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Particulate Versus Cross-Linked Collagenated Bone Substitutes for Guided Bone Regeneration: A Randomized Controlled Trial

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Keywords: dental implant | guided bone regeneration | horizontal ridge augmentation | radiographic analysis | randomized controlled clinical trial

ABSTRACT

Aim: To compare the dimensional outcomes of horizontal augmentation with the retentive-flap technique using particulate and cross-linked collagenated bone substitutes.

Materials and Methods: This two-centre, two-arm randomized clinical trial investigated 69 subjects: 34 in the particulate group and 35 in the collagenated group. Patients were randomly assigned to receive single implant placement with simultaneous guided bone regeneration (GBR) using either particulate deproteinized porcine bone material (DPBM) or cross-linked collagenated DPBM. Quantitative evaluations were conducted for horizontal width, augmented area, and augmented volume in both hard and soft tissue dimensions.

Results: Immediately after surgery, the collagenated group exhibited higher hard tissue dimensions in terms of horizontal width and augmented area. After 4 months, the difference between the two groups decreased to a non-significant level, mainly attributable to the high shrinkage rate of the collagenated group (32.32 [20.79] %) compared to the particulate group (19.90 [14.33] %). No significant difference was observed regarding the soft tissue contour analyses between the two groups after 4 months.

Conclusions: There were no significant differences between cross-linked collagenated and particulated DPBMs regarding the dimensional outcomes of horizontal augmentation with the retentive-flap technique. The high resorption rate of the collagenated bone substitute negates its initial superiority in both radiographic and soft tissue dimensions (no. KCT0005348).

1 | Introduction

Collagenated bone substitutes are now widely used in various clinical applications, including guided bone regeneration (GBR) and other bone grafting procedures (Nevins et al. 2003; Araújo et al. 2010, 2011; Friedmann et al. 2021; Lee et al. 2021). Initially, these substitutes were primarily used for alveolar ridge preservation (ARP) (Araújo and Lindhe 2009; Araújo et al. 2010), with the expectation that materials incorporating collagen will enhance bone regeneration while improving clinical manageability. Based on robust scientific evidence demonstrating the clinical success of ARP with

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collagenated bone substitutes, several groups have expanded their clinical applications to include GBR procedures (Sapata et al. 2020; Benic et al. 2022; Lee, Jung et al. 2022), which have been reported to provide comparable volume augmentation at both the hard- and soft-tissue levels.

The incorporation of binding agents with other materials has emerged as a useful strategy for preventing the scattering of particulate materials. Synthetic fibrin sealant and platelet-rich fibrin are well-known binders for particulate bone substitutes in GBR; they are expected to create a mouldable, sticky mass and stabilize the materials within the grafted site (Yoon et al. 2014; Amaral Valladão Jr. et al. 2020; Park, Hong, et al. 2023). Collagen in collagenated bone substitutes also acts as a binder to stabilize the mass so as to make it easily adaptable to the defect configuration. However, this approach comes with the critical risk of volume shrinkage due to the rapid degradation of collagen. To mitigate the risk of volume shrinkage, the conjugation of cross-linked collagen has emerged as a promising option (Naenni et al. 2021). Our recent study has also found that using cross-linked collagen as a binder in collagenated bone substitutes resulted in improved volume maintenance and enhanced bone formation at the graft site (An et al. 2024).

One of the most-important factors for successful GBR is stable space provision, through the use of either scaffolding materials or covering membranes. In current GBR procedures using a collagen membrane, oral surgeons may fix the membrane (Urban et al. 2016; An et al. 2022; Park et al. 2022) or control flap tension (Lee, Park, et al. 2022; Park et al. 2022; Park, Chung, et al. 2023) to stabilize the grafted material. Successful outcomes were obtained in recent clinical studies involving both horizontal and vertical augmentation procedures using the retentive-flap technique (Lee, Park, et al. 2022; Park, Chung, et al. 2023), though horizontal shrinkage was pronounced in horizontally augmented sites (26% and 42% volume reductions at 4 months and 1 year, respectively) (Park, Chung, et al. 2023). The use of collagenated bone substitutes may be a suitable option for horizontal augmentation with the retentive-flap technique due to their self-stabilizing property, and so further investigations are required to understand their impact.

Therefore, this study aimed to determine and compare dimensional changes at augmentation sites during horizontal GBR procedures performed using the retentive-flap technique with particulate and cross-linked collagenated porcine bone substitutes through a randomized clinical trial (RCT).

2 | Materials and Methods

2.1 | Study Design

This study was designed as a two-centre RCT with two parallel treatment groups and a follow-up duration of 4 months. The trial involved 70 patients, with 46 and 24 individuals from Yonsei University Dental Hospital (Centre 1) and the Veterans Health Service Medical Center (Centre 2), respectively. Patients were randomly assigned to receive either particulate or cross-linked collagenated bone substitute. Ethical approval was granted by the institutional review boards of Centre 1 (no. 2-2020-0034) and Centre 2 (BOHUN 2020-06-028-001). The trial was registered in the Clinical Research Information Service of the National Research Institute of Health, South Korea, on August 25th, 2020 (no. KCT0005348). To ensure consistency with and adherence to the trial protocol, two participating surgeons (one from each centre) and all participating researchers attended a calibration meeting covering each step of the trial, including all of the surgical steps, prior to commencing the trial. This manuscript is consistent with the CONSORT guidelines for reporting parallel-group randomized trials (Moher et al. 2012).

2.2 | Sample-Size Determination

The required sample size was calculated using software (G*Power version 3.1.9.7, Heinrich-Heine-Universität Düsseldorf, Germany) as described by the previous study based on the buccal hard tissue thickness measured at 6 months after the surgery (Benic et al. 2022). This study has included 20 patients per group, considering the dropout rate of 15%. To find a difference of 0.5 mm with a standard deviation of 0.5 mm (two-sided alpha level of 5% and a statistical power of 95%), 27 patients per group were estimated to be needed. Based on an assumed dropout rate of 15% (Faul et al. 2007), it was determined that 35 participants were appropriate for each group.

2.3 | Inclusion and Exclusion Criteria

Patients meeting the following inclusion criteria were enrolled: (a) age ≥ 18 years and (b) at least one tooth missing from the maxilla or mandible accompanied by horizontal alveolar defects. The following exclusion criteria were applied: (a) partially edentulous ridge requiring more than three implant installations; (b) bone metabolic disorder; (c) periodontal disease contraindicating implant placement; (d) history of antiresorptive medication usage within the previous 4 months; (e) smoking more than 20 cigarettes daily or smoking a pipe or cigars; (f) history of malignancy, radiotherapy, or chemotherapy within the past 5 years; (g) pregnant or lactating; or (h) poor oral hygiene status (full-mouth plaque score ≥ 25%).

2.4 | Randomization and Allocation Concealment

Eligible participants were randomly assigned to one of two groups using sealed envelopes that each contained a computer-generated random number. The allocated random numbers were generated following a stratified block randomization protocol with variable block sizes (2, 4, and 6), ensuring a 1:1 group allocation ratio within each centre. The enrolled participants at each centre were assigned to one of the following groups:

- Particulate (control) group, in which sites were augmented using demineralized porcine bone mineral (DPBM) particles with sizes ranging from 0.25 to 1.0 mm (The Graft, Purgo Biologics, Seongnam, South Korea).
- Collagenated (test) group, in which sites were augmented using a 10-mm × 11-mm × 12-mm soft-type DPBM block (0.25–1.0 mm granules; 85%) conjugated with cross-linked collagen (15%) (The Graft Collagen, Purgo Biologics).

Patients remained blinded to the group allocation throughout the experimental period, while this was not the case for investigators since the two bone graft materials had different appearances. To reduce the possible risk of bias during the analyses, all patient data, including group allocation, were encrypted.

2.5 | Surgical Procedures

Cone-beam computed tomography (CBCT) images were acquired preoperatively using parameters of 85 kV and 11 mA with an exposure time of 14 s and a field of view of 100 mm x 100 mm (Rayscan Alpha Plus, Ray, Seongnam, South Korea), while three-dimensional profilometric data were obtained using an optical scanner (Trios 3, 3Shape, Copenhagen, Denmark). All dental implants were placed followed by GBR procedures by a single clinician at each centre (J.S.L. in Centre 1 and D.W.L. in Centre 2). The allocated materials were grafted onto the peri-implant horizontal defects and covered with a collagen membrane (Bio-gide, Geistlich, Wolhusen, Switzerland). In the test group, the cross-linked collagenated bone substitute was customized to fit the defect area by trimming it with a scalpel (Mir-Mari et al. 2017). Primary closure was achieved with the retentive flap technique (Lee, Park, et al. 2022; Park, Chung, et al. 2023) without using additional fixation devices. Through apical flap advancement and periosteal releasing incisions just to the necessary amount, dead space could be minimized, thereby preventing the scattering and apical migration of the graft material.

Regular follow-up visits were performed at the following designated post-operative time points: 1 week (suture removal), 1 month, 3 months, and 4 months (Figure 1). At 4 months after the surgery, healing abutments were connected by flapless approach, and intraoral scan data were obtained afterwards. In cases with low vestibule formation due to the GBR, buccal flaps were partially elevated and apically positioned along with the healing abutment connection to aid in the achievement of peri-implant health.

2.6 | Defect Width Measurement

After superimposition of each patient's axial sectional CBCT views at different timepoints, the reference line was defined as the tangent line connecting the buccal alveolar bone contour of the adjacent teeth and was regarded as the original ridge envelope boundary (Figure S1). The baseline defect width was measured as the distance from the reference line to the innermost part of the horizontal defect.

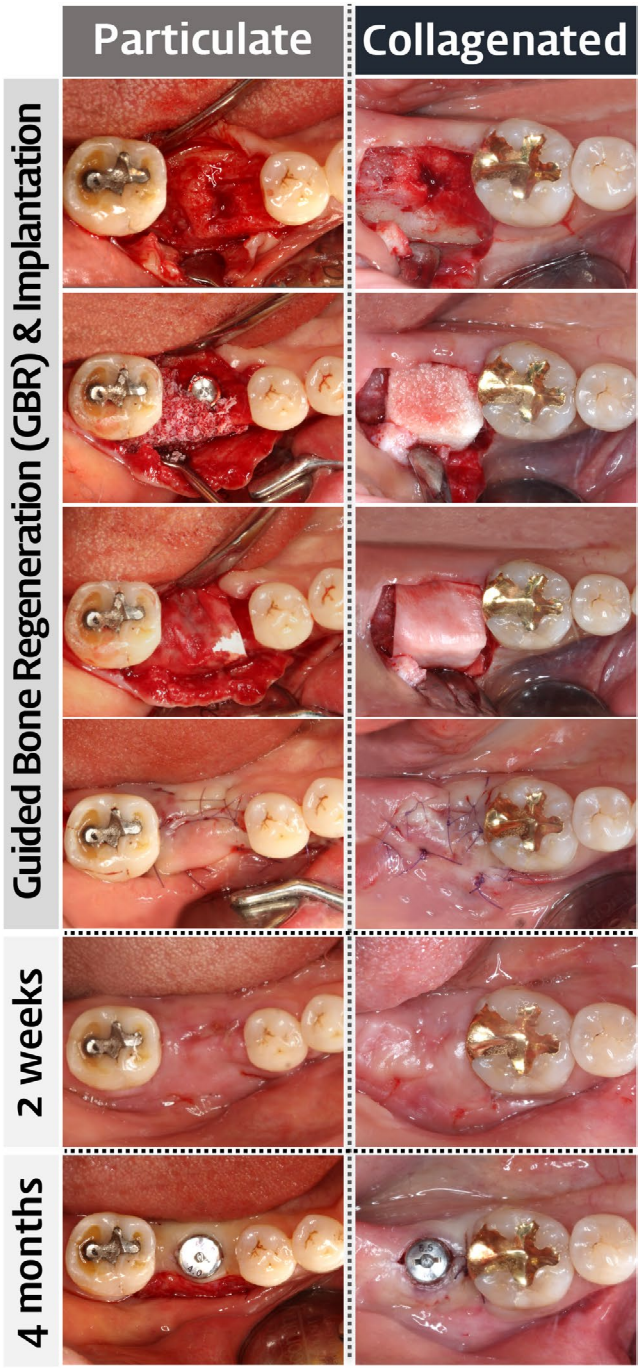

FIGURE 1 | Clinical photographs taken at the simultaneous guided bone graft (GBR) procedure, 2 weeks and 4 months after the surgery.

2.7 | Radiographic Analysis

The radiographic analysis was performed by a single researcher (J.Y.J.). CBCT images were obtained in Centres 1 and 2 at three time points during the experimental period: before the surgery (baseline), immediately post-operatively, and 4 months after the surgery. The dimensions of the augmented region were measured on the immediate post-operative and 4-month CBCT images by superimposing the baseline images using computer software (OnDemand 3D version 1.0.10.7510, Cybermed, Seoul, South Korea). The following parameters were measured (Figure 2A–C):

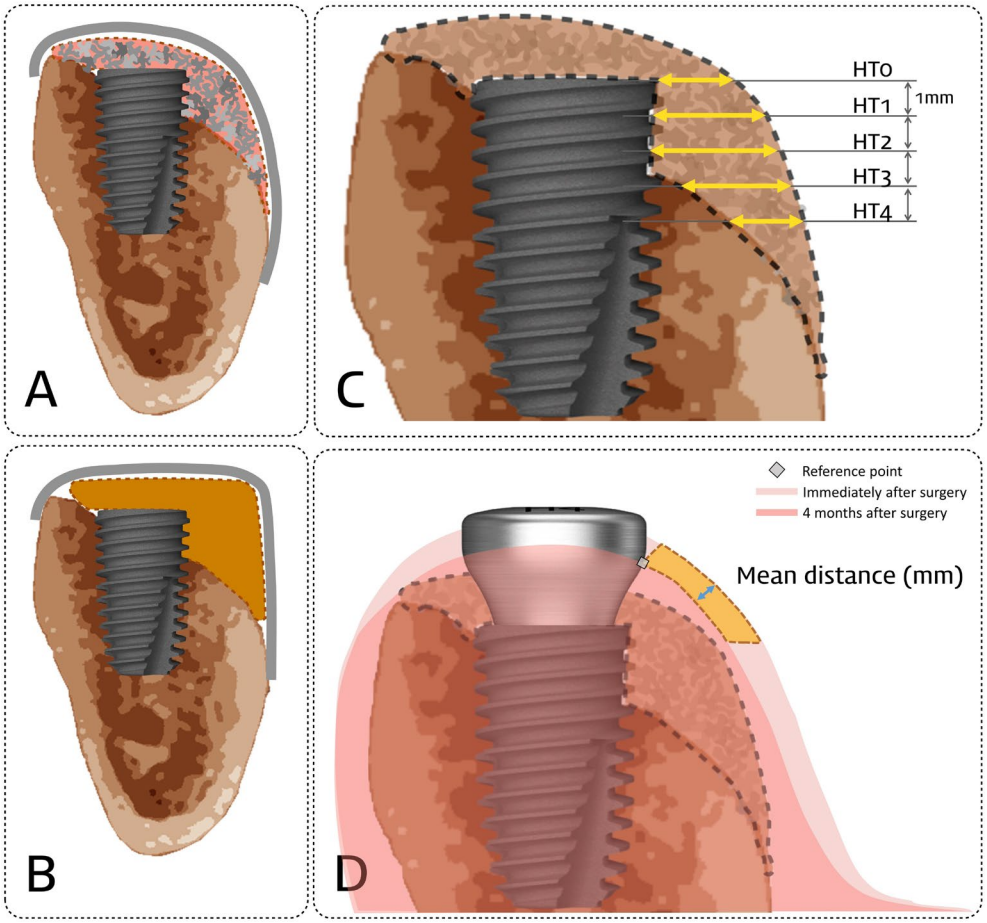

FIGURE 2 | Schematic illustration showing how the dimensional measurements were performed. (A) augmented area (AA; mm^2) and augmented volume (AV; mm^3) in the particulate group. (B) AA and AV in the collagenated group. (C) Horizontal distance from the buccal implant surface to the outermost augmented region at the level of 0, 1, 2, 3, and 4 mm (HT0, HT1, HT2, HT3, and HT4; mm) from the implant platform. (D) Schematic illustration showing how the soft tissue contour analysis was performed. The selected region of interest (ROI) coloured in orange was defined for evaluating the changes in soft tissue contour at two different timepoints (post-op and 4 months follow-up). The crestal border was set as the mucosal margin of the healing abutments connected at 4 months follow-up.

- Horizontal thickness (HT; mm), corresponding to the horizontal distance from the buccal implant surface to the outermost augmented region at 0, 1, 2, 3, and 4 mm (designated as HT0, HT1, HT2, HT3, and HT4) from the implant platform (Mir-Mari et al. 2016).
- Augmented area (AA; mm^2), corresponds to the area of the augmented region demarcated by the outermost augmented line, the floor of pre-existing alveolar bone, and the implant surface.
- Augmented volume (AV; mm^3), corresponding to the three-dimensional volume of the augmented region formed by subtracting the alveolar ridge volume of the baseline CBCT data from the immediate post-operative or 4-month data.

HT and AA were measured on the most-central image of the CBCT data, and AV was measured using three-dimensionally reconstructed CBCT data. The average value of HT0-4 (mean value of horizontal thickness at 0, 1, 2, 3, and 4 mm below the platform) at 4 months after surgery was considered the primary outcome of the study.

2.8 | Soft Tissue Contour Analysis

Scan data were obtained using an intra-oral scanner (Trios 3, 3Shape, Copenhagen, Denmark) at three distinct time points: before the surgery (baseline), immediately post-operatively, and 4 months after the surgery (Figure 2D). The STL datasets were superimposed over the baseline and another time point in the SMOP software (Swissmeda, Zurich, Switzerland) using the best-fit algorithm at the adjacent tooth surfaces. For the appropriate scan data showing acceptable superimposition outcomes, a single investigator (J.Y.J.) performed the soft tissue measurements using designated regions of interest (ROI), which were defined based on prior studies (Schneider et al. 2014; Bienz et al. 2017).

The linear change in the soft tissue contour within the ROIs was quantified as the mean distance between the two surfaces at baseline and 4 months (Zeltner et al. 2017) (Figure 2d). The changes in the area of ROIs and the volume outlined by the ROIs were also recorded as the planimetric and volumetric measurements, respectively.

2.9 | Statistical Analysis

All statistical analyses were conducted using SPSS software (version 25.0, IBM, Chicago, IL, USA) and R software (version 4.3.1, R Foundation for Statistical Computing, Vienna, Austria). Normality of the data distribution was confirmed for all measured parameters using the Shapiro–Wilk test. The Analysis of Covariance (ANCOVA) was performed for the possible confounders (type of arch: maxilla or mandible, surgical site: anterior, premolar, or molar site) that could influence the outcome variables (linear, areal, and volumetric increase of hard and soft tissue dimension) used in this study. The repeated-measures analysis of variance (ANOVA) was employed to assess differences between the two groups in all parameters with adjusted values based on the ANCOVA, and post hoc analyses were performed for the variables with statistically significant differences. Paired-samples *t*-tests were performed to compare different time points (immediate post-operative and 4 months) within the same group. The significance threshold in all statistical analyses was set at 0.05.

3 | Results

3.1 | Demographic Results

Among 86 participants who were initially assessed for eligibility (60 and 26 at Centres 1 and 2, respectively), 70 participants were enrolled and randomly assigned to the particulate and collagenated groups (Figure 3). After performing the GBR procedures, one participant showing compromised healing had undergone earlier re-entry of the surgery site than scheduled, and was not able to perform radiographic and volumetric analyses at the intended timepoint. Therefore, 69 participants were finally included in the statistical analyses of the study: 34 in the particulate group and 35 in the collagenated group (Figure 3).

The demographic characteristics of the included participants are presented in Table S1. There were no differences between the two groups except for the distribution of the type of jaw (8 maxillae and 26 mandibles for the particulate group, and 17 and 18, respectively, for the collagenated group). In both groups, there was a predilection for the participants to be male and for the use of molar sites. The participants were aged 65.8 [10.4] and 60.5 [15.3] years in the particulate and collagenated groups, respectively. The baseline defect width was 3.35 [1.85] mm and 2.49 [1.23] mm in the particulate and collagenated groups, respectively.

Considering the unequal distribution of baseline characteristics, the ANCOVA regarding overall parameters was performed and the results are summarized in Table S2. Involvement of the mandibular arch exhibited a negative correlation with two-dimensional outcome values (HT4, AA) compared to when performed in the maxilla. Additionally, procedures in the molar area showed a positive correlation with the HT values compared to those conducted in the anterior area.

3.2 | Clinical Findings

All included sites healed uneventfully except for one in the particulate group that exhibited delayed wound healing and had a healing abutment connected earlier than the time specified in the experimental schedule. The sites that received collagenated DPBM demonstrated significantly greater augmentation at the crestal level immediately post-operatively. However, at 4 months after the surgery, the clinical

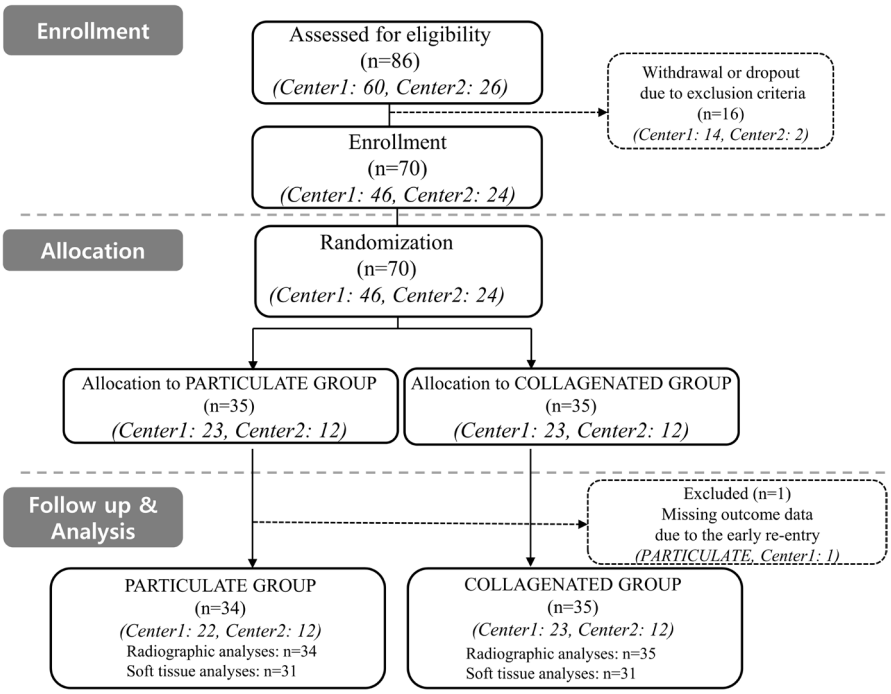

FIGURE 3 | CONSORT flowchart of the study.

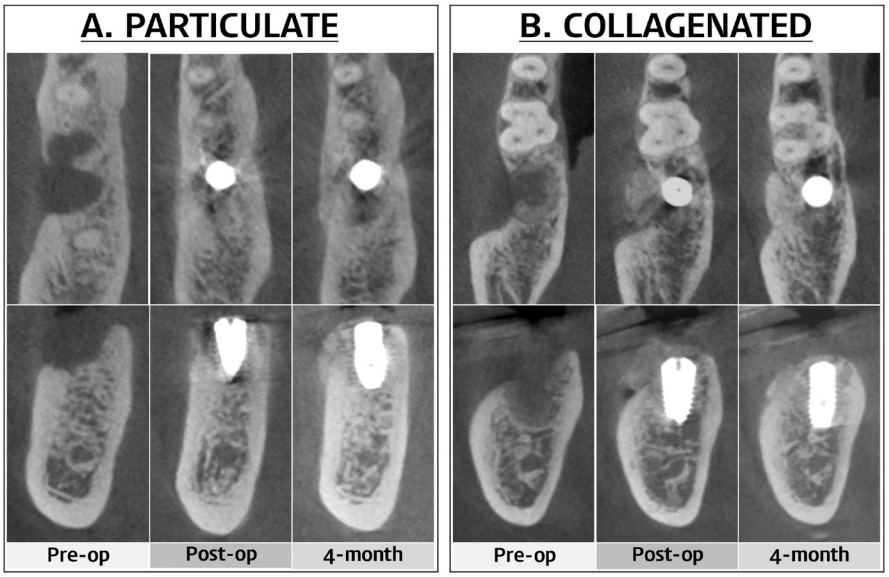

FIGURE 4 | Representative cone-beam computed tomography (CBCT) cross-sections in the two groups. After superimposition of the obtained data, dimensional measurements (linear, planimetric, and volumetric) were performed.

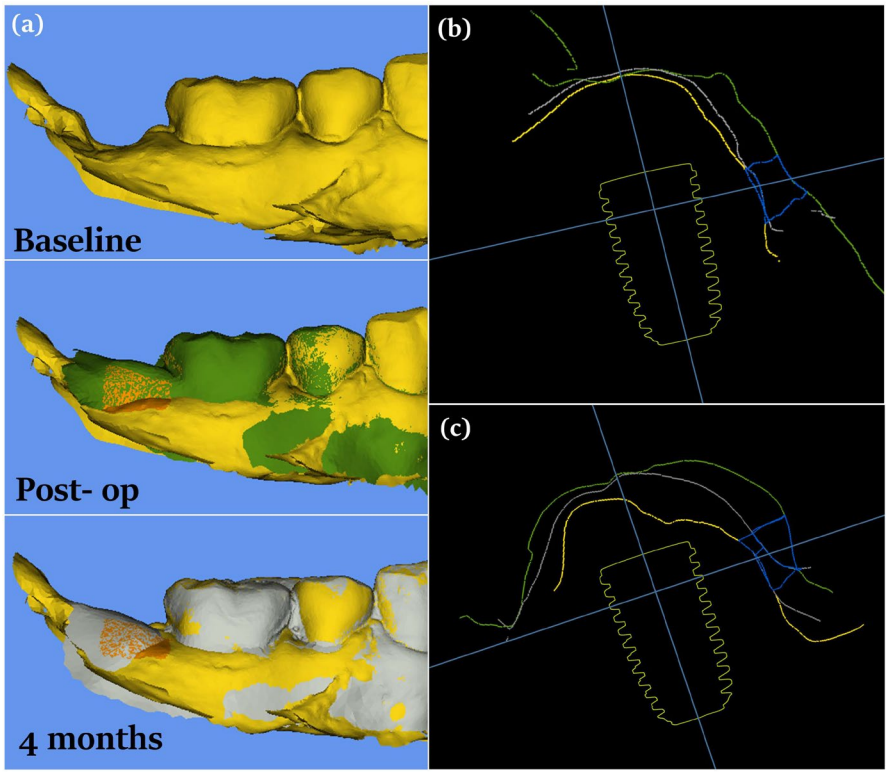

FIGURE 5 | (a) Soft tissue contour analysis was performed after superimposition of the STL files at three different timepoints: Baseline (yellow), post-op (green) and 4 months follow-up (grey). (b, c) Representative cross-sectional images of (b) the particulate group, and (c) the collagenated group.

volume augmentation was indifferent between the two groups (Figures 4 and 5).

3.3 | Radiographic Findings and Measurements

The results of the linear, planimetric, and volumetric measurements are presented in Table 1 and Figure 6a–c.

3.3.1 | Linear Measurements of Dimensional Alterations

The collagenated group showed a mean HT value of 3.81 [1.15] mm, while the particulated group showed 3.10 [1.07]mm immediately after the surgery. At 4 months after the surgery, all HT values in both groups had reduced significantly compared with those measured immediately post-operatively ($p < 0.001$).

TABLE 1 | Cone-beam computed tomography measurement of the augmented tissue at sequential time points.

			Particulate ($n=34$)		Collagenated ($n=35$)		
			Post-op	4-month follow up	Post-op	4-month follow up	p^b
Linear	HT0	mm	2.79 (1.02)[a,c]	1.96 (0.79)[a,c]	3.64 (1.07)[a,c]	2.43 (1.02)[a,c]	0.031[b]
	HT1	mm	3.14 (1.05)[a]	2.41 (0.88)[a]	3.84 (0.99)[a]	2.63 (1.04)[a]	0.168
	HT2	mm	3.25 (1.07)[a]	2.71 (1.05)[a]	4.01 (1.22)[a]	2.72 (1.12)[a]	0.071
	HT3	mm	3.21 (1.12)[a]	2.74 (1.12)[a]	4.01 (1.19)[a]	2.76 (1.20)[a]	0.066
	HT4	mm	3.12 (1.08)[a]	2.65 (1.04)[a]	3.55 (1.23)[a]	2.31 (1.09)[a]	0.050
	Avg.	mm	3.10 (1.07)[a,c]	2.49 (1.01)[a]	3.81 (1.15)[a,c]	2.57 (1.10)[a]	0.050[b]
Area		mm^2	30.54 (10.78)[a]	22.23 (8.61)[a]	40.09 (14.83)[a]	23.02 (9.36)[a]	0.052
Volume		mm^3	484.39 (222.31)[a]	313.52 (157.86)[a]	498.60 (281.58)[a]	263.47 (179.18)[a]	0.461

Note: Values are presented as mean (SD).
[a]Comparison between 'Post-op' and '4-month follow up' within the same group, statistically significant ($p<0.001$).
[b]p-values from the repeated-measure ANOVA analysis representing the interaction effect between time and group are statistically significant ($p<0.05$).
[c]Post hoc analysis showing a statistically significant difference between the particulate group and the collagenated group at the corresponding timepoint (adjusted $p<0.05$).

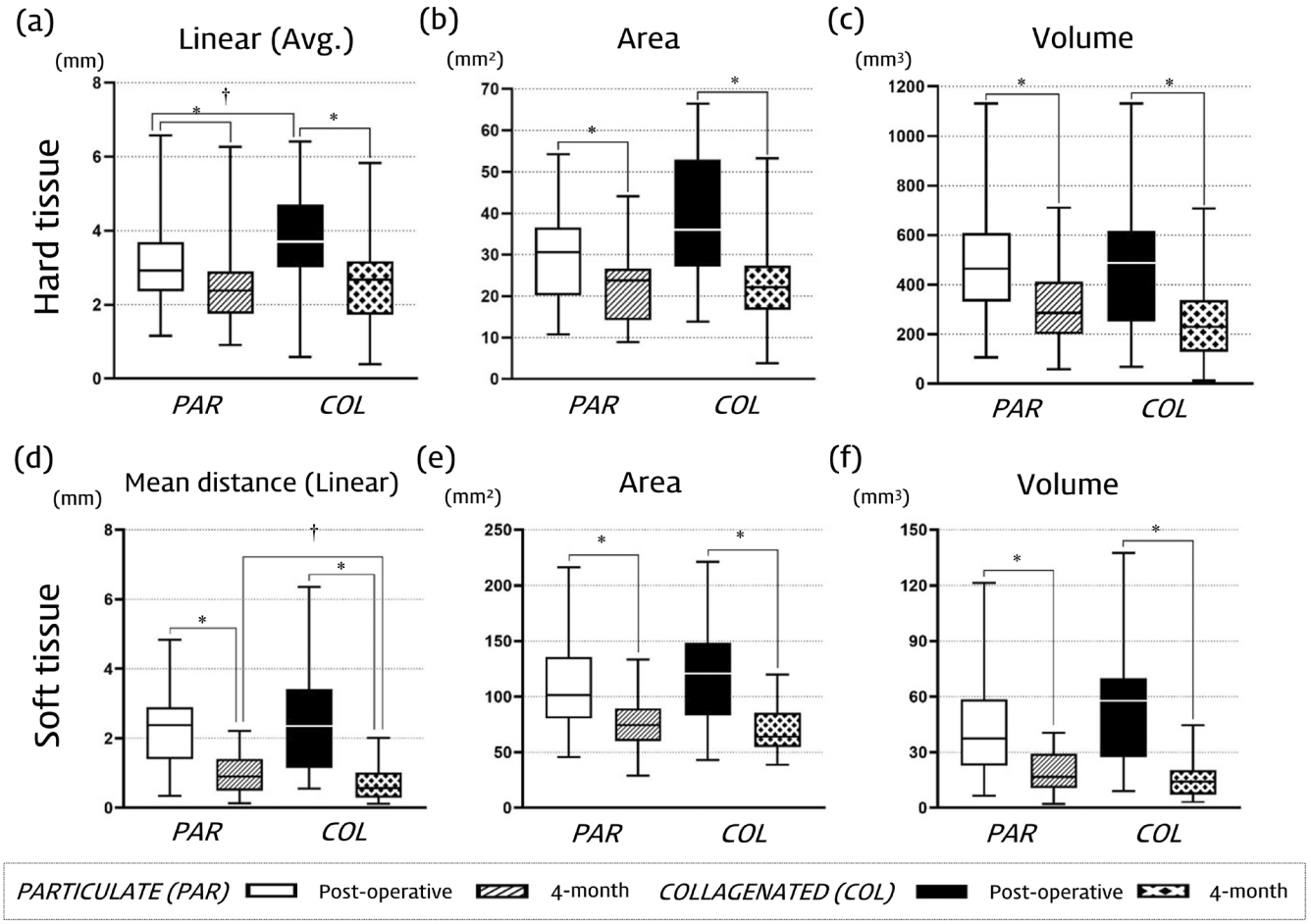

FIGURE 6 | (a–c) Box plots showing the radiographic dimensional outcomes of augmented tissues in (a) the average horizontal thickness (HT), (b) Augmented area (AA), and (c) Augmented volume (AV). (d-f) Box plots showing the changes in the soft tissue contour of augmented tissues with respect to (d) mean distance, (e) area of ROIs and (f) volume outlined by the ROIs. Abbreviations: PAR, the particulate group; COL, the collagenated group. * Comparison between 'Post-op' and '4-month follow up' in the same group, statistically significant ($p<0.05$). † Comparison between 'Particulate group' and 'Collagenated group' at the same time point, statistically significant ($p<0.05$).

The HT values in both groups were indifferent at all levels except the most-coronal level (HT0, $p = 0.031$) and the average value (average HT, $p = 0.050$). The post hoc analysis of HT0 demonstrated that the HT0 values were significantly higher in the collagenated group compared to the particulate group immediately after the surgery ($p = 0.0021$; 3.64 [1.07] mm and 2.79 [1.02] mm for the collagenated and particulate group, respectively) and 4 months after the surgery ($p = 0.030$; 2.43 [1.02] mm and 1.96 [0.79] mm for the collagenated and particulate group, respectively). Regarding the post hoc analysis of average HT, the collagenated group showed a significantly higher value immediately after the surgery (3.81 [1.15] mm) compared to the particulate group (3.10 [1.07] mm).

3.3.2 | Planimetric Measurements of Dimensional Alterations

AA showed no statistically significant difference between the collagenated group (40.09 [14.83] mm^2 at immediately after surgery, 23.02 [9.36] mm^2 at 4 months after surgery) and the particulate group (30.54 [10.78] mm^2 at immediately after surgery, 22.23 [8.61] mm^2 at 4 months after surgery) ($p = 0.052$). Both groups exhibited significant reductions in AA ($p < 0.001$) until the 4-month follow-up visits.

3.3.3 | Volumetric Measurements of Dimensional Alterations

The AV values in the particulate and collagenated groups did not differ significantly ($p = 0.461$). Both groups exhibited significant reductions in AV until the 4-month follow-up visit ($p < 0.001$).

3.4 | Soft Tissue Contour Measurements

The results of soft tissue analyses are presented in Figure 6d–f and Table S3. Sixty-two patients (31 patients in each group) with scan images showing an appropriate superimposition rate between baseline and 4 months after the surgery were included in the analyses. The increase in the mean distance was significantly different between the two groups. The post hoc analysis showed that the increase in the mean distance immediately after the surgery was not significantly different between the collagenated group (2.50 [1.44] mm) and the particulate group (2.15 [1.13] mm). After 4 months, the increase in the mean distance had reduced to 0.68 [0.50] mm (collagenated group) and 0.99 [0.56] mm (particulate group), showing a significant difference due to the high shrinkage rate of the collagenated bone substitute.

The planimetric and volumetric measurements tended to show a similar tendency, with high proportional shrinkage rates of 23.00 [19.17]% (particulate group) and 36.61 [22.46]% (collagenated group) for the area of ROIs, and 41.94 [36.62]% (particulate group) and 63.00 [26.25]% (collagenated group) for the volume of ROIs. Intergroup comparison analyses found no significant difference between the two groups.

4 | Discussion

This study compared the dimensions and changes therein of augmented sites that received collagenated or particulate DPBM after a 4-month healing period following the application of GBR to a horizontal defect around dental implants. The main findings of this study are multifaceted: (1) there was no significant difference in the dimensional outcomes between the two graft materials, but HT was larger at the implant platform level at sites that received collagenated DPBM; (2) collagenated DPBM induced greater post-operative augmentation in the immediate vicinity of the implant fixture, despite an insignificant difference in the total volume of post-operative augmentation; and (3) augmentation with collagenated DPBM resulted in greater reductions in both hard and soft tissue dimensions.

Regarding the use of collagenated bone substitute, a previous RCT (Benic et al. 2022; Song et al. 2023) has assessed dimensional changes in both the hard and soft tissues after GBR procedures accompanied by collagenated and particulate bone substitutes with the use of a resorbable membrane and fixation pins. Despite the significantly higher increase of post-operative hard tissue dimensions in the collagenated group, no significant difference was found in hard-tissue dimensions between the two treatment modalities after a 6-month follow-up (Benic et al. 2022). The high biodegradation rate of collagenated bone substitute may have played an important role in these previous findings, eventually leading to the apical migration of the bone substitute (Benic and Hämmerle 2014; Kwon et al. 2023). Consistent with the result of the above-described studies, the present study also found that the quantitative radiographic outcomes after 4 months were not significantly different between using collagenated and particulated bone substitutes. Regarding the shrinkage rate, the linear dimension of the augmented portion in the collagenated group decreased by an average of 32.32%, which was clearly a larger proportional change than that in the particulate group (19.90%) (Table S4).

To stabilize the augmented bone materials, the two surgeons who participated in the present trial applied the specific retentive-flap management technique that has been verified in previous studies performed by the same research group (Lee, Park, et al. 2022; Park, Chung, et al. 2023). This concept involves achieving coverage of the augmented bone substitute through the utilization of a mucoperiosteal flap with appropriate tension, which allows for passive primary closure and also secure stabilization of the materials without any fixation devices. A previous retrospective study using this technique achieved successful horizontal augmentation outcomes, with a notable increase in bone width of 2.48 mm observed at 1 year after the surgery (Park, Chung, et al. 2023). A systematic review of horizontal augmentation identified about 1.5 mm of width loss at re-entry, possibly due to the tendency for an excessive amount of augmentation being prone to resorption following the natural anatomy of the original alveolar ridge (Naenni et al. 2019). These results are broadly consistent with the present study achieving substantial horizontal width gains of 3.64 mm immediately post-operative and 2.43 mm after 4 months. It is worth noting that this study is the first randomized clinical trial to achieve a notable horizontal width gain using the retentive-flap technique,

producing quantitative outcomes comparable with those of the previous RCT that employed fixation pins (Benic et al. 2022; Song et al. 2023).

Despite the high resorption rate of collagen substitute in augmentation procedures, the addition of a soft-block bone substitute has shown to be beneficial in maintaining the buccal contour at surgery sites (Mir-Mari et al. 2017). Previous studies showed that overaugmentation beyond the ridge contour was advantageous for maintaining the ridge contour (Lee et al. 2021; Arnal et al. 2022; Zuercher et al. 2023). The results of clinical studies evaluating quantitative outcomes of GBR need to be interpreted with caution since the defect morphology and flap characteristics may vary significantly between subjects so as to markedly influence the achievable amount of augmentation (Fu and Wang 2011; Benic et al. 2019). Nevertheless, it is important to stress that most related clinical studies have achieved significantly larger post-operative augmentation widths using collagenated bone substitute compared with using particulated bone (Benic et al. 2022; Song et al. 2023), and the collagenated group in the present study also exhibited greater post-operative augmentation in the immediate vicinity of the implant fixture. Moreover, an intergroup difference was found in the alveolar crest width (i.e., HT0) after 4 months of follow-up, suggesting a potential benefit of using collagenated bone substitute in terms of coronal augmentation.

Comparing the changes in soft tissue contour of peri-implant mucosa has shown that similar horizontal tissue width gain could be obtained in both groups at 4 months after the surgery (Figure 6d–f). The use of collagenated bone substitute has been highlighted as an effective option for preventing volumetric shrinkage after teeth extraction (Schneider et al. 2014), and a previous paper performing GBR using deproteinized bovine bone material and collagen membrane reported that a horizontal contour increase of approximately 1.00–1.20 mm could be achieved after 3 months (Benic et al. 2017). This aligns with the results of this paper, showing horizontal gains of 0.99 [0.56] mm and 0.68 [0.50] mm for the particulate and the collagenated group, respectively (Table S3). It should be mentioned that the previous RCT with a similar study design to the present study had shown superior outcomes using soft bone block at 6 months after the surgery, showing a somewhat contrasting tendency compared to the findings of the present study (Song et al. 2023). The authors attributed the difference in changes of soft tissue contour to the higher initial amount of augmentation in the collagenated group due to the variations in defect configuration of both groups. In the current trial, the initial superiority of soft tissue volume in the collagenated group was not as pronounced, which may have led to the opposing results at 4 months after the surgery.

The present study had several limitations that should be mentioned. First, the clinical end point of the study was 4 months, which is a relatively short observational period for fully assessing GBR outcomes. A previous study with a similar design using particulate bone observed that horizontal bone gain decreased from 3.98 [2.06] mm immediately after surgery to 3.02 [2.06] mm at 4 months and 2.48 [2.09] mm at 1 year after the GBR (Park, Chung, et al. 2023). This notable reduction over time highlights the potential variability in long-term dimensional outcomes, suggesting the need for a longer observation period in the present study. Secondly, at 4 months after the surgery, intraoral scan data were obtained after healing abutment connection and, if necessary, a vestibuloplasty procedure involving apical positioning of the buccal flap. This may have had a considerable impact on the soft tissue contour. Third, only the radiographic parameters were fully analyzed, and so further controlled studies involving histologic and clinical parameters need to be performed. Moreover, this study followed a per-protocol analysis by excluding data from the patient who underwent earlier re-entry of the surgical site, possibly causing a bias of excluding non-compliant subjects.

Within the study limitations, it can be concluded that the increases in augmentation dimensions over 4 months after the surgery with the retentive-flap technique were not significantly different between the collagenated and particulate groups. The overall dimensional outcomes of this study using the retentive-flap technique were consistent with those obtained in conventional studies utilizing fixation pins. The high resorption rate of the collagenated bone substitute negates its initial superiority in either radiographic or soft tissue dimensions.

Author Contributions

Ji-Young Jung: data curation, writing – original draft, formal analysis, software. **Seung-Hyun Park:** investigation, writing – original draft, validation, visualization. **Kwan-Jung Kim:** data curation. **Kyung-A Ko:** formal analysis, data curation. **Dong-Woon Lee:** writing – review and editing, methodology. **Jung-Seok Lee:** conceptualization, methodology, writing – review and editing, validation, funding acquisition.

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Ethics Statement

The trial was registered in the Clinical Research Information Service of the National Research Institute of Health, South Korea, on August 25th, 2020 (no. KCT0005348; https://cris.nih.go.kr/cris/search/detailSearch.do?seq=17908&search_page=L).

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Supporting Information

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