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Alveolar ridge regeneration in two-wall-damaged extraction sockets of an in vivo experimental model

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Abstract

Aim: To determine the healing outcome following grafting with deproteinized porcine bone mineral (DPBM) with or without collagen membrane coverage in two-wall (both buccal and lingual)-damaged extraction sockets.

Materials and methods: Distal roots of three mandibular premolars in six beagle dogs were extracted, and the whole buccal and lingual bony walls were surgically removed. Three treatment protocols were then applied according to the following group allocation: no graft (None), grafting DPBM (BG), and grafting DPBM with coverage by a collagen membrane (BG + M). Two observational periods (2 and 8 weeks) were used with the split-mouth design, and quantitative and qualitative analyses were performed by microcomputed tomography and histology.

Results: The dimensions of the alveolar ridge at both grafted sites (BG and BG + M) remained similar to those of the pristine ridge in the histologic and radiographic analyses, whereas the ungrafted sites (None) collapsed both vertically and horizontally. Both grafting protocols produced substantial bony regeneration, but the addition of a covering membrane enhanced the proportion of mineralized tissue within the augmented area, and the BG + M group also showed a significantly larger area of regenerated ridge than the None group ($p < .05$).

Conclusions: Bone grafting with collagen membrane can maintain the alveolar ridge dimensions with substantial bone regeneration in a two-wall-damaged extraction socket.

KEYWORDS
alveolar ridge augmentation, bone regeneration, collagen membrane, damaged extraction socket, tooth extraction

1 | INTRODUCTION

The indications for extraction socket grafting have widening from limited cases of conventional ridge preservation in an anterior

intact extraction socket (Barone et al., 2008; Iasella et al., 2003; Ten Heggeler et al., 2011) to the posterior region (Kim et al., 2011; Walker et al., 2017) and sites with damaged extraction sockets (Guarnieri et al., 2019; Lee et al., 2015; Zhao et al., 2018). From a

clinical perspective, extraction socket grafting at posterior/damaged sites also significantly reduces the need for additional augmentation surgeries and so reduces both the invasiveness (Cha et al., 2019; Rasperini et al., 2010) and the likelihood of complications (Kim et al., 2017). While a dimensional collapse occurs at the entire site of a buccal-bone-deficient extraction socket, grafting bone substitutes with or without a collagen membrane can comparably maintain the alveolar ridge dimension and allow for substantial bone regeneration (Lee et al., 2015; Lee, Choe, et al., 2018; Scheyer et al., 2016; Sisti et al., 2012). However, despite various types of defect morphologies at tooth extraction sites being encountered in clinical settings, there is little evidence for the occurrence of healing after extraction socket grafting in the presence of a deteriorated condition such as when the bony walls are deficient.

One clinical trial that performed extraction socket grafting at a damaged site with severe periodontitis found the dimensional maintenance of the alveolar ridge in 100 patients (Lee, Cha, et al., 2018). However, a follow-up study of the histologic results revealed that the bone regeneration varied widely from 0% to 40% (Koo et al., 2020). Various clinical and host factors including the characteristics of the defects and the healing potential are expected to influence the bony regeneration that occurs at grafted sites (Kim et al., 2004). The defect morphology is directly related to the healing source to the grafted site, and their regression analysis showed that the tendency for regeneration of the bone tissue increased slightly with the height of the residual alveolar bony wall in either a buccal or a lingual aspect (Koo et al., 2020). A previous preclinical study evaluated the sequential healing following grafting bone substitutes within the buccal-bone-deficient extraction socket (Lee, Choe, et al., 2018), which also demonstrated that the bone formation appeared to start and sprout from the preexisting bone of the lingual wall and the floor of the socket. Therefore, the residual socket wall can be considered to be a critical factor for bony regeneration in extraction socket grafting.

The predominant clinical protocol for conventional ridge preservation in an intact extraction socket involves grafting osteoconductive biomaterials with or without covering biomaterials. On the other hand, there is no consensus for the protocol to apply in extraction socket grafting at damaged sites. Several clinical trials used a resorbable collagen membrane to cover the defect and to stabilize the grafted biomaterial (Barone et al., 2015; Guarnieri et al., 2019; Lee, Cha, et al., 2018). Another animal study of the buccal-bone-deficient extraction socket also found that bone regeneration was enhanced by collagen membrane coverage in the outermost area of the grafted site (Lee et al., 2015). However, another preclinical study of the same model found that applying bone grafting without collagen membrane maintained the volume comparably to the pristine alveolar ridge, with the bone regeneration extending throughout the grafted area (Lee, Choe, et al., 2018).

The above situation demonstrates the need to determine how collagen membrane coverage in various types of damaged extraction sockets affects the healing processes. The present study aimed to radiographically and histologically determine the healing outcomes after grafting deproteinized porcine bone mineral (DPBM) with or without collagen membrane coverage in a two-wall (both buccal and lingual)-damaged extraction socket model in beagle dogs at two observational periods (2 and 8 weeks).

2 | MATERIALS AND METHODS

2.1 | Animals

Six male beagle dogs weighing 15 kg and aged 15–24 months were used in this study. The sample size was determined based on the previous studies (Araujo et al., 2009; Lee, Choe, et al., 2018) to minimize an included animal number and to evenly distribute the samples of each group for three experimental sites of premolars. The study protocol was approved by the Institutional Animal Care and Use Committee, Yonsei Medical Center, Seoul, Korea (IRB No. 2018-0265).

2.2 | Study design

Two-wall-damaged extraction sockets were surgically induced by performing total ostectomy of the buccal and lingual walls after removal of the distal roots of bilateral mandibular second, third, and fourth premolars. Each mesial root was retained as a reference pristine site for each corresponding distal root. Three damaged extraction sockets in the unilateral alveolar ridge were rotationally allocated in the following groups to produce an even distribution of three other premolar sites: (a) no graft (None), (b) grafting DPBM (THE Graft, Purgo Biologics, Seoul, Korea) (BG), and (c) grafting DPBM with coverage by a collagen membrane (Biocover, Purgo Biologics) (BG + M). Each experimental group showed similar dimensions of the defect involved (Table S1 in Appendix S1). Two observational periods (2 and 8 weeks) were applied to right and left unilateral alveolar ridges, respectively. Finally, six experimental sites (distal part of each premolar) per beagle dog (total 36 sites) were allocated for three groups in each observational period.

2.3 | Surgical protocol

Three premolars in the unilateral mandible of six animals were hemisectioned. The distal roots were removed using surgical forceps, and the mesial roots were maintained with decoronation. In the distal root area, both the buccal and lingual bony walls were completely removed according to the height and width of the extraction socket in order to form the two-wall-damaged standardized model (Figure 1a,b). One of the three treatments was applied at each site according to the group allocation. DPBM particles were packed within the site up to the imaginary line between the adjacent bone walls, and the collagen membrane covered over the grafted site without fixation. The periosteal flap was repositioned and sutured (Monosyn 6-0). Antibiotic medication and wound dressing with saline irrigation
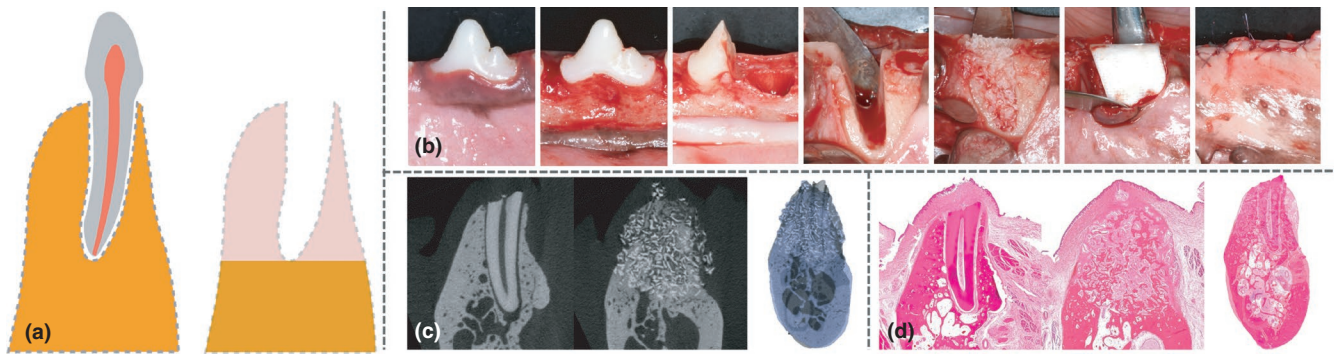
FIGURE 1 (a) All of the buccal and lingual alveolar bones were removed to produce two-wall-damaged defects in which the mesial and distal walls remained after the removal of each distal root. The vertical level on the defects was defined based on the preexisting root apex. (b) Surgical procedure and group allocation. (c and d) Each mesial root retained as a reference pristine ridge (left side of each image) and the experimental site (in the middle of each image) are shown in micro-CT images (c) and histologic sections (d). Superimposed images on the right side of each figure were used for morphometric analyses [Colour figure can be viewed at wileyonlinelibrary.com]
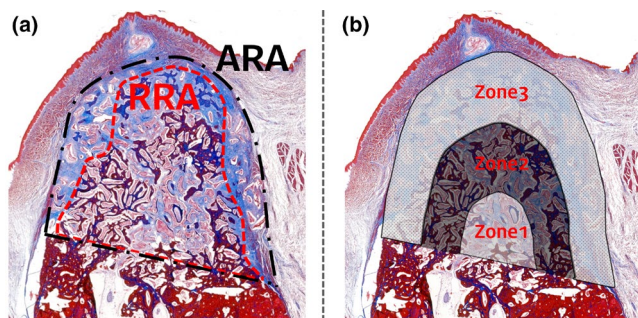

FIGURE 2 (a) Augmented ridge area (ARA) is indicated by the black dotted line showing the outermost margin of grafted biomaterials. Regenerated ridge area (RRA) is indicated by the red dotted line showing the outermost mineralized area. (b) ARA was divided into three zones from the inner core of ridge to the outer area for evaluating whether or not the presence of a covering membrane affects the bone quality: zone 1 (whitish area), 2 (dark area), and 3 (dotted area) [Colour figure can be viewed at wileyonlinelibrary.com]

were applied for 1 week, and then, the sutures were removed. The animals were killed for radiographic and histologic analyses at 8 and 2 weeks after performing the experimental procedures in the left and right mandibles, respectively. The acquired specimens were fixed in 10% neutral buffered formalin for 2 weeks.

2.4 | Micro-CT radiographic analysis

Micro-computed tomography scanning (micro-CT; Skyscan 1173, Skyscan) was performed (FOV = 6.2 cm; Projection time = 00:40:41; Number of projections = 799; Frame averaging = 4) at a resolution of 35 μm (achieved using 100 kV and 100 μA). The micro-CT images were used in DICOM to retrieve and interpolate the cross-sectional slides for morphometric evaluation at three-dimensional software (On-Demand3D, Cybermed). The bucco-lingual coronal planes parallel to the long axis of the mesial dental root and distal extraction socket were selected at the most-central region, and the

two bucco-lingual sections were obtained. These images were superimposed with the aid of reference anatomical structures such as the mandibular canal and the outermost margin of the mandible (Figure 1c,d). On the merged images, the areas of the pristine and grafted alveolar ridges were measured using computer software (Adobe Photoshop CS5, Adobe Systems), and each dimension at the distal experiment site was calculated as a percentage of that at the reference mesial site.

2.5 | Histologic preparation and analysis

The specimens were sectioned into six blocks containing the mesial roots or the experimental extraction sockets after decalcification using high-speed decalcifier (Calci-Clear Rapid, National Diagnostics Inc.), which was changed every 48 hr, and the samples were then dehydrated and embedded in paraffin. The most-central bucco-lingual sections were cut along the dental root axis or the extraction socket at a thickness of 4 μm and then stained with hematoxylin and eosin and Masson's trichrome (Figures 1d and 2). Histologic slides were scanned at an original magnification of ×200 (Panoramic 250 Flash III), and histomorphometric analysis was performed using computer software (Adobe Photoshop CS5). Superimposition was performed in the same method as the aforementioned micro-CT. (ridge side of Figure 1d.)

Two types of dimensional alteration were measured histologically: the augmented ridge area (ARA) and the regenerated ridge area (RRA). ARA was demarcated by the outermost line of grafted biomaterials, and RRA was demarcated by the outermost newly formed bone within the augmented ridge (Figure 2a). These dimensions were calculated as percentages of the pristine alveolar ridge area at the reference mesial-root site. For qualitative analysis, the percentage contributions of the following components to ARA were measured and calculated as follows: mineralized tissue (newly formed bone area), residual biomaterials, and fibrovascular tissue. To evaluate the effects of using a coverage membrane on new bone formation within the augmented area, three zones were defined by trisecting the distance from the center of the defect baseline,

and qualitative analyses were performed in each zone separately (Figure 2b).

2.6 | Statistical analyses

All statistical analyses were performed using computer software (version 20.0, SPSS), and all parameters are presented as mean ± standard-deviation values. The Kolmogorov–Smirnov test and Mauchly's sphericity test were applied to evaluate the normality of the data and the sphericity assumption, respectively. Repeated measured ANOVA was used for all groups, and Bonferroni p value correction (post hoc test) was applied to detect significant differences between experimental groups at each observational period. The paired t test was used to compare between the same groups at the 2- and 8-week observational periods. The cutoff for significance was set as a p value of .05. For data that did not conform to normality, the corresponding nonparametric analyses were used the Friedman test and the Wilcoxon signed-rank test with the p value correction between groups and Wilcoxon signed-rank test between two observational periods.

3 | RESULTS

3.1 | Clinical findings

All experimental sites showed uneventful healing without any inflammation or wound dehiscence. Horizontal collapse of the alveolar ridge dimension only appeared at sites without grafting (None), while the dimensions at the two experimental sites (BG and BG + M) were similar to those at the adjacent reference sites in the residual mesial-root region.

3.2 | Quantitative analyses of the superimposed micro-CT images

Alveolar bone fractures were found in micro-CT images at two experimental sites (one site in the None group at 8 weeks and one site in the BG + M group at 2 weeks), which were excluded from the radiographic and histologic analyses. Two-wall-damaged extraction sockets (None group) healed with substantial collapse of the alveolar ridge dimension (Figure 3): the alveolar ridge dimension had recovered by up to 50% (47.78 ± 19.08%; Table S2 in Appendix S1) in the most-central section at 8 weeks, which was a significantly larger increase ($p < .05$) compared with at 2 weeks (13.66 ± 6.76%; Figure 3). On the other hand, in the two grafted groups (BG and BG + M), the dimensions were maintained comparably with those at the pristine alveolar ridge after both 2 weeks (105.84 ± 11.45% and 103.70 ± 12.70% respectively) and 8 weeks (104.47 ± 28.13% and 100.02 ± 12.55% respectively). The alveolar ridge dimension did not differ significantly between the two grafted groups, in which it was higher than that in the None group ($p < .05$ between the BG + M and None groups at both periods and between the BG and None groups at 2 weeks).

3.3 | Quantitative analyses of the superimposed histologic images

The pattern of the augmented ridge dimension was similar in the histologic and radiographic analyses (Figures 4 and 5). ARA was significantly lower in the None group (23.37 ± 18.32%; Table S2 in Appendix S1) than in the BG group (103.22 ± 13.44%) and BG + M group (101.68 ± 11.35%) at 2 weeks ($p < .01$). At 8 weeks, ARA in the None group was increased (44.72 ± 22.24%) compared with the 2-week value, but it remained significantly lower than those in the BG group (110.74 ± 28.33%) and BG + M group (107.70 ± 6.21%). ARA did not differ significantly between the two experimental groups (BG and BG + M groups), but its variation was wider in the BG group than the BG + M group, in which the values were concentrated around 100% of the pristine ridge volume. There is no significance between 2 and 8 weeks in each group of ARA.

There was limited newly formed bone around the defect base in all 2-week groups (Figure 4), and RRA was lower in the two grafted groups (7.95 ± 2.15% and 4.90 ± 3.73% in the BG and BG + M groups) than in the None group (23.37 ± 18.32%, $p = .10$). However, this healing pattern had clearly reversed at 8 weeks, with RRA being significantly higher in the BG + M group (82.93 ± 9.63%) than in the
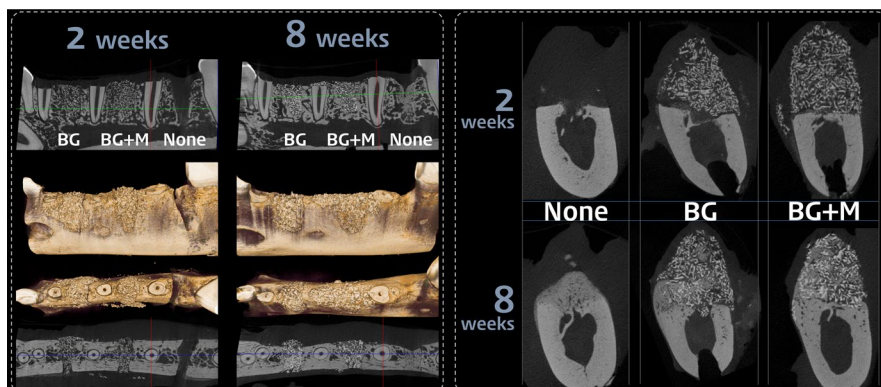

FIGURE 3 Images on the left show panoramic, axial, and three-dimensionally reconstructed micro-CT images of the entire quadrant of the dog mandible in the three groups allocated at each distal site. The images on the right side are cross-sectional micro-CT images with the three groups aligned according to the healing periods [Colour figure can be viewed at wileyonlinelibrary.com]

None group (44.72 ± 22.24%, *p* = .03). RRA was also high in the BG group (72.15 ± 29.23%), but it did not differ significantly from the values in the other groups due to the wide range of RRA values. RRA differed significantly between the 2- and 8-week observational periods in both the BG (*p* < .01) and BG + M (*p* < .01) groups.

3.4 | Qualitative histomorphometric analysis

The proportion of mineralized tissue within the augmented area showed a similar pattern to RRA at 2 weeks. The proportion of mineralized tissue was significantly higher in the None group (24.70 ± 8.05% and 72.95 ± 5.97% at 2 and 8 weeks, respectively; Table S3 in Appendix S1) than in the two grafted groups (2.63 ± 0.67% and 30.27 ± 8.49% in the BG group, respectively, and 1.88 ± 1.42% and 35.72 ± 7.22% in the BG + M group) at both observational periods (*p* < .05) (Figure 5). Also, there was a significant difference between the BG and BG + M groups at 8 weeks (*p* < .05), unlike the other results. All groups at 8 weeks showed significantly increased proportions of mineralized tissue compared with at 2 weeks (*p* < .01).

The proportions of residual biomaterials were 10.09 ± 2.78% and 10.78 ± 3.03% in the BG and BG + M groups, respectively, at 2 weeks (*p* = .60), and 7.76 ± 3.34% and 7.34 ± 1.99% at 8 weeks (*p* = .79). There were no significant differences between the two grafted groups. In addition, there was a tendency for the proportion of residual biomaterials to reduce from 2 to 8 weeks, but this was significant only in the BG + M group (*p* < .05). All groups showed significant reductions in the proportion of fibrovascular tissue from 2 to 8 weeks (*p* < .01): 75.30 ± 8.05%, 87.28 ± 2.48%, and 87.34 ± 4.41% in the None, BG, and BG + M groups, respectively, at 2 weeks, and 27.05 ± 5.97%, 60.64 ± 7.98%, and 56.94 ± 7.41% at 8 weeks. The None group also showed a
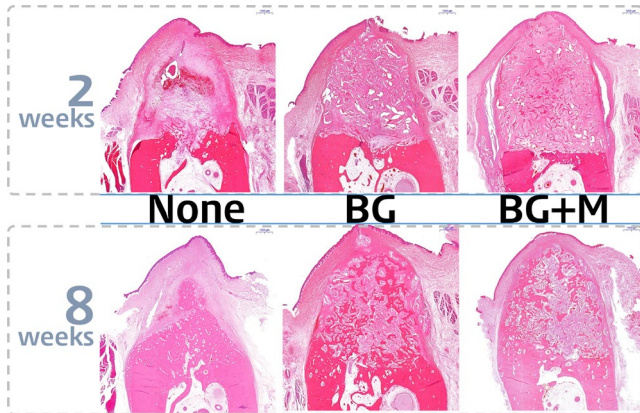

FIGURE 4 Histologic sections stained with hematoxylin and eosin and obtained at the middle portion of the defects. Sections after 2 weeks of healing show obvious defect margins and little mineralized tissue. Sections after 8 weeks of healing exhibit larger dimensions at the grafted sites than at the not-grafted sites [Colour figure can be viewed at wileyonlinelibrary.com]
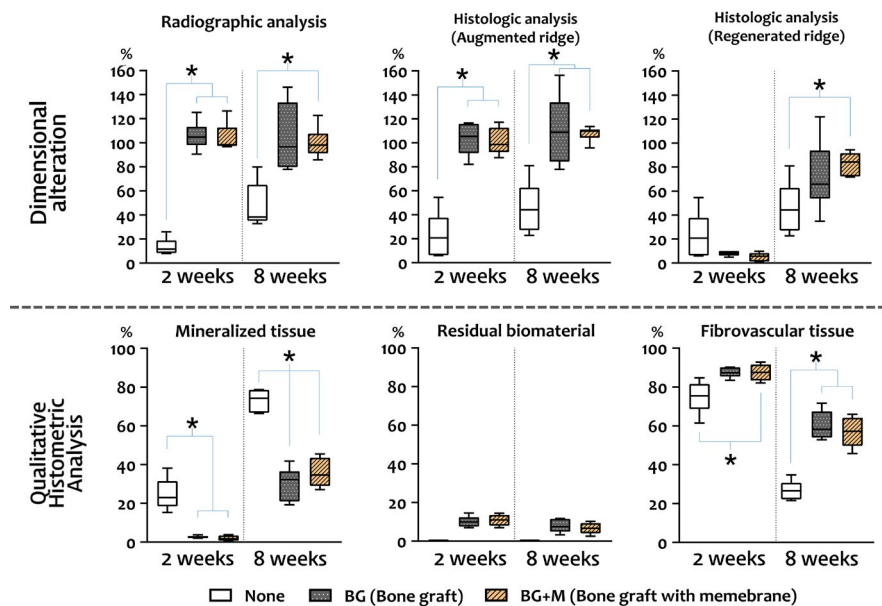

FIGURE 5 Dimensional alterations (upper row) and results of the qualitative histometric analyses (lower row). The dimensional alteration in the BG and BG + M groups differed significantly from that in the None group for radiography (at 2 weeks) and histologic analysis (augmented ridge, at both 2 and 8 weeks), as well as the qualitative measurements of mineralized tissue (at both 2 and 8 weeks) and fibrovascular tissue (8 weeks). There was a significant difference between the BG and BG + M groups for the mineralized tissue at 8 weeks. The augmented ridge areas were measured slightly over 100% compared with the pristine alveolar ridge (mesial-root site) in both BG and BG + M groups, with the placement of the grafted biomaterials beyond the original shape of the ridge due to the deficiency of bucco-lingual bony plate. The dimensional alteration was significantly greater in the BG + M group than the None group for radiography (at 8 weeks) and histologic analysis (regenerated ridge, at 8 weeks). *p* < .05 [Colour figure can be viewed at wileyonlinelibrary.com]

significantly reduced proportion of fibrovascular tissue compared with the two grafted groups at 8 weeks ($p < .01$), while only the BG + M group showed a significantly increased proportion at 2 weeks ($p = .01$).

To evaluate regional differences in new bone formation within the entire whole grafted area, the augmented area was divided into three zones in both grafted groups, and subgroup analysis for the proportion of each component was performed in each zone (Figure 6 and Table S4 in Appendix S1). There were no significant either regional or inter-group differences, but there was a slight increasing tendency in the proportion of mineralized tissue in zone 3 at the membrane-applied sites ($25.37 \pm 6.84\%$ in the BG group and $33.63 \pm 11.26\%$ in the BG + M group, $p = .13$) and slight difference between the grafted groups at 2 weeks in the residual biomaterials of zone 1 ($8.15 \pm 3.90\%$ in the BG group and $10.96 \pm 2.85\%$ in the BG + M group, $p = .07$).

4 | DISCUSSION

Preclinical and clinical studies of damaged extraction sockets have revealed that the alveolar ridge dimensions can be preserved by grafting xenogeneic biomaterials (Lee, Cha, et al., 2018; Lee, Choe, et al., 2018; Lee et al., 2015). However, the bone quality in the grafted area of damaged sockets is heterogeneous (Koo et al., 2020), and there are still insufficient data on the defect morphology of the socket and bone regeneration. The present study induced a two-wall (both buccal and lingual)-damaged extraction socket model to evaluate the bone healing pattern following two types of grafting and found (a) ungrafted two-wall-damaged sockets collapsed with a volume of <50% from the pristine alveolar ridge, (b) grafting xenogeneic biomaterials with and without membrane coverage similarly maintained alveolar ridge volume with substantial bone regeneration, and (c) membrane coverage reduced the variation in the range of ARA and RRA values while enhancing the bone quality within the augmented area.

An intact extraction socket reportedly healed with dimensional shrinkage within a limited area of the coronal region (overall 14%–17%; Araujo & Lindhe, 2009a), and the one-wall-damaged extraction socket (buccal-bone deficient) shrank over the whole area from the apex to the coronal regions (20%–40%; Lee, Choe, et al., 2018). The present study demonstrated substantial alterations in dimensions both vertically and horizontally (Figures 3 and 4), with the dimension of the ridge collapsing by 50% in the middle of the socket at 8 weeks (Jovanovic et al., 2007). This pattern of the amount of dimensional healing being affected by the amount of socket damage can be interpreted in line with previous findings of periodontal healing deteriorating progressively according to the number of residual walls of the defect (Kim et al., 2004). The hallmark study of Schenk et al. (1994) induced a similar (saddle) type of alveolar bone defect and that also demonstrated severely pronounced collapse of both vertical and horizontal dimensions (Stavropoulos et al., 2004).

Grafting xenogeneic bone substitutes have reduced dimensional shrinkage of the dimensions in the extraction socket in various preclinical and clinical studies (Koo et al., 2020; Lee, Cha, et al., 2018; Lee, Choe, et al., 2018; Lee et al., 2015). In a previous study of fresh socket grafting, the alveolar ridge dimension was maintained up to about 90% in the coronal region compared with 65% without a grafting procedure (Araujo & Lindhe, 2009b). In contrast, grafting biomaterials in the one-wall (buccal bone)-damaged extraction socket clearly maintained the ridge dimensions at more than 100% relative to the pristine ridge (Lee, Choe, et al., 2018). The present study also found that grafting biomaterials resulted in excess of 100% of the pristine alveolar ridge dimensions (Figures 3–5). The absence of a bony wall in the socket might allow the placement of biomaterials in the outermost region corresponding to the pristine alveolar ridge and could enhance the maintenance of alveolar ridge dimensions compared with performing a ridge preservation technique in the intact extraction socket.

ARA may correspond to a clinical ridge volume, and RRA can be identical to the clinical tissue that supports a dental implant. After 8 weeks of healing in a dog model, a one-wall-damaged extraction
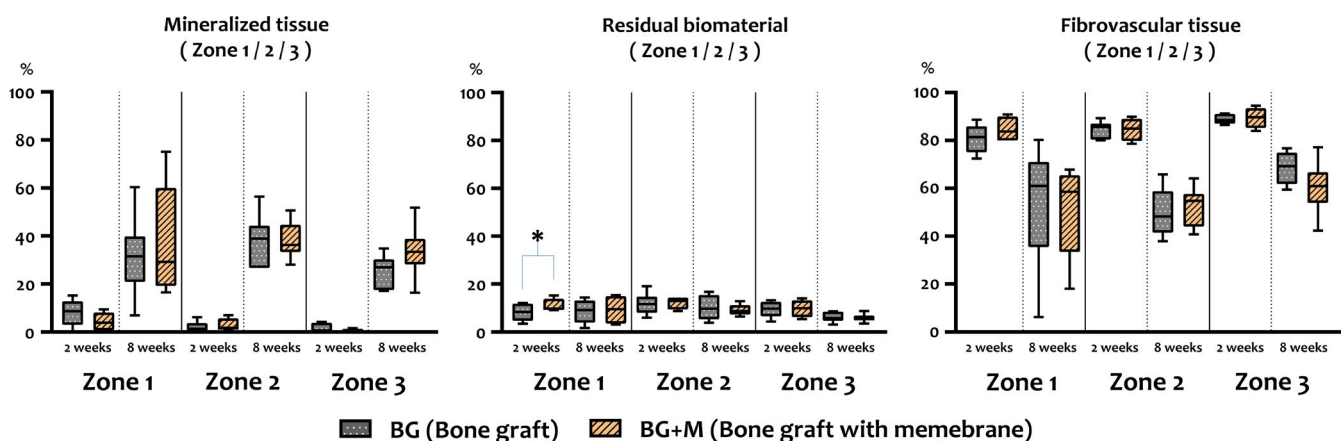

FIGURE 6 The proportions of the three components according to the divided zones. *$p < .05$. There was a significant difference between the BG and BG + M groups in the residual biomaterial of zone 1 at 2 weeks [Colour figure can be viewed at wileyonlinelibrary.com]

socket showed almost complete regeneration of the ridge within the augmented area: 93% at the coronal level and 100% at both the middle and apical levels (Lee, Choe, et al., 2018). However, in the present study, two-wall-damaged sockets healed with an incomplete regenerated ridge volume (72%–83%) regardless of whether or not there was coverage by collagen membrane. These observations are potentially relevant to the heterogeneous results in histologic biopsies from a clinical trial of damaged extraction sockets (Koo et al., 2020). New bone formed from the preexisting alveolar bone defect or the proximal walls, and the defect morphology or dimension can affect the regeneration within the augmented area such as in a periodontal regeneration. Therefore, an appropriate healing time for damaged extraction socket grafting needs to be determined separately based on the defect morphology.

A covering membrane is known to act as a tissue barrier that excludes adjacent unnecessary cells (Nyman, 1991). Although both grafted sites in the present study (BG and BG + M) demonstrated substantial mineralized tissue formation, the proportion of mineralized tissue was higher in the BG + M group than the BG group ($p = .03$, Figure 5). This is consistent with the basic concept of guided bone regeneration using a barrier membrane in a similar (saddle) type of defect (Dahlin et al., 1988). However, the role of the membrane in bone regeneration remains controversial (Benic et al., 2017; Brkovic et al., 2012; Jones et al., 2006). Another study of the same type of defect model found that coverage by the membrane resulted in a dimensional increase but had no impact on the bone quality within the regenerated area (Bornstein et al., 2007). The results for sequential healing in a one-wall-damaged extraction socket may corroborate this by bony regeneration with favorable bone quality (about 38%) found at sites that received xenogeneic bone substitutes only (Lee, Choe, et al., 2018).

Collagen membrane seems to act in a way other than simply as a tissue barrier, by increasing the stability of the grafted biomaterials. In terms of the regional qualitative results, no significant differences in the proportion of mineralized tissue were found between the two experimental sites according to coverage of the collagen membrane even in the outermost region far from the healing sources. However, the BG group demonstrated large variations in ARA and RRA, and we speculate that an inadequate bony wall can adversely affect the dispersion of the biomaterials over the grafted area and result in slight deterioration of the bone quality. Nevertheless, there were smaller deviations in the BG + M group in the quantitative analyses, which is comparable to previous findings in intact and one-wall-damaged sockets (Araujo & Lindhe, 2009b; Lee, Choe, et al., 2018). Together these results suggest that covering the defect with a collagen membrane stabilizes the grafted biomaterials and enhances the bone quality in the augmented two-wall-damaged extraction socket.

This study was subject to some limitations. Firstly, although extraction socket grafting has been addressed by animal studies, the relatively small dimensions of the extraction socket and the socket entrance can enhance the regeneration in the defect area. Therefore, the present preclinical results should be interpreted with caution when considering clinical applications. This may be relevant to the wide variation in the histologic results found in clinical trials of damaged extraction sockets, in contrast to the successful regeneration seen in preclinical studies. Secondly, only one type of collagen membrane was used in this study. Recent studies have found that the use of different covering membranes has different biologic impacts on the augmented area (Elgali et al., 2017; Omar et al., 2019), and so further comparative studies are needed to confirm the treatment of choice in two-wall-damaged extraction sockets. Third, the present results were produced from the 2D analyses rather than 3D volumetric analyses, and these should be interpreted conservatively.

5 | CONCLUSION

Bone grafting with collagen membrane can maintain the alveolar ridge dimensions with substantial bone regeneration in the two-wall-damaged extraction socket (i.e., deficient in both buccal and lingual bone). The use of a covering membrane might reduce variations in the dimensions of the regenerated alveolar ridge by stabilizing the grafted biomaterials, as well as increase the bone quality within the augmented area of damaged extraction sockets.

CONFLICT OF INTEREST
The authors declare that they have no conflicts of interest.

AUTHOR CONTRIBUTIONS
Hsu Kuo Tien: Data curation (lead); Investigation (equal); Writing-original draft (equal). **Chang-Sung Kim:** Formal analysis (supporting); Writing-review & editing (supporting). **Seong-Ho Choi:** Formal analysis (supporting); Writing-review & editing (supporting). **Reinhard Gruber:** Formal analysis (supporting); Writing-review & editing (supporting). **Jung-Seok Lee:** Conceptualization (equal); Data curation (supporting); Funding acquisition (lead); Investigation (lead); Project administration (lead); Writing-original draft (equal); Writing-review & editing (lead).

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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