

## Research article

# Lateral Guided Bone Regeneration Using a Novel Synthetic Bioresorbable Membrane: A Two Center Prospective Randomized Controlled Trial

## Running title: A novel membrane for ridge augmentation

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### Abstract

The aim of this study was to evaluate the outcomes of lateral guided bone regeneration (GBR) using a novel resorbable synthetic polyethylene-glycol/methacrylate (PEG/MET) membrane compared to a non-cross-linked collagen membrane (CM). Twenty-eight patients with a potential implant site exhibiting insufficient bone width of  $\leq 5$  mm were included. Ridge width was measured intraoperatively at 1 mm and 4 mm apical to the crest and via cone-beam computed tomography at baseline and 6 months following GBR using either a PEG/MET or a CM in conjunction with an allograft. During implant placement, core biopsies were harvested and analyzed histomorphometrically. Width changes were calculated. Differences between groups were analyzed using two-sided t-test and Mann-Whitney U-test. The PEG/MET membrane was moldable and exhibited higher strength and stability compared to the CM. Nevertheless, it displayed higher exposure rate of 12/15, compared to 2/13 in the CM sites. At the time of implant insertion, 6 months following GBR, significant gain in bone width was observed in both groups. Mean ridge width at 1 mm and 4 mm apical to the crest was increased significantly from  $2.06 \pm 0.77$  mm and  $3.84 \pm 1.23$  mm to  $3.84 \pm 1.52$  mm and  $6.06 \pm 2.03$  mm ( $p = 0.0006$  and  $p = 0.0009$ , respectively), with no clinical or radiographic differences between groups. Experimental sites contained more residual scaffold material than the controls ( $17.4 \pm 3.3\%$  and  $8.6 \pm 2.0\%$ ,  $p = 0.0566$ ). However, bone and connective tissue area fraction were not statistically different between the groups. Overall, despite the higher exposure rate, the new PEG/MET membrane was as successful as a standard collagen membrane in lateral GBR and may have potential use in bone augmentation procedures. This study suggests the feasibility of synthetic membranes, which are not associated with disease transmission, as an attractive alternative to the commonly used CM of bovine or porcine origin.

### Keywords

Alveolar ridge reconstruction; Bone augmentation; Guided bone regeneration; Randomized controlled trial; Bioresorbable membrane

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## 1. Introduction

Guided bone regeneration (GBR) is the most commonly used technique to treat edentulous ridges with insufficient bone volume prior or in conjunction with endosseous dental implant placement [1–7]. Endosseous dental implants placed in defect sites previously augmented using GBR, have been shown to have survival rates of 87% to 95%, comparable to those encountered with native bone [8, 9]. The basic concept of GBR involves the placement of a barrier membrane to exclude down-growth of soft tissue cells, maintaining space for cells capable to promote tissue regeneration [10].

The use of non-resorbable expanded polytetrafluoroethylene membranes (ePTFE), membranes for GBR procedures, has been extensively documented in the past decades. Adequate lateral ridge augmentation and favorable long-term survival of subsequently inserted implants have been demonstrated using this membrane [3, 11–13]. However, it is a technique-sensitive procedure with high compli-

cation rates such as premature exposure associated with diminished results [3, 11, 14, 15]. To overcome these limitations, new materials are currently explored [16–19].

In the recent years, resorbable barrier membranes became popular for GBR procedures; these membranes are made of porcine-derived native type I and type III collagens and are currently the membranes of choice for many clinicians [17, 20], due to its hemostatic, chemotactic, tissue integration and semi-permeability functions, thus facilitating nutrient transfer during the early stages of wound healing [21, 22]. Despite the good results using collagen membranes [5], several drawbacks still exist. First, they may lack volume stability, an important requirement for barrier function in GBR procedures [23]. Second, the inconsistent and often rapid absorption rate, results in a reduced ability to maintain space, thus compromising the results [21, 24–26]. Third, the raw material of their production is derived from animal tissues, involving risk of

transmission of infectious agents, costs and objection by animal rights organizations.

The introduction of synthetic polymers for use as barrier membranes in GBR offers several advantages over natural collagen-based materials. Due to the fact that donor tissue is not required, these materials can be prepared in large quantities without supply limitations and with greater safety and robustness. In addition, chemical modifications allow the production of membranes with improved mechanical and physical properties [19, 27]. Synthetic barrier membranes composed of polylactic or polyglycolide acid have been investigated and demonstrated slower degradation rates compared to collagen membranes [28, 29]. Another membrane composed of polyglycolic acid/trimethylene carbonate (PGA/TMC) has been widely studied for GBR [30–32] and its subsequent long-term prototype has demonstrated comparable results to collagen membrane (CM) both in animal [33] and human [32] studies. However, some studies have shown therapeutic problems using these polymers mainly associated with pro-inflammatory fragments that appear upon degradation [34, 35].

Polyethylene glycol (PEG) hydrogel was later developed for use as a barrier membrane in GBR, exhibiting new features compared to other polymer-based membranes [19, 29, 36–38]. It was shown to be highly biocompatible and is customized intra-operatively, according to defect morphology. It has a long-term barrier function and its degradation is through a non-acidic hydrolytic process [39]. PEG membranes have been used in the past few years for GBR in the treatment of bony dehiscence defects around dental implants with comparable results with natural collagen membranes regarding implant survival, clinical soft tissue parameters, and marginal bone levels after a follow-up period of up to 5 years [40, 41]. It was also found effective in protecting bone grafts in sinus augmentation resulting in enhanced vital bone formation [42]. However, PEG membranes showed a significantly higher exposure rate compared to sites grafted with a collagen membrane [43]. Its tendency to rupture following polymerization is another inherent limitation that may lead to soft tissue penetration and proliferation between graft particles and implant surfaces and may result in reduced BIC values [44]. Moreover, the ability of PEG membranes to maintain barrier functions over time in long-span lateral ridge defects and their performance as a standalone GBR procedure without implant placement, have not yet been addressed [43].

The aim of the present study was to evaluate clinically, radiographically, histologically, and histomorphometrically, the efficacy of a new resorbable synthetic membrane composed of ammonio methacrylate copolymer type A and polyethylene glycol (PEG/MET), used in conjunction with allogenic bone substitute for lateral GBR in humans, compared with a collagen membrane.

## 2. Materials and Methods

This prospective, two-center, randomized controlled clinical study was conducted at the Departments of Periodontology at Hadassah Medical Center and at Rambam Health Care Campus from May 2013 through February 2015. The protocol was initially approved by the Institutional Review Boards of the Ethical Committee of Rambam Health Care Campus, Haifa, Israel as well as Hadassah Medical Center (approval #0074-13-rmb and #0230-12-HMO, respectively), and all subjects signed a written informed consent form prior to the commencement of the study.

### 2.1. Subject population

Subjects requiring an endosseous dental implant in a healed bony site that exhibited adequate ridge height but insufficient ridge width, (defined as less than 5 mm in cone beam computed tomography) were approached to participate in the study.

Subjects were excluded for the following reasons: (i) < 18 years old; (ii) history of systemic disease that would contraindicate oral surgical treatment; (iii) smoking of more than 10 cigarettes per day; (iv) intravenous or oral bisphosphonate therapy; (v) pregnant or lactating women; (vi) unwillingness to return for the follow-up examination; (vii) full mouth plaque score above 25%; (viii) acute dento-alveolar infection; and (ix) alcoholism or chronic drug abuse.

### 2.2. Ridge augmentation procedure

Prior to enrollment, all patients were referred for a cone beam computed tomography (CBCT) scan (i-CAT, Imaging Sciences, USA) in order to confirm an alveolar ridge width less than 5 mm. The scan was made with the following technical parameters: 120 kV acceleration voltage, 5 mA beam current, field of view (FOV) diameter of 16 cm, FOV height of 4 cm, 360° rotation and voxel size of 0.125 mm.

An acrylic stent had been fabricated to ensure that pre- and post-augmentation measurements were taken at the same anatomic location. All subjects received an antibiotic (Amoxicillin 2 g, or if allergic, clindamycin, 600 mg) and analgesics (Ibuprofen 800 mg) 30–60 minutes before the ridge-augmentation surgery. After administration of local anesthesia, a crestal incision was made at the treatment site, and full-thickness flaps were reflected to allow access to the site. The acrylic stent was placed and ridge width was measured 1 mm and 4 mm sub-crestally of each future implant site using a caliper (3M™ESPE™MDI Ridge Mapping Calipers). Clinical measurements were performed only in one research center (Rambam).

Decortication of the buccal cortical plate was initially performed and periosteal release incisions were made to allow for tension-free closure over the membrane and graft. Freeze-dried bone allograft (OraGRAFT® Cortical particulate mineralized FDBA, LifeNet, Virginia Beach, VA, USA) was then used as the grafting material in both the control and test groups.

Subjects were randomly assigned to either the experimental group (T) where ammonio methacrylate copolymer type A/polyethylene glycol (AMCA Regenecure® membrane, Jerusalem, Israel) membrane was placed over the bone graft and extended 2 mm beyond, or to the control group (C) in which collagen membrane (Bio-Gide®, Geistlich AG, Wolhusen, Switzerland) was placed. The membranes were shaped and fitted to the area requiring augmentation and were anchored using fixation pins, screws, tacks or resorbable sutures. Primary wound closure was obtained with horizontal mattress and interrupted ePTFE sutures (Fig. 1).

An antibiotic was prescribed as a continuation of the premedication regimen that included amoxicillin 500 mg, every 8 hours for 5 days or clindamycin 300 mg, every 8 hours for 5 days. The patients received ibuprofen (400 mg three times a day for the first 2 days) according to individual needs to manage postsurgical discomfort. Subjects were instructed to rinse their mouth with a 0.2% chlorhexidine gluconate mouth-rinse twice daily for 2 weeks. In addition, patients were instructed to refrain from mechanical plaque removal

in the area of implantation for 1 week. Sutures were removed 14 days postoperatively.

Patients were followed up at 1, 2 weeks and at 1, 2, 3, 4, 5, and 6 months following the augmentation procedure. During the follow-up visits, data were recorded regarding: (i) membrane exposure, (ii) healing process, (iii) local infection, and (iv) side effects.

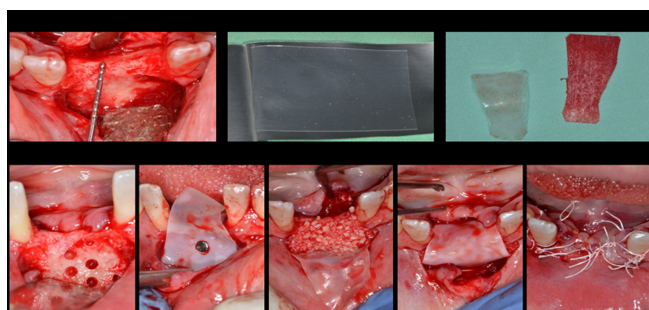


Fig. 1. Clinical photographs illustrate the treatment rendered to the experimental group. (a) Insufficient alveolar bone ridge of 3 mm at baseline. (b, c) AMCA RegeneCure® barrier membrane before and after trimming. (d) Decortication of the buccal cortical plate. (e) Anchorage of AMCA RegeneCure® barrier membrane with a tack. (f) Application of OraGRAFT® Cortical particulate mineralized FDBA, LifeNet. (g) Placement of AMCA RegeneCure® barrier membrane over the bone substitute. (h) Augmentation site closure using ePTFE sutures.

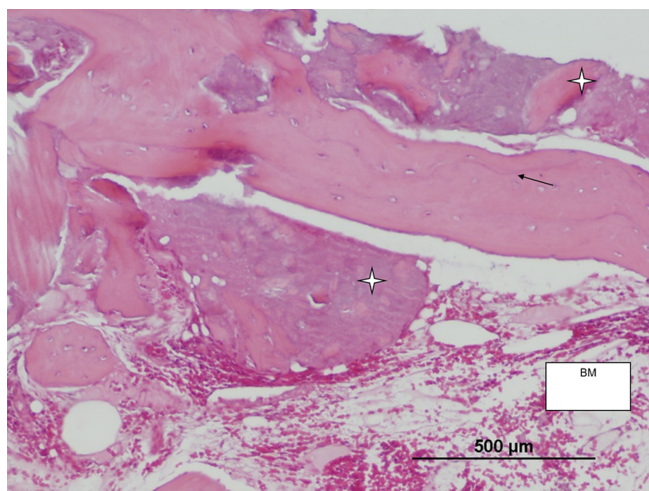


Fig. 2. A representative image of H&E histological slide obtained from control group (scale bar 500 µm). Intimate contact between newly formed vital bone (arrow pointing on osteocytes) and residual scaffold (asterisk) was observed. Bone marrow (BM) spaces were also present.

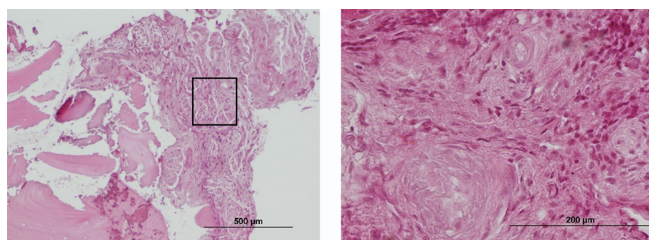


Fig. 3. Nonspecific inflammatory infiltrate was observed in the connective tissue (coronal part) of two biopsies obtained from the experimental group.

## 2.3. Re-entry and implant placement procedure

Endosseous implant surgery was performed at least 6 months following lateral ridge augmentation procedures. All patients were referred for a second CBCT scan prior to implant installation. Full-thickness flaps were reflected in the former augmentation site. The dimensions of the alveolar ridge were measured and recorded using the original acrylic stent as described in surgical procedure section. Next, bone core biopsies (6 mm length and 1 mm in diameter) were harvested from the center of the grafted site in the same position and at the same angle planned for the endosseous implants using a 2-mm trephine. The biopsy specimens were transferred to a 4% buffered formalin solution. Subsequently, endosseous implant was inserted after final preparation of the osteotome. Subjects received the same drug prescription as after the initial surgery.

## 2.4. Histological processing

All biopsies were fixed in 4% paraformaldehyde for 2 days and decalcified in 10% EDTA, (Sigma-Aldrich, MS, USA) for 4 weeks, cut into two halves in the midline, embedded in paraffin, and sectioned (8 µm). For determination of bone morphology, sections were stained with Masson's trichrome and Hematoxylin and Eosin (H & E).

## 2.5. Histomorphometric analysis

Histomorphometric evaluation of the samples was performed on two nonconsecutive sections from each specimen, under a light microscope (Zeiss Axioskop, Carl Zeiss, Jena, Germany) using software (image J, NIH, Bethesda, Maryland) for image analysis. The following values were measured: (i) total bone area, (ii) connective tissue, (iii) residual bone graft, and (iv) bone marrow. The measurements were expressed as percentage of the total sample area.

This study complies with the CONSORT checklist for reporting clinical trials [45].

## 2.6. Statistical analysis

Descriptive statistics were initially tabulated for patients' demographics, baseline and final measurements. Mean changes in the alveolar ridge dimensions at 1 and 4 mm apical to the crest, were calculated using t-test for paired observations for both absolute values as well as percentiles of the original values. Next, these changes were compared between the experimental and control groups using Mann-Whitney non-parametric test. Pearson correlation coefficient test was employed to evaluate the association between the radiographic and clinical measurements and also to explore the relationship between various demographic and clinical variables on the magnitude of these changes. A five percent significance level was used for all of these comparisons.

## 3. Results

Twenty-eight subjects (7 males, 21 females; mean age: 51.9 ± 13.0 years; age range, 18 to 77 years) completed the study and were included in this analysis. Only 3 were smokers (light to moderate) with lifetime exposure of 5–15 pack years. At the final visit (during implant surgery), only the PEG/MET membrane remnants were detected.

Baseline and final clinical and radiographic dimensional ridge values are depicted in Table 1. At baseline, mean values (± SD) for



Table 1. Clinical and radiographic horizontal alveolar ridge width at baseline and 6 months following augmentation

Variable	Mean (mm)	S.D. (mm)	Minimum (mm)	Maximum (mm)	Median (mm)
Baseline clinical bone width at 1 mm	2.06	0.77	1.0	3.0	2.0
Baseline clinical bone width at 4 mm	3.84	1.23	2.0	6.0	4.0
Final clinical bone width at 1 mm	3.84	1.52	1.5	7.5	3.75
Final clinical bone width at 4 mm	6.06	2.03	2.0	11.0	6.0
Baseline radiographic width at 1 mm	2.86	1.24	1.0	6.0	3.0
Baseline radiographic width at 4 mm	4.77	1.49	2.0	5.0	7.0
Final radiographic width at 1 mm	4.75	1.49	2.0	8.0	5.0
Final radiographic width at 4 mm	7.04	1.93	3.0	7.25	11.5

Table 2. Clinical and radiographic horizontal alveolar ridge width and the change 6 months following augmentation

Variable	N	Mean baseline ( $\pm$ SE) mm	Mean final ( $\pm$ SE) mm	Mean changes ( $\pm$ SE) mm	p-value*
Clinical bone width at 1 mm	16	2.06 $\pm$ 0.19	3.84 $\pm$ 0.38	1.78 $\pm$ 0.41	0.0006
Clinical bone width at 4 mm	16	3.84 $\pm$ 0.31	6.06 $\pm$ 0.51	2.22 $\pm$ 0.54	0.0009
Radiographic bone width at 1 mm	28	2.86 $\pm$ 0.23	4.75 $\pm$ 0.28	1.89 $\pm$ 0.29	0.0001
Radiographic bone width at 4 mm	28	4.77 $\pm$ 0.28	7.04 $\pm$ 0.36	2.27 $\pm$ 0.32	0.0001

\*T-test for paired-observations.

alveolar ridge width 1 mm and 4 mm apical to the crest were  $2.06 \pm 0.77$  mm and  $3.84 \pm 1.23$  mm, respectively. Six-months following the lateral ridge augmentation procedure, these dimensions increased to  $3.84 \pm 1.52$  mm and  $6.06 \pm 2.03$  mm, respectively. Likewise, baseline and final radiographic measurements in these sites were  $2.86 \pm 1.24$  mm and  $4.77 \pm 1.49$  mm as well as  $4.75 \pm 1.49$  mm and  $7.04 \pm 1.93$  mm, respectively.

A significant clinical gain in bone width was found (Table 2):  $1.78 \pm 0.41$  mm ( $p = 0.0006$ ) and  $2.22 \pm 0.54$  mm ( $p = 0.0009$ ) at 1 mm and 4 mm apical to the crest, respectively. Likewise, the corresponding radiographic values for these sites were very similar:  $1.89 \pm 0.29$  mm ( $p = 0.0001$ ) and  $2.27 \pm 0.32$  mm ( $p = 0.0001$ ), respectively. At baseline, both treatment groups exhibited similar clinical and radiographic dimensions ( $p > 0.05$ ). A sizeable increase in the ridge width as a result of the regenerative procedure was observed for both groups (Table 3). The horizontal dimensions of the ridge have increased by approximately 50% to 150% of the original width. These changes were not statistically different between the groups for both the clinical and radiographic measurements.

Sixteen patients were included in the histological analysis. Fig. 2 shows a representative histologic section prepared from the biopsy specimens. Histologic evaluation revealed the formation of mature lamellar bone characterized by the presence of osteocytes, blood vessels and bone marrow spaces. Intimate contact was observed between the newly formed bone and the residual bone graft. In most of the specimens, an inflammatory reaction was not evident, however in 2 slides (from the experimental group), non-specific inflammatory infiltrate was found in the coronal part of the biopsy (Fig. 3). The quantitative histomorphometric analysis of the specimens revealed that vital bone occupied more than half of the sampled area ( $58.1 \pm 7.9\%$  and  $53.3 \pm 6.7\%$  for the experimental and control groups, respectively,  $p = 0.5254$ ). Also, the proportions of connective tissue and bone marrow spaces did not differ between groups (Table 4). In contrast, the experimental sites' biopsies contained more residual scaffold material than the controls ( $17.4 \pm 3.3\%$  compared to  $8.6$

$\pm 2.0\%$ ,  $p = 0.0566$ ). Histomorphometric analysis showed similar amounts of vital bone, connective tissue and marrow spaces among the groups. However, percentage of residual scaffold was higher in the test group.

Overall, membrane exposure occurred in 12/15 of the experimental sites (80%) and in 2/13 of the control sites (15%). Membrane exposure did not appear to be correlated with lower GBR outcome scores. Age did not correlate with any of the clinical, radiographic or histologic parameters, while the baseline dimension of the ridge was found to positively correlate with the percent of bone gain both clinically ( $r = 0.64$ ,  $p = 0.008$  and  $r = 0.59$ ,  $p < 0.0164$  for the 1 and 4 mm sites, respectively) and radiographically ( $r = 0.64$ ,  $p = 0.0002$  and  $r = 0.60$ ,  $p = 0.0007$  for the 1 and 4 mm sites, respectively).

## 4. Discussion

In the present prospective randomized control clinical trial, we evaluated a new resorbable, synthetic PEG/MET membrane, used in conjunction with a bone allograft to augment alveolar ridges. The use of a synthetic PEG/MET membrane has significantly increased bone width without causing significant inflammatory response and adverse reaction. GBR using a polyethylene glycol membrane and an allograft was reported to provide effective ridge augmentation in dogs [28] and in human [37, 40] studies. However, to the best of our knowledge, the present study represents the first human clinical investigation using polyethylene glycol and ammonio methacrylate membrane. Our findings demonstrate a significant clinical and radiographic increase in alveolar ridge width of approximately 86% and 58%, 6 months following lateral ridge augmentation at 1 mm and 4 mm apical to the crest, respectively. No significant differences were observed between the experimental and control groups. In a recent meta-analysis, Sanz-Sanchez *et al.* [9], evaluated horizontal bone width dimensions following lateral GBR procedures and the influence of several variables of interest on the outcomes. They reported a mean increase in alveolar ridge width of 3.9 mm for all staged approach GBR procedures using a variety of membranes and

Table 3. Clinical and radiographic changes in alveolar ridge width: Comparison between treatment groups

Variable	Mean ( $\pm$ SE) changes experimental group	N	Mean ( $\pm$ SE) changes (mm) control group	N	p-value*
Clinical bone width change at 1 mm	2.00 $\pm$ 0.60	8	1.56 $\pm$ 0.59	8	0.5215
Clinical bone width change at 4 mm	2.06 $\pm$ 0.68	8	2.19 $\pm$ 0.71	8	1.000
% Clinical bone width change at 1 mm	144.8 $\pm$ 59	8	86.5 $\pm$ 29	8	0.7105
% Clinical bone width change at 4 mm	60.13 $\pm$ 26	8	53.75 $\pm$ 29	8	0.7518
Radiographic width change at 1 mm	1.80 $\pm$ 0.43	15	2.00 $\pm$ 0.42	13	0.6243
Radiographic width change at 4 mm	1.90 $\pm$ 0.41	15	2.69 $\pm$ 0.50	13	0.2650
% Radiographic width change at 1 mm	106.6 $\pm$ 39	15	90.4 $\pm$ 22.5	13	0.4730
% Radiographic width change at 4 mm	51.60 $\pm$ 15.6	15	65.7 $\pm$ 15.8	13	0.1645

\*Mann-Whitney U test (adjusted for ties).

Table 4. Comparison between treatment groups: Histological variables

Variable	Mean $\pm$ sechanges experimental group	N	Mean $\pm$ SE changes control group	N	p-value*
% Vital bone	58.1 $\pm$ 7.9	7	53.3 $\pm$ 6.7	9	0.5245
% Residual scaffold	17.4 $\pm$ 3.3	7	8.6 $\pm$ 2.0	9	0.0566
% Connective tissue	4.7 $\pm$ 4.7	7	14.3 $\pm$ 6.8	9	0.2467
% Bone marrow	7.1 $\pm$ 3.3	7	7.3 $\pm$ 5.2	9	0.5598

\*Mann-Whitney U test (adjusted for ties).

bone substitutes. More specifically, 3.5 mm increase in bone width was demonstrated using particulate allograft and a resorbable membrane. The maximum bone width gain of 5.68 mm was reported for the combination of particulate xenograft, autologous bone and resorbable membrane, whereas the minimum bone width gain of 1.1 mm was found for the combination of particulate synthetic graft with non-resorbable membrane [9]. The results of the present study fall within this range for collagen and PEG/MET membranes. Differences in bone width gain among studies may be attributed to numerous variables including: the phenotype of the soft tissue, surgical technique, and the experience of the surgeons. An additional factor that might influence the results is the initial bone width and defects anatomy. Indeed, according to the results of the present study, bone gain was positively correlated with baseline bone width.

In the present study, membrane exposure was observed in 80% and 15% of the cases in the experimental and control groups, respectively. In a recent review, Jensen *et al.* [46], found an overall membrane exposure rate of 25.9% in staged horizontal ridge augmentation procedures using both resorbable and non-resorbable membranes in humans. Nevertheless, the most common complication associated with such procedures was the need for additional augmentation procedure (that was reported in 37% of the cases) [46]. Although the experimental group in the present study showed a relatively high exposure rate, the need for an additional augmentation was lower than the above mentioned review (26%). Even lower values (15%) were observed in the control group. Most of the studies in this field suggest that membrane exposure is negatively correlated with regenerative outcomes. In their meta-analysis from 2015, Sanz-Sanchez *et al.* [9], found that exposed sites gained 3.1 mm less than non-exposed sites. This finding is in accord with previous clinical investigations [16, 47–50]. The sites that required additional augmentation procedures were those exhibiting inflammation associated with membrane exposure. It can be assumed that as long as the membrane remains intact fol-

lowing its exposure, its stability and functionality can be maintained without jeopardizing the regenerative outcome [32]. This notion was previously suggested by Gerus *et al.* [32], who found an exposure rate of 42% of the sites. They showed that when exposure did not lead to membrane removal, the mean gain in ridge width was similar to the sites where the membrane remained covered. In contrast, premature removal of the membranes because of infection, negatively impacted gain in bone width. Our results failed to find an association between membrane exposures and diminished regenerative outcomes. This result can be attributed to the fact that clinical signs of inflammation were not observed in areas of exposed membrane.

Collagen membrane (CM) was the first resorbable membrane used in GBR. It has been used in conjunction with autogenous bone, hydroxyapatite, xenografts and allografts, and showed comparable success rates to those achieved with non-resorbable ePTFE membranes which had been considered to be the gold-standard. In addition, the use of a resorbable membrane may reduce the risk for membrane infection if a soft tissue dehiscence occurs postoperatively [14]. However, CMs have several shortcomings; they have relatively short absorption time thus having a short barrier function of 2 to 3 months [14]. Therefore, they may not provide sufficient time for the completion of bone regeneration process. In addition, the pronounced biodegradation of CMs may decrease their barrier function, thus enabling a premature ingrowth of connective tissue [33]. Indeed, in the present study the percentage of connective tissue was 2-fold higher in the CM group (14% and 7% in the control and experimental groups, respectively), although these differences were not statistically significant [26, 51]. In addition, CMs are manufactured from animals, whereas synthetic membranes are produced without quantity limitations and with no risk for disease transmission.

On average, the histomorphometric analysis of the present study showed that the experimental bone biopsies consisted of 58% vital bone. A histomorphometric study by Gerus *et al.* [32], of specimens

obtained 6 months after the GBR procedure using a synthetic polyglycolic acid/trimethylene carbonate (PGA/TMC) barrier membrane and combination of assayed demineralized bone matrix and cortical cancellous chips uniformly dispersed in a thermoplastic biologic carrier, yielded similar results of 57% bone. In the present study, no differences were found between the experimental and control group regarding the percentages of vital bone. However, the proportions of the residual graft were significantly higher in the experimental group when compared to control ( $17.4\% \pm 3.3\%$  and  $8.6 \pm 2\%$ ,  $P = 0.0566$ ). This may be explained by the differences in membrane composition, degradation and porosity that might influence bone graft resorption by recruitment of cells that participate in allograft degradation (such as monocytes) and penetration of blood vessels from the flap to the grafted zone.

The study has some limitations in terms of the relatively small sample size. Moreover, samples for histological and histomorphometric analysis were not available from all participants. Finally, BIC values could not have been evaluated in this study due to its nature; a human clinical investigation.

## 5. Conclusion

The results of the current prospective randomized controlled study demonstrate that the use of an innovative synthetic resorbable polyethylene glycol/ammonio metacrylate membrane in conjunction with an allograft was effective as CM in lateral ridge augmentation prior to endosseous dental implant placement, although exposure rate was significantly higher. Larger cohort studies are warranted to fully appreciate the virtues and vices of the material.

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## Conflict of Interest

The authors declare that they do not have conflict of interest regarding the present study. The study was supported by a research grant from RegeneCure.

All authors declare that they had substantial contributions to the design of the work, drafting the paper or revising it and finally approved the version to be published. All authors agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any parts of the work are appropriately investigated and resolved.

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