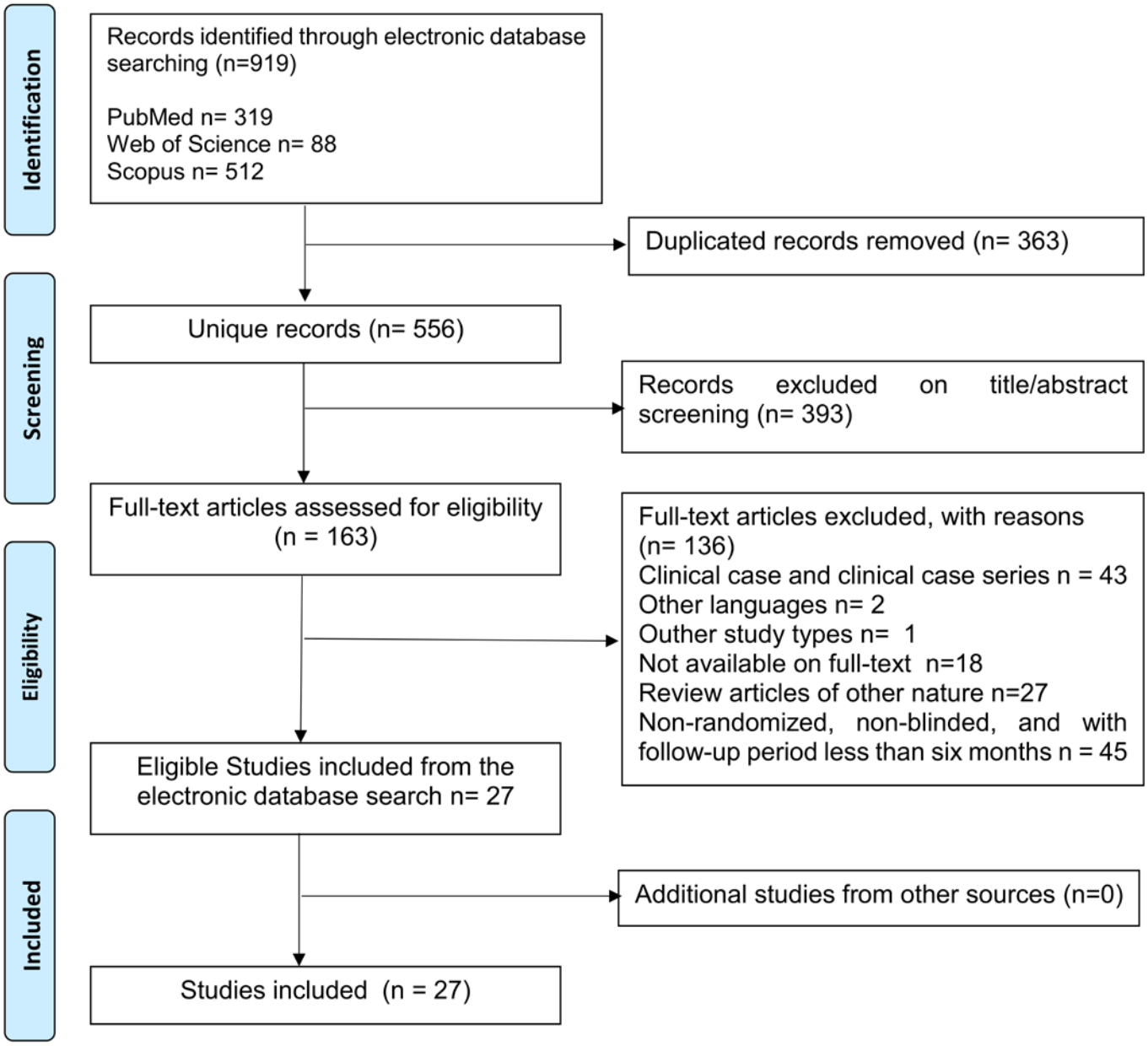

Figure 1. Flow diagram for the review of papers (adapted from Moher *et al*., 2009)

Characteristics of the Studies

The studies were categorized according to the following results: membranes for preservation of alveolar bone, membranes for endodontic application, membranes with application in dental implants, and membranes for furcation and intraosseous lesions. Information was recorded for each study, including authorship and year of publication, study design, sample size and age, follow-up period, surgical treatment, evaluation method, results and study considerations.

Twenty-seven studies addressing membranes for guided bone regeneration in dental practice were identified. In a chronological analysis, not considering the categories surveyed, according to the eligible studies, one study was identified published in 1996 and twelve published over a 10-year period: 1998 (n = 3), 2000 (n = 1), 2002 (n = 2), 2004 (n = 1), 2007 (n = 4), 2008 (n = 1). Between 2009 and 2015, 14 studies were reported in the literature: 2009 (n = 3), 2010 (n = 02), 2011 (n = 4), 2012 (n = 1), 2013 (n = 1) and 2015 = 3). The timeline of the results shows a growing interest in membranes for GBR in dentistry. However, we did not identify randomized blinded trials in humans that were published from 2016-2017.

GBR Membranes Used for Alveolar Bone Preservation

According to the proposed methodology, six publications were identified, which are presented in table 3. These studies correspond to randomized blinded[36-39] and blinded split-mouth trials.[17,18,40]

Table 3. Characteristics of the studies on alveolar bone preservation displayed in chronological order (n = 6)

Author/year	Study Type	Sample and age	Follow-up	Treatment	Assessment methods	Results	Study considerations
Lekovic *et al*. 1998	BRCSMCT	16P(10M/6W); MA =52,6 ± 11,8	6Mo	EG: SD filled with BMGLP; CG: without membrane.	Titanium pins were placed on the outer surface of the BBP of the DA after extraction at a distance of 2 to 5 mm from the coronal border of the bone wall. Measurements with PP were performed: 1) EVM = more coronal distance from the pin to the coronal edge of the buccal bone plate; 2) IVM: distance from the most apical end of the DA after extraction and the coronal border of the BBP; and 3) HM: distance from the coronal border of the buccal bone to the coronal edge of the buccal or palatal bone plate	Significant differences in relation to EVM (1.81 ± 0.19 versus 3.31 ± 0.23); IVM (3.00 ± 0.18 versus 6.94 ± 0.34 mm) and HM (2.94 ± 0.19 versus 7.50 ± 0.26 mm). Measurements between the CG and the EG showed that the EG presented significantly lower changes in EMV (P <0.0005), greater changes in IMV (P <0.00001) and lower changes in MH (P <0, 00001).	Treatment of DA after extraction with glycolic and BMGLP is valuable in preserving and preventing defects in alveolar bone in dental extractions.
Aimet, Pigella e Romano, 2007	BRCSMCT	15P (10W/M); MA = 24,9 ± 5,46	12Mo	EG: SRP + BMGLP (n=15); CG = SRP (n=15)	Measurements with PP were performed: 1. Distance from the CEJ to the most apical point of the crest of the BBP; 2. Distance from the CEJ to the most apical point of the ridge of the LBP; 3. Distance from the CEJ to the most apical point of the crest of the DBP; 4. Mesiodistal defect width; 5. Mesio-buccal defect width; 6. Depth of defect to buccal bone crest; 7. Depth of defect to buccal bone crest.	BMGLP showed statistically significant bone gain compared to the control group (P <.0001)	It would be of significant benefit to patients if defects in the distal second molars were treated and regenerated with BMGLP after extraction of adjacent third molars.

Samartino *et al*., 2009	ECRC	18P(9W/9W); AR = 21-25	18We	EG: DA filled with PRP + RM (Bio-Gide; Geistlich Biomaterials, Wolhusen, Switzerland); CG: only PRP.	Measurements with 3-position periodontal probe (distal, distal-buccal and disto-ligual); Depth of survey was evaluated; level of insertion to the gingival probing and recession.	There was a statistically significant difference in the values of the insertion level to the probing in both groups. However, the resorbable membrane did not confer any additional clinical benefit to the bone repair process.	Although the clinical results of comparison of platelet-rich plasma alone versus platelet-rich plasma + resorbable membrane can be considered histologically similar, platelet-rich plasma + resorbable membrane showed earlier signs of bone maturation, but not a grade higher bone regeneration.
Mardas, Chadha e Donos, 2010	BRCT	27P(6M/21W); (MA of EG = 39.5 - 7.8; MA of CG = 34.9 _ 14.2)	8Mo	EG: DA with SBC (Straumann AG, Basileia, Switzerland) + MR (Bio-Gide, Geistlich, Switzerland); CG: AD with DBBM (Geistlich Biomaterials, Wollhusen, Switzerland) + + MR (Bio-Gide, Geistlich, Switzerland).	Horizontal and vertical dimensions of the alveolar bone crest were reevaluated and biopsies were performed for histological analysis in all patients.	patients completed the study. Both materials preserved the mesio-distal height of the alveolar bone crest. Histological analysis showed new bone formation in the apical part of the biopsies, which in some cases was in direct contact with particles of Straumann Bone Ceramics and Deproteinized Bovine Bone Bio-Oss. The coronal part of the biopsies was occupied by a dense fibrous connective tissue that surrounds the particles of Straumann Bone Ceramics and Bio-Oss Deproteinized Bovine Bone.	Straumann Bone Ceramics and Deproteinized Bovine Bone Bio-Oss + Membranes partially preserved the width and the interproximal bone height of the alveolar bone crest.
Friedman *et al*., 2011	BRCT	37P (MA:53)	6 Mo	EG: 17P – BCP + RCLCM; CG: BCP + NCLM.	The primary endpoint was to quantify the effect of the membrane on the dimensional changes of the bone margins at the alveolar crest level of implants. Bone gain in width and height was calculated.	The increase of mineralized tissue in the alveolar bone crest was significantly higher in the lateral test group (1.8 vs 0.7 mm, p = 5,046) and in vertical dimensions (1.1 vs 0.2 mm, p = 5.035) compared to controls.	Ribose crosslinked collagen membranes supported the mineralization and remodeling process even at sites showing impaired healing as indicated by the morphometric result.
Cortell-Ballester *et al*., 2015	BRCT	30P (MA = EG: 35.6 - 6.3; CG = 33.8 - 6.9)	6Mo	EG: RM; = Without RM.	PD of the lower second molar was measured at 3 sites: distal-vestibular, distal, disto-lingual and distal-vestibular insertion level.	PD of the lower second molar the distance from the cemento-alveolar junction and the alveolar bone crest to the base of the defect showed greater improvement in the experimental group ($p < 0.05$).	The use of a bio-guide collagen membrane after extraction of the third molar or mesioangulated or impacted third molars stimulates bone regeneration, improves insertion level and bone filling distal to the lower third molar.

AR = Age Range; BBP = Buccal Bone Plate; BCP = Biphasic Calcium Phosphate; BMGLP = Bioabsorbable Membrane of Glycolic and Lactide Polymers; BRCSMCT = Blinded and Randomized controlled split-mouth clinical trial; BRCT = Blinded and Randomized clinical trial; CEJ = Cementum-Enamel Junction; CG = Control Group; CRCM = Non-Ribose crosslinked collagen membranes; CRCM = Ribose Crosslinked Collagen Membranes; DA = Dental Alveolus; DBBM = Deproteinized Bovine Bone Mineral; DBP = distal bone plate; EG = Experimental Group; EVM = External Vertical Measurements; HM = Horizontal Measurement; IVM = Internal Vertical Measurement; LBP = Lingual Bone Plate; M = Men; MA = Mean Age; Mo = Months; P = Patients; PD = Probing Depth; PP = Periodontal Probe; PRP = Platelet-rich plasma; RM = Resorbable Membrane; SBC = Straumann Bone Ceramics; SC = Surgical Defect; SRP = Scaling and Root Planning; W = Women; We = Weeks.

Some studies suggest that the treatment of the alveolar bone with membranes after surgical procedures constitutes a valuable approach to preserve and prevent defects after dental extractions[17], improving the clinical attachment and bone levels in the region[36] through supporting bone formation.[37] Thus, the treatment of these defects with membranes could exert significant benefit to the patients.[38]

However, there is evidence that GBR membranes exerted a partial effect on the preservation of bone width and height,[25] without additional clinical benefit to the bone repair process when compared to treatment approaches such as platelet-rich plasma[37] or grafts alone.[38]

We also observed different approaches and membranes for GBR, such as absorbable membrane of glycolic and lactic polymers,[18,38] resorbable collagen membranes[35,37,38] and ribose cross-linked membranes.[39] Thus, the results should be interpreted with caution due to the risk of bias.

GBR Membranes Used for Endodontic Application

The literature research reported only two randomized and blinded clinical studies[41,42] on membrane applications for guided bone regeneration in endodontics, published in 2002 and 2011 (Table 4). The results of the bibliographic research are conflicting.

Table 4. Characteristics of the studies on GBR with endodontic application displayed in chronological order (n = 2)

Author/year	Study Type	Sample and age	Follow-up	Treatment	Assessment methods	Results	Study considerations
Garret *et al*., 2002	BRCT	26P (EG: 16P; CG: 9P); AR =24-67	12Mo	EG: PABRM (Guidor, Besenville, IL) CG: without PABRM.	Periapical surgeries were performed where the non-surgical root canal therapy failed and a periapical lesion occurred. Follow-up radiographs at 3, 6 and 12 months were compared to radiography performed immediately after surgery, using digital images and a densitometric relationship that gave a numerical estimate of bone healing	There was no statistical difference between the rate of bone healing in cases where the resorbable membrane based on polylactic acid was used and in cases where no membrane was used.	A polylactic acid resorbable membrane has no beneficial effect on the rate of bone healing and the additional expense to the patient would not be warranted in such cases.
Goyal *et al*., 2011	BRCT	30P. AR = 17-45.	12Mo	CM (n = 10); PRP (n = 10); CS + PRP (n = 10).	The study compared the use of PRP, PRP + CS and a CM in the treatment of apicomarginal defects. Clinical and radiographic measurements were determined at baseline and every 3 months after surgery up to 1 year. The cases were defined as healed when there were no clinical signs or symptoms, and the radiographs showed complete or incomplete (scar tissue) healing of previous radiolucencies.	All three treatments had highly significant reductions (P <0.05) in periodontal pocket depth, clinical insertion level, at the position of the gingival margin; in the periapical lesion size, in the percentage reduction of periapical rarefaction and periapical healing. There were no significant differences between the three groups for these parameters (P> 0.05).	Platelet-rich plasma or platelet-rich plasma + collagen sponge leads to improvements in clinical outcomes of apical margins in terms of periapical healing, clinical insertion level, periodontal pocket depth reduction. PRP may be an alternative treatment to the collagen membrane in AM treatment.

AR= Age Range; BRCT = Blinded and Randomized clinical trial; CG = Control Group; CM = Collagen Membrane; CS = Collagen sponge; EG = Experimental Group; MA = Mean Age; Mo = Months; P = Patients; PABRM = Polylactic acid based reabsorbable membrane; PRP = Platelet Rich Plasma.

In a one-year evaluation study, Garret *et al*.[41] with 26 patients between 24 and 67 years of age, found that there was no statistically significant difference between bone healing in cases where a polylactic acid-based resorbable membrane was or was not used in periapical surgeries. It suggests that the use of this membrane would not have an additional beneficial effect in relation to the bone formation. Therefore, not justifying the additional expense for the patient.

Goyal *et al*.,[42] 30 patients were compared of the use of platelet-rich plasma in a combination with collagen sponge and a collagen membrane for the treatment of apical-marginal defects. It was observed that all treatment modalities presented significant reductions, with no significant differences between the three groups in relation to periapical healing.

It is important to highlight that, even when applying similar methodologies in both studies, the results should not be extrapolated due to the different treatments and membranes used, as well as the limited number of available publications identified according to the methodology used in this literature review.

GBR Membranes Applied in Dental Implants

Five studies regarding the use of membranes for guided bone regeneration with dental implant application (Table 5) were found. Four blinded randomized clinical trials[43-46] and one blinded and randomized multicenter clinical study.[47]

Table 5. Characteristics of the studies on GBR used in dental implants displayed in chronological order (n = 5)

Author/ year	Study Type	Sample and age	Follow-up	Treatment	Assessment methods	Results	Study considerations
Merli, Migani e Esposito, 2007	BRCT	22P (MA in the EG:44.6; MA in the GC = 49.9).	6Mo	EG (11P): CM (Bio-Gide; Geistlich Pharma, Wolhusen, Switzerland); GC (11P): ABG + NRM (e-PTFE, W.L. Gore & Associates, Flagstaff, AZ);	Failure or mobility in the dental implant were manually verified; Vertical bone regeneration was measured in mm with a periodontal probe on the day of surgery and at the pillar connection	EG and CG obtained significant bone gain and with desired results, 2.2 mm (SD=1.5; P <0.001) on average for RRM and 2.5 mm (SD 1.1) for NRM (P <0.001). There was no SSD in bone gain between the 2 procedures (P = 0.58). Complications occurred in 40% of patients. There was no difference in the occurrence of complications between the procedures (P> 0.99).	Both techniques were effective in bone gain. However, both were associated with complications. Clinicians and patients should carefully balance risks and benefits when considering GBR use.
Jung *et al*., 2008	BRCT	37P (MA=48)	6Mo	EG: (19P; PGRM - Institut Straumann AG, Basel, Switzerland) GC: (18P; CRM, Bio-Gide, membrane; Geistlich Pharma AG)	The study was performed with patients who required implant treatment with BD. The height of the BD was measured and BD of 3 mm were excluded from the study. The alteration in VBG was evaluated: Height (mm) = of implant surface for bone-implant contact; Width (mm) = Distal and mesial alveolar bone crest of bone; defect depth (mm): from the alveolar bone crest to the surface of the implant; ID height (mm): from Alveolar bone crest for bone-implant contact;	Bone regeneration was similar to native bone. Vertical bone regeneration was 5.63 ± 1.84 mm in the experimental group and 4.25 ± 1.16 mm in the control group. More complications were observed with the polyethylene glycol resorbable membrane, but all were recovered without intercurrences.	The PGRM was as successful as a collagen membrane in the treatment of bone dehiscence defects in dental implants with simplified clinical handling.
Agelis *et al*., 2011	BRCT	80P MA in EG: 46.4 (20-77) MA in CG: 47.7 (24-75).	12Mo	EG: 40P; GBR + CRM (OsseoGuard, Biomet 3i). GC: 40P; GBR + CRM (OsseoGuard, Biomet+ BS (Endobon; Biomet 3)	The measures evaluated were implant failures, complications, pink aesthetics, patient satisfaction and marginal peri-implant bone levels.	After implant placement, mean bone levels were -0.21 mm in GBR + BS and -1.92 mm GBR, while at 1 year after loading were -1.04 and -1.76, respectively. When comparing the two groups, GBR + BS implants showed 0.70 mm more peri-implant marginal bone than GBR implants. Aesthetics was statistically significantly better for the GBR + BS.	The use of bone substitute (Endobon) with resorbable collagen membrane (OsseoGuard) in bone dehiscence around the Intraosseous Defect improves the aesthetic result.

Ramel *et al*., 2012	BRCT	37P	36Mo	EG: PGRM (MembraGel, Institut Straumann) CG: MRC (Bio-Gide membrane, Geistlich Pharma)	Form, color, and coverage of peri-implant soft tissues were examined by visual assessment of clinical appearance. The marginal bone level (the distance from the abudment-implant to the first BIC) was measured in the mesial and distal aspects. The abudment-implant junction was designated as reference point (0 mm).	The mean changes in the distance between the first BIC at the transition point were 0.43 ± 0.56 mm (PGRM) and 0.21 ± 0.36 mm (CRM) at 1 year and 0.61 ± 0.89 mm (polyethylene glycol reabsorbable membrane) and 0.33 ± 0.64 mm (CRM) at 3 years. The respective differences between groups were 0.13 mm (1 year) and 0.31 mm (3 years), which were not significant at both times.	PGRM showed better results than collagen resorbable membrane in the treatment of bone dehiscence around dental implant in relation to clinical parameters of soft tissue and marginal bone levels after a 3-year follow-up period.
Gassling *et al*., 2013.	BRCT	6P MA (54-69)	12Mo	CG: CRM (Bio-Gide, porcine collagen types I and III); EG: PRFM	The study evaluated the effect of two resorbable membranes, platelet-rich plasma membrane and Bio-Gide, on the bone formation of bone autografts. The results were assessed clinically (visually) and histomorphometrically.	The mean bone formation after 5 months was 17.0% and 17.2%, for the EG and CG, respectively. The mean residual bone substitute was 15.9% and 17.3% for EG and CG, respectively. No local complications, such as dehiscence or membrane exposure, were found at any site in any of the treated patients. After 12 months, all implants achieved primary stability on the maxillary sinus floor increased without any inflammation of the peri-implant tissue.	The different absorbable membranes resulted in a similar amount of bone formation.

ABG = Autogenous Bone Graft; BD = Bone Dehiscence; BIC= Bone-Implant Contact; BRCT = Blinded and Randomized clinical trial; BS = Bone Substitute; CG = Control Group; CM = Collagen Membrane; CRM = Collagen Resorbable Membrane; EG = Experimental Group; ID = Intraosseous Defect; MA = Mean Age; Mo = Months; NRM = Non-Resorbable Membranes; P = Patients; PGRM = Polyethylene Glycol Resorbable Membrane; PRPM = Platelet Rich Plasma Membrane; RM = Resorbable Membrane; SD = Standard Deviation; SSD = Statistically Significant Difference; VBR = Vertical Bone Regeneration.

Merli, Migani and Esposito[43] evaluated a resorbable and a non-resorbable membrane and both treatments were effective in bone augmentation for dental implants. However, the membranes employed were associated with complications. The authors emphasize that the risks and benefits when considering the use of GBR membranes should be carefully balanced.

Comparing resorbable and polyethylene glycol membranes, Jung *et al*.[44] found that polyethylene glycol membranes presented simplified clinical handling and enhanced bone gain results. This corroborates with Ramel *et al*.,[45] whose study compared the clinical performance of a polyethylene glycol and a collagen resorbable membrane and it was found a statistically significant evidence that the polyethylene glycol membrane present better results than the collagen membrane in the treatment of bone dehiscence around dental implants.

Gassling *et al*.[46] evaluated a platelet-rich plasma membrane and a collagen membrane and found that the two resorbable membranes resulted in a satisfactory and similar amount of bone formation. The use of resorbable collagen membranes has also been associated with a better aesthetic gain around dental implants.[47]

GBR Membranes Used for the Treatment of Furcation and Intraosseous Defects

Table 6 shows the main characteristics of the 14 studies included on membranes for bone regeneration in furcation and intraosseous defects according to: authorship, type of study, follow-up period, sample, methodology, results and considerations. These studies are blinded randomized clinical trials[48-58] and blinded randomized split-mouth clinical studies.[59-61]

Table 6. Characteristics of the studies on GBR in intraosseous and furcation defects in chronological order (n = 14)

Author/year	Study Type	Follow-up	Sample	Methods	Results	Study considerations
Cortellini, Prato e Tonetti, 1996	BRCT	12Mo	36P (18BD)	The EG was treated with RCM positioned coronal to the interproximal bone crest; CG was treated with coronally applied NRM (ePTFE) to the alveolar bone crest; The third group was treated with FS. At the time of surgery and after the debridement of the defects were measured: 1) distance from the CEJ to the defect; 2) distance from the CEJ to the more coronal extension of the interproximal bone crest.	All groups resulted in clinically significant improvements in CAL and reductions in PD; 2) a statistically significant treatment effect (P <0.0001, ANOVA) was observed comparing the EG (4.6 ± 1.2 mm), CG (5.2 ± 1.4 mm) and FS (2.3 ± 0.8 mm) in terms of CAL; the differences in terms of AL between the EG and the CG were not statistically significant (P = 0.19); EG and CG gained significantly more CAL (P <0.0001, t-test). AL> 4 mm were observed in 83.3% of the cases in both GBR groups EG + CG), while gains of AL to the probing of this magnitude were not detected in the SF.	Clinically significant insertion-to-probe level gains can be obtained with GBR procedures using absorbable collagen membrane and non-resorbable membrane. Patient morbidity, however, was lower in the group treated with absorbable collagen membrane
Christgau *et al*., 1998	BRCSMCT	12Mo	25P (50BD)	Patients were treated with PAM or with Polyglactin-910 membrane. They were recorded using PP: PBI (ISP), gingival recession (gingival recession, probing depth, insertion level to the probe; relative vertical insertion gain was calculated as% of the insertion level to the maximum related probe of insertion gain (expressed by the measured depth of shape of the bone defect) Standard intraoral radiographs were quantitatively evaluated for bone changes (density, area) in the region of bone defect	PAM and polyglactin-910 membrane provided significant reductions in PD and level of clinical insertion. 60% relative vertical insertion gain on polylactic acid membrane and 58% relative vertical insertion gain on polyglactin-910 membrane. Standardized intraoral radiographs revealed a significant gain in bone density, 58.3% of the initial defect area in PLA, and 54.0% of the initial defect area in the polyglactin-910 membrane showed bone density gain. Neither clinical nor radiographic data revealed a significant difference between the 2 types of membranes	Polyacrylic acid membrane and polyglactin-910 membrane demonstrated similar favorable results in bone regeneration of intraosseous defects
Kim *et al*., 1998	BRCT	12Mo	26P (26 BD)	EG: DBB + CSM (13P). CG: FS (13 P). PD, CAL, gingival recession and bone level were recorded after oral hygiene orientation and SRP	The reduction of the PD (mean ± SD) for EG and CG was 4.3 ± 0.5 and 3.0 ± 1.3 mm; The CAL was 2.9 ± 0.8 and 1.7 ± 1.5 mm; and the increase in the level of bone was 2.9 ± 1.4 and 1.2 ± 1.2 mm, respectively. Clinical improvements were significantly different from surgery for both groups (P <0.01). There were no significant differences between the groups in the reduction of PD and CAL. The bone level increase was significantly higher in the demineralized bovine bone + CSM group compared to CG (P <0.05).	Demineralized bovine bone + calcium sulfate membrane resulted in reduced probing depth and improved clinical insertion level comparable to surgical flap. However, bone gain in deep periodontal pocket assessed by clinical parameters was greater than that observed only by the surgical flap. These changes were observed at 6 and 12 months after surgery. This regenerative technique needs further biological evaluation before it is generally accepted.

Eickholz *et al.*, 2000	BRCT	12Mo	21 (44 BD) MA: 22-64.	The study compared 2 resorbable membranes: control group = PLATC; experimental group: PDO. Gingival index, plaque index, PD, loss of vertical clinical insertion, loss of horizontal clinical insertion and standard intraoral radiographs were measured	Four weeks after surgery, 61% of all barriers were exposed to some degree. However, both treatments revealed a significant reduction of gingival index (P <0.005), reduction of PD (-3.08 ± 2.29 mm [EG], -3.52 ± 2.67 mm [GC] P <0.001) and gain of loss of vertical clinical insertion (2.44 ± 2.29 mm [EG], 2.80 mm ± 2.21 [CG], P <0.001) 12 months after surgery on all defects. Within the intraosseous defects, significant bone filling (2.03 ± 1.70 mm [EG], 1.91 ± 1.20 mm [CG], P = 0.001), and within the furcation, an insertion loss gain (0.79 ± 0.68 mm [EG], 1.13 ± 1.44 mm [CG], P <0.05).	Regarding the reduction of gingival index and probing depth, as well as to the increase of loss of vertical clinical insertion and loss of horizontal clinical insertion, this study did not reveal statistically significant or clinically relevant differences between the experimental group and the control group. Thus, the use of both resorbable membranes in GBR therapy may be recommended.
Joly *et al.*, 2002	BRCSMCT	8Mo	10P MA=35-65.	The study evaluated the effect of GBR using RM in the treatment of ID. Prior to the surgical phase, patients were enrolled in a rigorous maintenance program, including guidance on oral hygiene and SRP (PI and GI <10%). Clinical measurements were performed with an electronic probe. Measurements included: CAL, gingival margin level, PD, bone level at sowing and level of ACB. EG = GBR; CG = FS. Standard intraoral radiographs were taken at baseline and 8M. Digital images were analyzed by subtraction to evaluate changes in area (A) and optical density	Statistically significant differences were found in both groups when comparing baseline and posttreatment levels for clinical insertion, gingival margin level, depth of probing and bone level to soda (P <0.01). Higher reductions in bone level, sizing and area gain and optical density were observed in the GTR group when compared to control (P <0.01). Both therapies were effective in improving the clinical parameters evaluated	The clinical and radiographic findings of this study demonstrated greater bone filling at GTR treated sites
Vouros, Aristodimou e Konstantinidis, 2004	BRCT	12Mo	34P	The study compared two RM (RM and PAM) combined with BBM with FS alone to treat ID. The ECI (depth of probing and level of clinical insertion) was performed 2 months after completion of conservative treatment to verify the depth of the defect. The patients were divided into three groups: resorbable membrane + BBM, PAM + BBM and surgical flap. The results of the clinical treatment were finally evaluated 12 months after surgery for changes in depth of probing and level of clinical insertion. Baseline and 12-month radiographs were compared using nonstandard digital radiography	PD of 5.08 mm and mean gain of CAL of 4.39 mm occurred In RM + BBM. The corresponding values for the PAM + BBM group were 4.72 and 3.71 mm. FS produced values of 2.50 and 2.43 mm. All improvements in clinical parameters were statistically significant (p> 0.001) in groups for all variables. Both RM produced a statistically greater reduction in PD and gain CAL compared to FS (p> 0.05). The comparison between the RM did not reveal a statistically significant difference in the reduction of PD (p = 0.56) or in the gain of CAL (p = 0.34).	Placement of the resorbable membranes in the present study in combination with the BBM graft significantly improved the clinical and radiographic parameters of the deep periodontal pocket, which was superior to the surgical flap

Dori *et al*., 2007	BRCT	12Mo	24P	The study evaluated the effect of PRP on the healing of deep ID treated with IBMB and GBR with a NRM (ePTFE). 24P with advanced chronic periodontal disease and IO were randomly treated with a combination of PRP + IBMB + GBR or IBMB + GBR. They were evaluated at the beginning and 1 year after treatment: plaque index, gingival index, bleeding probing, PD, gingival recession and CAL.	No differences were observed in any of the parameters studied at the baseline between the groups. PRP + IBMB + GBR showed a reduction in mean PD of 8.6 - 1.7 mm to 3.1 - 1.3 mm (P <0.001) and a change in CAL, mean of 10.3-1.4 mm to 5.7-1.6 mm (P <0.001). In the group treated with IBMB + GBR, mean PD was reduced from 8.8 - 1.7 mm to 3.1 - 1.0 mm (P <0.001) and mean CAL changed from 10.4-2.6 mm to 5.9-1.8 mm (P <0.001). In both groups, all sites gained ‡ 3 mm CAL. No statistically significant differences were observed in any of the parameters studied between the two groups.	Ideal clinical results were obtained with inorganic bovine mineral bone + GBR with non-resorbable membrane, with or without addition of platelet rich
Yassibag-Berkman *et al*., 2007	BRCT	12Mo	2P (30 ID)	The study evaluated the efficacy of PRP in combination with ABTPG and RCM in the treatment of anterior interproximal ID. ID were divided into three groups: ABTPG, ABTPG + PRP and RCM + PRP + ABTPG. The following were evaluated: plaque index, gingival index, clinical insertion level, PD.	At the end of 12 months, the clinical insertion level was 2.4, 2.1 and 2.5 mm in the three treatment groups, respectively. No statistically significant differences were observed in the clinical and radiographic measurements between the groups	All treatments were effective in the treatment of anterior interproximal ID. The results also suggested that platelet rich plasma did not add any clinical benefit to Alloplastic B-Tricalcium Phosphate Graft used alone or in combination with GBR.
Paolantonio *et al.,* 2008	BRCT	12Mo	51P	The study compared the clinical results of GBR with CSG in terms of gain of CAL in ID. The subjects had a ID with PD ≥ 6 mm and divided into 3 equal groups: FS, FS + CSG, FS + RCM. One year after the surgical treatment, a complete clinical examination and a surgical re-entry were performed. Pre- and post-therapy clinical parameters including PD, CAL, surgical flap and bone defect level were compared	SSD in all parameters evaluated (PD and CAL, P <0.001, gingival recession and level of bone defect, P <0.05). Differences (PD, CAL and bone defect level, P <0.001, GR, P <0.05) were also observed in the three groups. The RCM and CSG groups had values of PD, CAL and bone defect level significantly lower than those treated with only FS. Significantly greater reduction and decrease in clinical insertion level and bone defect level in GBR compared to FS. No SSD were observed between RCM and CSG.	Both regenerative treatments produced additional clinical benefits on surgical flap alone. In addition, the use of calcium sulphate graft can minimize post-surgical recession
Santana, Matos, Dyke, 2009	BRCT	12Mo	60P	The study evaluated the clinical response of Class II furcation lesions with GBR. CERT (n = 30) was compared to the FS (n = 30). The CERT was a combination of absorbable hydroxyapatite and tetracycline (3: 1), an NRM and FS. Plaque index, bleeding probing, gingival recession, PD, CAL, loss of horizontal clinical insertion vertical clinical insertion loss, vertical furcation height, horizontal furcation depth and the amount of tissue under the NRM.	Both treatments resulted in improvements in all clinical variables evaluated. Reduction in DP of 3.65 - 0.6 mm and 0.60 - 1.0 mm; Vertical gains of 3.05 - 0.6 mm and 0.65 - 0.6 mm and horizontal gains of 3.45 - 1.3 mm and 0.55 - 0.7 mm in CERT and SF, respectively. In the CERT, significant positive correlations were found between initial PD and reduction of PD, and the initial vertical furcation height correlated positively with the reduction of PD and horizontal height gain. The horizontal furcation depth and the amount of tissue formed under the NRM were positively correlated with the reduction of the PD and the horizontal furcation height and vertical furcation height gains. For the FS group, the initial PD correlated positively with the reduction of PD and the gains of furcation vertical height and horizontal furcation height and correlated negatively with the gingival recession. The initial vertical furcation height correlated positively with reductions of PD.	Experimental combined regenerative therapy presented significantly better clinical results, with greater reduction of depth of probing, vertical furcation height gains and horizontal furcation height, and greater frequency of furcate closure compared to surgical flap, and it was shown to be promising as a treatment technique regenerative.

Nygaard-Østby *et al*., 2010	BRCT	10y	40P (36BD)	The study evaluated the stability of autogenous bone results with or without GBR in the treatment of deep intraosseous defects.	Significant improvements in PD and CAL were observed for both groups. The results were maintained over the 10-year follow-up. However, the intergroup comparisons at 10 years showed that autogenous bone + ROG showed significantly greater reduction of depth of probing and level of clinical insertion than only autogenous bone	Statistically significant difference were found with adjunct use of GBR with autogenous bone at 10 years. However, these results should be interpreted with caution in light of their clinical relevance and biological rationality
Siciliano *et al*., 2011	BRCT	12Mo	40P (35 BD)	The study compared the healing of intraosseous defects treated with enamel matrix derivative (EMD) or ROG. ID were treated with EMD alone or with reinforced titanium non-resorbable membrane. No graft materials were used. At the baseline and after 12 months, depth of probing and level of clinical insertion were recorded.	At the baseline, ID were 8.5-2.2 mm at sites treated with EMD and 8.6-1.7 mm at sites treated with reinforced TNRM (P = 0.47). The average gain of CAL with reinforced TNRM was significantly higher (P <0.001) than EMD (4.1-1.4 mm versus 2.4-2.2 mm, respectively). NRM of reinforced titanium compared with EMD, significantly (P = 0.01) increased the probability of increasing clinical insertion CAL (79.2% vs. 11.3%, respectively).	Although the surgical flap had not been investigated the application of enamel matrix derivative alone appeared to produce less reduction of depth of probing and increase of insertion level to the probe compared to reinforced titanium non-resorbable membrane in the treatment of intraosseous defects.
Esposito *et al*., 2015	BRCT	12Mo	97P	The study evaluated the efficacy of a BS covered with a RM versus surgical flap for ID. Patients were allocated: BS + RCM (49P) or surgical flap (48P). Dental loss, complications, patient satisfaction with treatment and aesthetics, CAL, PD, gingival recession, radiographic bone level in standard intraoral radiographs, plaque index and gingival bleeding index were evaluated	At the baseline, there were more teeth with mobility in the BS + RCM (29 versus 15). One year after treatment, two patients abandoned the BS + RCM group. Three complications (minor dehiscence of the postoperative wound) occurred in the bone BS + RCM versus none in the surgical flap group, where the difference was not statistically significant. The b BS + RCM group obtained a statistically significant difference in the CAL (mean difference = -0.8 mm, 95% CI [-1.51, -0.03], P = 0.0428), reduction of DP (mean difference = -1.1 mm, 95% CI [-1.84, -0.19], P = 0.0165) and radiographic bone level (mean difference = -1.2 mm, 95% CI [-2.0, -0.4], P = 0.0058) compared to the surgical flap group. No SSD were observed between groups for gingival recession.	The use of bone substitute + resorbable membrane compared with the than surgical flap produced statistically significant difference in the treatment of intraosseous defects, which was superior to 3 mm, in relation to the gain of the clinical Insertion level, reduction of probing depth and gain of radiographic bone level.
Kiany e Moloudi, 2015	BRCSMCT	6Mo	10 (20 BD)	The study evaluated and compared the effectiveness of amniotic membrane with BBM and a resorbable membrane with BBM in GBR for the treatment of intraosseous defects. The 10 patients with chronic periodontitis and bilateral intraosseous defects ≥ 4 mm and depth of probing ≥ 6 mm were divided: experimental group: amniotic membrane + BBM and control group: resorbable membrane + BBM. Periodontal clinical parameters were recorded at baseline and at 6 months after treatment	PD, CAL and bone level to soda showed significant improvements after 6 months in the experimental group and control group. Surgical delivery showed a significant increase in the control group, but not in the experimental group. The changes in the median depth of depth and level of preoperative and postoperative clinical insertion between the groups were not significant. There was no significant relationship between the depth of the basal bone defect and the gain level of clinical insertion	Amniotic membrane and resorbable membrane in conjunction with BBM provided improvements in clinical periodontal parameters. Amniotic membrane did not induce significant surgical flap and is suggested as a novel barrier membrane in GBR treatment.

ABC = Alveolar Bone Crest; ABTPG = Alloplastic B-Tricalcium Phosphate Graft; AL = Attachment Level; BBM = Bovine Bone Mineral ; BD = Bone Defect; BRCSMCT = Blinded and Randomized controlled split-mouth clinical trial; BRCT = Blinded and Randomized clinical trial; BS = Bone Substitute; CAL = Clinical Attachment Levels; CEJ = Cement-Enamel Junction; CERT = Combined Experimental Regenerative Therapy; CG = Control Group; CSG = Calcium Sulfate Graft; CSM = Calcium Sulphate Membrane; DBB = Demineralized Bovine Bone; EG = Experimental Group; FSP = Flap

Surgery; IBMB = Inorganic Bovine Mineral Bone; ID = Intraosseous Defects; MA = Mean Age; Mo = Months; NRM = Non-resorbable Membrane; P = Patients; PAM = Polylactic Acid Membrane; PBI = Papillary Bleeding Index; PD = Probing Depth; PDO = Polidioxanon; PLATC= polylactic acetyl tributyl citrate; PP = Periodontal Probe; PRP = Platelet Rich Plasma; RCM = Resorbable Collagen Membrane; RM = Resorbable Membrane; SD = Standard Deviation; SRP = Scaling And Root Planning; SSD = Statistically Significant Difference; TNRM =Titanium Non-Resorbable Membrane; Y = Years.

Significant and positive gains in bone attachment levels can be obtained with the use of GBR membranes in furcation and intraosseous lesions with lower complications and morbidity for the patient.[48] Eickholz *et al*.[58] analyzed the clinical performance of two resorbable membranes and observed a reduction in plaque index and probing depth, thus recommending their use for the treatment of furcation and intraosseous defects.

There is evidence of greater bone filling in regions where treatment with bone regeneration was employed alone[57,60] or in combination with bovine bone[51,52] hydroxyapatite[55], bone substitute[58] or autogenous bone.[56] It also produced additional clinical benefits such as minimizing the post-surgery recession compared to single surgical flap techniques.[54] Polylactic acid or polyglactin-910 membranes also demonstrated similar favorable results in bone regeneration of intraosseous defects.[58]

When compared to surgical flap techniques, the use of calcium sulfate membranes in combination with demineralized bovine bone resulted in reduced probing depth and improved clinical attachment levels. It was also observed that the bone gain evaluated in deep periodontal pockets was greater compared with only surgical flap techniques.[49]

Yassibag-Berkman *et al*.[53] evaluated the platelet-rich plasma in combination with collagen-resorbable membranes in the treatment of anterior interproximal intraosseous defects and found that all treatment options were effective and that the addition of plasma platelet-rich combination did not add any additional clinical benefit when in combination with the GBR treatment.

Study Limitations

Although this review was carried out on randomized clinical trials, the difficulty of categorizing and standardizing the data presented an important limitation. However, the results offer a certain confidence since the selection and quality evaluation of the studies were strictly followed, reducing possible flaws in this process. It was emphasized that the adoption of strict inclusion and exclusion criteria had a significant impact on the results found as well as its applicability.

Another possible limitation of this systematic review was the use of only three electronic databases (PubMed, Web of Science and Scopus), not including the gray literature. However, the three included databases indexes a large amount of manuscripts that offer good quality of scientific evidence in the medical and dental area. Data meta-analysis was not performed and may also be considered a limitation of this study. However, an accurate synthesis with deep critical assessments of these studies prevailed in order to make this review more informative and reliable.

In view of the number of studies that were disregarded for analysis due to the proposed methodology, it would be plausible to conduct a study that contemplated a holistic view of the use of membranes for guided bone regeneration in dentistry, with different follow-up intervals. A review based on clinical cases could favor a more comprehensive view of this issue.

The number of studies that met the inclusion criteria on GBR membranes with application in endodontics (n=2), dental implants (n=6), and preservation of alveolar bone in surgical cases (n=6) were observed. This number may suggest the need for future controlled and randomized clinical trials, duly designed to better assess the potential of GBR use in patients undergoing this treatment approach, especially involving endodontic procedures.

Implications for Clinical Practice

The present literature review included different types of membranes and approaches combined with or without bone substitutes that guided bone regeneration in dentistry. Most of these studies showed significant differences between the membranes used considering the investigated parameters. It was seen to contribute to the role of GBR membranes in the preservation of the alveolar bone or bone gain in procedures for dental and periodontal procedures. However, in specific cases such as GBR membrane for endodontics, it was not possible to provide further considerations due to the lack of available clinical evidence. Randomized and blinded clinical studies are need in order to provide more reliable results with a minimum bias in its approach.

Regarding the treatment of furcation or intraosseous defects, these findings showed that guided bone regeneration through membranes was effective for resolution of cases when compared with flap surgery alone. These data corroborate a systematic review, meta-analysis,[30] and a systematic review[23] which demonstrated that GBR is more effective in gain of clinical attachment and reduction of probing depth in the treatment of intraosseous as well as furcation defects.

It is not fully explained in the scientific literature if the combination of barrier membranes and graft materials can contribute to the guided bone regeneration process when comparing membranes or graft materials alone. However, the combination therapies presented better results than the

isolated therapies, with small additional benefits.[22,28]

The small number of studies that met the inclusion criteria of this literature review limited the conclusions about GBR's success in certain dentistry areas. The diversity of techniques and membranes employed show the need for controlled clinical trials to support predictable and successful treatment protocols using membranes for guided bone regeneration.

Although most of the results corroborates with satisfactory clinical results, they should not be extrapolated, since there is a probability that there will be a continuous disagreement about clinical recommendations, techniques and membranes that should be used when considering its application. Therefore, the decision to conduct guided bone regeneration therapy using barrier membranes requires caution and individual assessment of each patient. The decision-making process, whether or not to consider the use of GBR membranes should be based on the available scientific evidence combined with the clinical experience of the professional.

Conclusion

The small number of studies that met the inclusion criteria limited the conclusions on the success of membranes for guided bone regeneration in specific dentistry areas. However, there is a strong evidence of the important role of the use of GBR membranes in procedures involving dental implants in aesthetic areas as well as in treatment of intraosseous or furcation defects, which suggests their indication in these cases.

It has not been showed to what extent the use of membranes combined with or without graft materials can contribute to the process of bone regeneration. The variety of techniques and membranes employed as well as the small number of studies surveyed show the need for properly controlled clinical trials designed to determine predictable and successful treatment protocols when considering GBR as a treatment approach.

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