Histologic analysis following grafting of damaged extraction sockets using deproteinized bovine or porcine bone mineral: a randomized clinical trial

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Histologic analysis following grafting of damaged extraction sockets using deproteinized bovine or porcine bone mineral: a randomized clinical trial

Directed by Professor Chang-Sung Kim

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감사의 글

치의학 분야 최고의 교육 기관인 연세대학교에 입학하여 세계적으로 가장 활발히 우수한 연구 성과를 내시는 교수님들 가까이에서 배움의 기회를 갖게 된 것은 커다란 영광이었습니다.

먼저, 본 연구가 학위 논문으로 완성되기까지 연구에 매진할 수 있도록 면면히 지도해주신 김창성 교수님과 아낌없는 격려와 따뜻한 조언으로 많은 가르침주신 이중석 교수님께 진심으로 감사드립니다. 연구자로서 비판적 자세와 안목을 가질 수 있도록 이끌어주신 조규성, 최성호, 정의원, 차재국, 백정원 교수님께 깊이 감사드립니다. 또한, 바쁘신 와중에 심사를 맡아주신 이동원, 김영택, 임현창 교수님께 감사드립니다.

치과대학 학부 시절부터 자애로운 마음으로 보살펴주신 담임반 허경석 교수님께도 감사의 마음을 전합니다. 아울러, 연구가 무사히 진행되고 마무리될 수 있도록 도움을 준 치주과의 모든 선후배 의국원과 연구원들, 특히 송영우, 이관주 선생님에게 고마움을 전합니다.

마지막으로, 무한한 응원과 지지를 보내주시는 부모님, 좋은 자극을 주는 하나뿐인 동생, 언제나 믿음으로 곁을 지켜주는 사랑하는 아내까지 세상 무엇보다 소중한 가족들 덕분에 지금의 제가 있을 수 있었습니다. 감사한 마음 잊지 않고 겸손한 자세로 사회에 기여하는 사람이 되도록 더욱 노력하며 살겠습니다.

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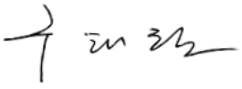

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Abstract

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Background: Extraction socket grafting has been developed as a treatment to prevent bone resorption after tooth extraction. Indication of this clinical procedure previously limited to the intact extraction socket at the anterior region, however, has been recently extended to the damaged sockets and posterior region.

Objectives: This study histologically analysed biopsy samples obtained from sites of damaged extraction socket grafting using deproteinized bovine bone mineral (DBBM) or deproteinized porcine bone mineral (DPBM) with coverage by a collagen membrane.

Material and methods: One hundred patients participated in this randomized controlled

clinical trial of extraction socket grafts performed in cases of periodontally compromised teeth. All participants were blinded to their group allocations, and each material was grafted with coverage by collagen membranes after extraction of the tooth and removal of granulation tissue. At implant placement at 4 months, a biopsy was harvested at the implant site using a trephine was analysed histologically.

Results: Eighty-five biopsy samples were acquired, of which 81 were finally included in the histologic analysis (42 in DBBM and 39 in DPBM group). Both DBBM and DPBM groups showed comparable proportions of residual biomaterial (12.37±5.67% and 12.21±5.75%, respectively), newly formed bone (15.07±10.52% and 18.47±11.47%, respectively), and non-mineralized tissue (72.56±10.07% and 71.55±15.47%, respectively). There were no significant differences in these histological parameters between the two groups with different biomaterials.

Conclusion: Comparable histologic bone formation was found in both socket grafted groups with DBBM or DPBM covered by collagen membranes in periodontally damaged extraction sockets. However, a wide variation of new bone formation was found after 4 months of postsurgical healing and a tendency of higher new bone formation were shown at damaged sockets that had an intact unilateral residual wall regardless of buccal or lingual side.

Keywords: extraction socket, bone regeneration, bone substitutes, clinical research, guided tissue regeneration

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I. Introduction

The clinical procedure that involves grafting bone substitutes into tooth extraction sockets is based on the rationale that the dimensional alterations of the alveolar ridge that occur after tooth extraction can be minimized by adding bone graft substitutes that provide a scaffold to the newly formed bone. Several animal studies have shown that a ridge preservation technique could attain dimensional preservation of the alveolar ridge and successful new bone formation in extraction sockets [1,2]. Similar studies were later performed as clinical trials and also reported clinical success [3-6]. In addition, grafting

various types of bone substitutes in extraction sockets in the anterior region exhibited dimensional stability of the alveolar ridge both at the time of implant installation [7-9] and a long-term follow-up [10]. However, the suggested clinical indications for this procedure have recently been expanded to the posterior sites or damaged extraction sockets as shown in several clinical studies [11,12].

Recent preclinical animal studies have suggested that socket grafting in extraction socket models with buccal bone deficiencies was able to restore the ridge dimensions by performing bone grafting immediately after tooth extraction [13,14]. The outcome of bone regeneration in the grafted area was yielded in final ridge dimensions comparable to the pristine osseous ridge. At histological observation, throughout sequential healing, it was revealed that sprouting new bone occurred from the preexisting alveolar bone and regenerated bone tissue that expanded to the outermost surface of the grafted area. On the contrary, significant dimensional collapse and reduced bone growth were shown in the ungrafted extraction sockets that had been previously compromised with buccal bone deficiency. Based on these results from the preclinical studies, the same authors performed a clinical trial to evaluate the outcome of alveolar ridge regeneration after bone grafting at periodontally compromised extraction sockets [11]. Both two types of xenogenic bone substitutes used in the study showed an outcome of comparable ridge augmentation from the damaged extraction sockets with minor postoperative vertical and horizontal bone loss (<2 mm linearly). Therefore, it can be stated that performing bone grafting immediately after tooth extraction even in the sites that have been damaged with bone deficiency could limit a drastic atrophy of the alveolar ridge.

Postextraction treatment methods have been developed primarily with the basis of both quantitative and qualitative aspects of evidence from animal studies. However, only few clinical studies have provided qualitative evidence regarding bone formation within the grafted extraction sites. One of the clinical studies with histological assessment showed that newly formed bone could be observed within a small apical part of the grafted sockets with fibrous tissue capsulation of biomaterials in the coronal area at 8 months after performing a ridge preservation [15]. Furthermore, a recent meta-analysis showed a high rate of heterogeneity in the outcome of histologic findings of this treatment [16]. This might be attributed to the large standard deviations (12.4–16.8%) found in the amount of new bone formation, yet with the similar mean amount of bone formation of the biopsy samples (24.6–35.3%) [17-20]. From this, it can be stated that this is relatively a high value of deviations among the biopsy results when compared to those of found in other clinical trials that performed conventional bone augmentation procedure such as sinus grafting (mean=26.0–38.0% and standard deviation=0.5–6.3%) [21-24]. In sum, qualitative evaluations that include histologic analysis appears to be necessary to assess and determine clinical application of the treatment since this procedure is often related to a following dental implant therapy that requires sufficient osseointegration within genuine bone tissue.

The objective of the present study was to histologically analyse the biopsy cores obtained from the implant installation site using a trephine 4 months after grafting deproteinized bovine bone mineral (DBBM) or deproteinized porcine bone mineral (DPBM) in periodontally compromised extraction sockets.

II. Materials and Methods

1. Study design

This study formed part of a randomized controlled clinical trial to compare the efficacy of DBBM (control group; 0.25–1.0 mm, Bio-Oss, Geistlich Pharma, Wolhusen, Switzerland) and DPBM (test group; 0.25–1.0 mm, THE Graft, Purgo Biologics, Seoul, Korea) as a grafting material in damaged extraction sockets. The dimensional results have already been published elsewhere [11] (Figure 1). The experimental design was based on the Tokyo version of the Helsinki Declaration and Good Clinical Practice Guidelines and approved by the Institutional Review Board for Clinical Research at the Dental Hospital of Yonsei University (approval no. 2-2015-0009).

2. Sample-size determination

The sample size of the clinical trial was originally calculated for a comparison of dimensional change as the primary outcome value in two experimental groups with a two-sided alpha level of 5%, a statistical power of 90%, and an effect size of 0.74, based on previous results [25]. Therefore, forty sites per group were found to be required in the clinical trial, and so 50 sites per group were enrolled on the assumption of a dropout rate of 20%. However, the present study compared histologic bone formation in both groups, and the appropriate sample size to draw a conclusion was recalculated based on the histologic

results [26] in extraction socket grafting. Effect size was determined at 0.98, and the necessary sample size for each group was calculated to be 29 sites with the two-sided alpha level of 5% and the power (1-β) of 95%. The present study finally included 39 and 42 samples for DPBM and DBBM group, therefore, the comparison could be drawn based on the sample size determination.

3. Study protocols

The study protocols are reported in detail elsewhere [11]. Briefly, patients who were chosen to receive tooth extraction due to severe periodontitis or a combined endodontic-periodontal lesion were included in the present trial. Group allocation was performed randomly with the aid of sealed envelopes, and the participants were blinded to the type of graft that they received. DBBM or DPBM was grafted with coverage by a collagen membrane (Biogide, Geistlich Pharma) after removing the teeth and the surrounding granulation tissue; material grafting within the sockets and membrane coverage after flap elevation, and suturing at the original position of the flap with the exposure of the membrane via the entrance of the socket. Prosthetically-oriented implant installation accompanied with bone preparation by trephine to obtain a bone biopsy sample for histologic evaluation at 4 months after surgery (Figure 2). After acquiring the biopsy sample, the sample information was concealed and researchers were reblinded before they performed the histologic analysis in order to reduce bias.

4. Defect size and classification by clinical features

Clinical features of defects were evaluated to determine effects on new bone formation; defect width and height of buccal/lingual wall were measured, and the grafted sockets were classified into the following six subgroups based on the height of the buccal and lingual walls (Figure 3).

- subgroup A: complete absence of both the buccal and lingual walls.
- subgroup B: complete absence of either the buccal or lingual wall and partial destruction of the other wall.
- subgroup C: partial destruction of both the buccal and lingual walls.
- subgroup D: complete absence of either the buccal or lingual wall with the other wall intact.
- subgroup E: partial destruction of either the buccal or lingual wall with the other wall intact.
- subgroup F: both the buccal and lingual walls intact.

5. Histologic and histomorphometric assessments

All biopsy samples were gently retrieved from each trephine and fixed in 4% paraformaldehyde solution for 2 days. The specimens were decalcified with Calci-Clear Rapid (National Diagnostics, Atlanta, GA, USA) and then embedded in paraffin before being cut into two central sections with a thickness of 4μm using a microtome (Model 2255, Leica, Wetzlar, Germany). Serial sections were stained using hematoxylin and eosin, and

Masson's trichrome. Histologic slides were observed under a light microscope (BX51, Olympus, Tokyo, Japan) and digitally scanned at a magnification of ×200 for histomorphometric analysis.

Four of the 85 biopsy core samples (1 in the DBBM group and 3 in the DPBM group) were excluded from the analysis since pristine bone sites rather than grafted sites had been harvested. The native bone was identified by the absence of graft materials and excluded from the analysis. The scanned images of the histologic slides were analysed histomorphometrically using computer software (Photoshop CS6, Adobe, San Jose, CA, USA). The total area of the specimens included new bone, residual biomaterials, and fibrovascular tissues. The amount of new bone was measured based on morphologic features of mineralized tissues and the identification of osteoblasts and osteocytes within or around the mineralized tissue. Small mineralized tissues with the appearance of discontinuous lamellar structure and lacunae without osteocytes were easily distinguished, and measured as residual biomaterial. Fibrovascular tissues were measured based on the unmineralized tissue area including connective tissues, vessels, and the other tissue components within the specimens. The proportion of each component within the total specimen area was calculated, and the proportion of the total specimen area relative to the internal size of the trephine was calculated as the harvesting proportion.

6. Statistical analysis

Statistical analysis was performed using standard software (SPSS version 23.0, SPSS,

Chicago, IL, USA). The means and standard deviations of all parameters were calculated. The independent *t*-test was used to compare the histologic parameters and harvesting proportion between the control and test groups. Pearson's correlation tests were applied to determine correlation between new bone formation and defect size or residual wall height. Subgroup results were evaluated their normality by Shapiro-Wilk test, and parametric and nonparametric statistical analyses among the subgroups were performed accordingly; one-way ANOVA for new bone formation and Kruskal-Wallis test for harvesting proportion. The criterion for statistical significance was set at $p<0.05$.

III. Results

1. Subject populations

The characteristics of the subject populations included in the present clinical trial have been described previously [11]. Briefly, 100 participants received extraction socket grafting, and dimensional analysis was performed in 94 of them (n=47 for each of the DBBM and DPBM groups). However, nine participants withdrew from the final procedure of the clinical trial (biopsy sample acquisition during implant surgery). Out of the remaining 85 biopsy samples (43 and 42 for the DBBM and DPBM groups, respectively) obtained from the finally included participants, 1 specimen from the DBBM group and 3 from the DPBM group were excluded from the histomorphometric analysis due to a low quality of the histology samples, the minimal inclusion of tissues, or the presence of severe artifacts in a critical area of the slide. Histomorphometric analyses were therefore finally performed in 81 specimens: 42 and 39 for the DBBM and DPBM groups, respectively (Table 1).

2. Histologic assessment

The histologic assessment found no evidence of marked inflammatory reactions and no occurrence of foreign-body reactions in any of the 81 histologic specimens. In addition, biomaterial particles could be visually identified based on their typical structure and

staining color, being integrated into the native bone and partially surrounded by connective tissue rich in cells and newly formed vessels.

In particular, new bone tissues were detected in various regions in the biopsy samples that spanned their lateral, apical, coronal, and central regions. Typical trabecular bone structures were observed across a broad expanse of each sample with clearly distinguishable osteocytes, which is indicative of the vitality of bone tissue.

New bone formation was primarily observed at the biomaterial–bone interface. DBBM and DPBM were observed as osseous tissue fragments with pale eosinophil staining and empty lacuna, whereas newly formed bone areas appeared with osteocytes in the lacunae and more-intense eosinophil staining. The remaining tissue present in the samples was connective tissue comprising fibroblasts, collagen fibers, and small capillaries. The DPBM particles were generally found to be more frequently surrounded by new vital bone than by connective tissue in comparison with DBBM particles (Figure 4).

3. Histomorphometric assessment

In all of the 81 bone biopsy cores obtained using a trephine, the histomorphometric measurements were exclusively performed around the areas of newly formed bone tissue, graft materials, and fibrous tissues. The percentages of newly formed bone, residual graft particles, and fibrous connective tissues were 15.07±10.52%, 12.37±5.67%, and 72.56±10.07%, respectively, in the DBBM group; the corresponding percentages in the DPBM group were 18.47±11.47%, 12.21±5.75%, and 69.32±10.02%. None of these values

differed significantly between the DBBM and DPBM groups (Table 2 / Figure 5a).

The harvesting proportion which is the obtained tissue in proportion to the total inner area outlined by trephine bur did not differ significantly between the DBBM (69.22±16.00%) and DPBM (71.55±15.47%) groups. The harvesting proportion of all samples showed a wide variation, ranging from 32% to 96%, and was evenly scattered regardless of the applied biomaterials. Although the harvesting proportion can be affected by the clinical bone density, a scatter plot of new-bone percentage versus the harvesting proportion revealed no correlation between the histologic bone quality and the harvesting proportion (Figure 5b).

Additionally, the outcomes did not vary significantly when the extraction socket defects were classified into the six subgroups of clinical defects. The percentages of harvesting proportions in subgroups A to F were 70.83±13.27%, 74.54±15.49%, 74.32±11.11%, 72.89±17.93%, 65.13±17.57%, and 63.80±13.53%, respectively (Table 3 / Figure 6a); the corresponding newly formed bone were 13.25±10.05%, 14.44±8.52%, 15.54±11.37%, 21.14±10.02%, 21.39±11.80%, and 14.14±12.15% (Figure 6b).

Defect width and residual wall height were presented in Table 4-5, and scatter plot and the correlation results between new bone formation and defect width or residual wall height were presented (Figure 7). The maximal residual wall height (defined as a higher height of the residual wall, either buccal or lingual wall) and bucco-lingual defect width showed significant but weak correlation with new bone formation (Pearson's coefficient=0.25 and 0.23; p=0.02 and 0.04, respectively).

IV. Discussion

This study histologically evaluated biopsy samples obtained using a trephine in a randomized clinical trial that compared the outcome of use of DBBM and DPBM in periodontally compromised extraction sockets from 100 participants [11]. Both DBBM and DPBM resulted in dimensional augmentation of the alveolar ridge with minimal volumetric shrinkage according to a previous study, but the histologic results obtained in the present study revealed low bone formation of less than 20% within these augmented areas after 4 months of postgrafting healing, regardless of the applied materials. When compared to many previous studies that reported around 30% of histologic new bone formation after performing ridge preservation techniques [17-20], relatively a low bone formation found in the present study might be attributed to delayed or interrupted initial healing by the materials applied at the damaged extraction sockets with limited healing sources. Comparing these results to the previous studies reporting 25% to 40% of mineralized tissue within biopsy samples in conventional alveolar ridge augmentation such as sinus grafting or guided bone regeneration [23,27-29], it remains questionable whether the augmented alveolar ridge attained by extraction socket grafting at periodontally compromised sites can be considered a sustainable bone bed for dental implants.

The present study found no significant difference in the outcome of new bone formation between DBBM and DPBM groups, which is in agreement with similar bone formation of 26.20±7.10% in DBBM and 29.7±9.3% in DPBM group that occurred when

both biomaterials were grafted in maxillary sinuses in the previous study [27]. However, in both groups, a wide range of different results were similarly shown not only in the outcome of new bone formation from 0% to 43%, but also in the harvesting proportion obtained from the trephine used to perform the biopsy. The residual materials occupied similar proportions of areas within the samples of both groups, with little evidence of resorption of the materials and minimal appearance of multinucleated osteoclasts on all histologic slides from both groups. According to the histomorphometric results, there was a less variation in the proportions of area occupied by residual biomaterials (12.37±5.67 and 12.21±5.75 for DBBM and DPBM, respectively) compared to that of the new bone proportions of area (15.07±10.52 and 18.47±11.47, respectively). Therefore, it is suggested that both DBBM and DPBM could provide a space within damaged extraction sockets with similar osteoconductive properties, while the amount of new bone formation were markedly varied in the maintained spaces.

A low mean proportion of regenerated bone and a large variation from 0 to 43% can be presented as clinical hurdles to the grafting at periodontally compromised extraction sockets. The protocol of a short healing period could be one of the reasons accounting for such a large deviation, since histological assessment at 4 month post-surgery revealed that it was not long enough to allow sufficient bone formation and the optimal growth of mineralized tissue. In a preclinical study, Lee et al. found that the amount of newly formed bone tissue within grafted damaged extraction sockets would increase over time indicating that longer healing periods should be considered for this procedure to be performed in

periodontally compromised extraction sites [14]. In a systematic review studying clinical trials that analysed bone quality at the sites of intact extraction socket grafting via histological assessment, a similar proportion of mineralized tissue formation was reported at spontaneously healed sites after 3 to 4 month healing periods before implantation [16]. Thus, to verify different results found in the current study, further clinical studies are needed to determine optimal healing periods after extraction socket grafting at periodontally compromised sites. Furthermore, since the histologic assessment that was performed in this study was not guided and analysed only a specific histological slide at a single cross-sectional plane rather than a volume of images, the comparison of our outcome with those of the previous literature should be interpreted with caution.

In a clinical setting, most clinicians rely on tactile determinations of bone density to evaluate the success of clinical outcome of bone grafting. With this respect in mind, the present study also included the harvest proportion of the trephine-based biopsy to indirectly assess the clinical bone density based on a phenomenon that a higher density of bone is likely to be collected with a larger volume of biopsy sample. However, no correlation, yet only characterized by a sparsely scattered pattern, between harvest and new bone proportions was found under the analysis of each DBBM and DPBM group. This indicates that clinical bone density cannot be a deciding factor when assessing the degree of bone regeneration within the grafted sites of periodontally compromised extraction sockets.

The present study performed an additional analysis evaluating effects of defect features on new bone formation, which can be served as a niche potentially providing both

healing sources and wound stability. The main aim of these additional analyses was to evaluate if there is any association between varied morphologies of sockets and the widely varied new bone formation. Pearson's analyses demonstrated correlations of bucco-lingual defect width and maximum residual wall height with new bone formation. However, only maximal residual wall height was confirmed to have a positive correlation by an additional t-test ($p<0.01$); intentionally two subgroups were divided by the mean 'maximal wall height' to confirm the correlation, the upper and the lower groups were compared. This coincides with the results from subgroup analysis that groups with an intact wall on either buccal/lingual side (subgroup D and E) showed the highest new bone formation compared to the other groups with completely or partially destroyed walls (A, B and C). In our previous preclinical study on the damaged extraction sockets, newly formed bone sprouted from the residual bone wall/floor in the initial healing phase and extended to the outermost surface of the stably grafted volume given the appropriate healing time [14]. It suggested that the height of residual defect wall can be a critical factor for histologic bone quality in the grafted extraction sockets, even in cases of complete destruction of counterpart defect wall.

The subgroup F, however, exceptionally showed a low proportion of new bone formation, despite high supports from both residual defect walls. This is contrary to the results of the other subgroups and the preclinical study, and might be caused by the three-dimensional complexity of extraction socket in molar region. The included teeth in this study were periodontally compromised ones that lost their support by apically involved lesion, and these extraction sites had severe loss of bone tissue in their specific parts

surrounding socket wall or septal bone. Most of the subgroup F were the teeth with apically involved circumferential defects induced by furcation involvement of retained inflammation, which might be related to have different outcomes from those found in other subgroups in this study and in the single-root region of the previous study. These multiple factors as well as systemic healing potential might act as confounding factors in the socket healing and could produce a wide variation of histologic bone formation in the present study. In addition, limited healing periods and a clinical protocol where every biopsy was taken in the different sites within the grafted volume could affect its wide variation. Therefore, further studies with longer healing time and the strict clinical protocol focusing on the evaluation of histologic bone formation should be needed for optimizing the clinical effects of the damaged extraction socket grafting.

V. Conclusion

Comparable histologic bone formation could be found in both periodontally damaged extraction sockets grafted with DBBM or DPBM and covered by collagen membranes. Although a wide variation of new bone formation was shown after 4 months of postsurgical healing, there was a tendency of higher new bone formation at a damaged socket with higher residual defect wall of either buccal or lingual side.

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Figure Legends

Figure 1. CONSORT flowchart of this study.

Figure 2. Method of harvesting the bone biopsy sample using a trephine at an augmented extraction socket. a, The grafted area was distinguished from the adjacent native bone by its different radiopacity (dotted line). A bone biopsy was performed at a site of implant installation, which would usually be at the center of the extraction socket. The region of interest (yellow rectangle) was prepared for obtaining the histologic sample after retrieving the specimen from the trephine. b, Micro-computed-tomography image of a biopsy specimen, showing the hard tissue harvested within the region of interest.

Figure 3. Classification of extraction socket defects according to defect morphologies. All of the included sites were classified into six subgroups to evaluate the effects of clinical defect morphologies on the histologic bone quality and harvesting proportion. Bone substitutes were grafted in the damaged extraction sockets up to an alveolar ridge shape extending from the height of the outer surfaces of the adjacent alveolar bone (area of oblique lines), regardless of the defect morphology. Bone regeneration can be influenced by the healing sources of the residual bone wall, and so the subgroup categories were based on the complete/incomplete presence of buccal/lingual bone wall surrounding the grafted area. (see main text for the details on subgroup classification)

Figure 4. Representative photomicrographs of histologic specimens from the DBBM and DPBM groups. Residual DBBM and DPBM particles were scattered and occupied spaces

in the coronal and middle regions of the specimens, and newly formed bone was present on the particles or within the spaces between the particles. However, in some specimens from both groups, fibrous encapsulated biomaterial particles were evident in the coronal region. Magnified views (boxed areas) were from the center region of each specimen. a, Residual bone graft material; b, Mineralized new bone; c, Bone marrow and fibrous tissue

Figure 5. Histomorphometric results in the DBBM (blue) and DPBM (red) groups. a, Box plots of qualitative histomorphometric results indicating median, first/third quartile, and maximum/minimum values for the residual graft material, new bone, and fibrous tissue. Each component of the histologic bone quality showed similar proportions in the DBBM and DPBM groups. b, Scatter plot of the harvesting proportion of the trephine (x-axis) versus the proportion of new bone formation (y-axis). Both the harvesting proportion and percentage of new bone were evenly distributed over ranges of 30–95% and 0–40%, respectively. While the harvesting proportion can be affected by the clinical bone density, the scatter plot indicates that there was no correlation between the harvesting proportion and new bone formation.

Figure 6. Subgroup analysis of histomorphometric results according to the classification of defect morphologies. a, Box plots of harvesting proportion according to classification. Each box plot indicates the median, first/third quartile, and maximum/minimum values of the data. b, Box plot of new-bone proportion according to classification. No statistically significant differences were found among the six subgroups in the comparison of the harvested proportion and new bone formation.

Figure 7. Correlation analysis with Pearson's correlation coefficient represented as r-values between defect size (width and residual wall height) and new bone formation. The maximal residual wall height and bucco-lingual defect width showed significant but weak correlation with new bone formation.

Tables

Table 1. Demographics of the study participants.

		Both groups	DBBM group	DPBM group
Number of patients		81	42	39
Age, years		55.02 (31–82)	54.29 (34–81)	55.82 (31–82)
Sex				
Male		53 (65.4)	27 (64.3)	26 (66.7)
Female		28 (34.6)	15 (35.7)	13 (33.3)
Jaw				
Maxilla		45 (55.6)	28 (66.7)	17 (43.6)
Mandible		36 (44.4)	14 (33.3)	22 (56.4)
Location				
Anterior	Incisor / canine	6 (7.4)	5 (11.9)	1 (2.6)
Posterior	Premolar	12 (14.8)	6 (14.3)	6 (15.4)
	Molar	63 (77.8)	31 (73.8)	32 (82.0)
Number of teeth extracted				
Single		70 (86.4)	37 (88.1)	33 (84.6)
Multiple		11 (13.6)	5 (11.9)	6 (15.4)
Amount of graft material, g		0.61 (0.20–1.75)	0.59 (0.20–1.50)	0.63 (0.25–1.75)

Data are *n* (%) or mean (range) values.

Table 2. Qualitative histomorphometric results in the DBBM and DPBM groups.

	Both groups (*n*=81)	**DBBM group** (*n*=42)	**DPBM group** (*n*=39)	**Confidence Interval**	***t*-test *p*-value**	**Effect size**
Residual bone graft material	12.29±5.71	12.37±5.67	12.21±5.75	-2.40, 2.71	0.648	0.028
Mineralized new bone	16.71±11.12	15.07±10.52	18.47±11.47	-8.31, 1.52	0.831	0.309
Bone marrow and fibrous tissue	71.00±10.18	72.56±10.07	69.32±10.02	-1.25, 7.74	0.559	0.323
Bone core harvesting proportion	70.34±15.79	69.22±16.00	71.55±15.47	-9.34, 4.76	0.884	0.148

Data are are mean±standard-deviation (%) values.

None of the parameters differed significantly between the DBBM and DPBM groups.

Confidence Interval was set at 95% confidence interval for the difference between the means of two groups.

Table 3. Qualitative histomorphometric results according to defect morphology.

	subgroup A (*n*=21)	**subgroup B** (*n*=12)	**subgroup C** (*n*=7)	**subgroup D** (*n*=18)	**subgroup E** (*n*=12)	**subgroup F** (*n*=11)
Residual bone graft material	12.22±5.83	12.67±5.00	13.00±4.40	11.67±5.98	13.14±6.09	11.67±5.87
Mineralized new bone	13.25±10.05	14.44±8.52	15.54±11.37	21.14±10.02	21.39±11.80	14.14±12.15
Bone marrow and fibrous tissue	74.53±8.93	72.88±9.35	71.46±9.19	67.19±9.50	65.47±9.31	74.19±11.15
Bone core harvesting proportion	70.83±13.27	74.54±15.49	74.32±11.11	72.89±17.93	65.13±17.57	63.80±13.53

Data are mean±standard-deviation (%) values.

None of the parameters differed significantly among the six groups.

Table 4. Defect size analysis in the DBBM and DPBM groups.

		Both groups (*n*=81)	**DBBM group** (*n*=42)	**DPBM group** (*n*=39)	**Confidence Interval**	***t*-test *p*-value**	**Effect size**
Defect width	Mesio-Distal	12.63±4.10	12.38±3.68	12.89±4.50	-2.34, 1.32	0.475	0.124
	Bucco-Lingual	11.27±2.29	11.33±2.54	11.21±1.97	-0.91, 1.14	0.175	0.053
Residual wall height	Buccal	4.20±2.56	4.14±2.53	4.26±2.59	-1.26, 1.03	0.407	0.047
	Lingual	4.96±2.86	4.72±3.13	5.22±2.52	-1.77, 0.78	0.188	0.176
	Maximam	5.74±2.81	5.49±3.07	6.02±2.46	-1.78, 0.73	0.136	0.191
	Minimam	3.42±2.11	3.38±2.17	3.47±2.05	-1.03, 0.85	0.878	0.043

Data are mean±standard-deviation (mm) values.

None of the parameters differed significantly between the DBBM and DPBM groups.

Table 5. Defect size analysis according to subgroups.

		subgroup A (*n*=21)	**subgroup B** (*n*=12)	**subgroup C** (*n*=7)	**subgroup D** (*n*=18)	**subgroup E** (*n*=12)	**subgroup F** (*n*=11)
Defect width	Mesio-Distal	13.73±4.31	11.96±4.36	16.41±6.49	12.25±3.12	11.80±1.85	10.37±1.86
	Bucco-Lingual	10.91±2.72	10.75±1.74	11.02±0.95	11.71±2.02	12.78±1.51	10.34±2.68
Residual wall height	Buccal	2.21±1.38	2.58±1.53	4.28±1.14	4.67±2.71	6.35±2.21	6.61±1.46
	Lingual	2.38±1.23	4.68±1.66	4.98±1.86	5.99±3.13	6.94±3.19	6.37±2.07
	Maximam	2.83±1.48	4.81±1.46	5.52±1.67	7.58±2.21	7.87±2.93	7.13±1.70
	Minimam	1.76±0.82	2.45±1.54	3.74±0.82	3.08±1.74	5.42±1.92	5.85±1.65

Data are mean±standard-deviation (mm) values.

Figures

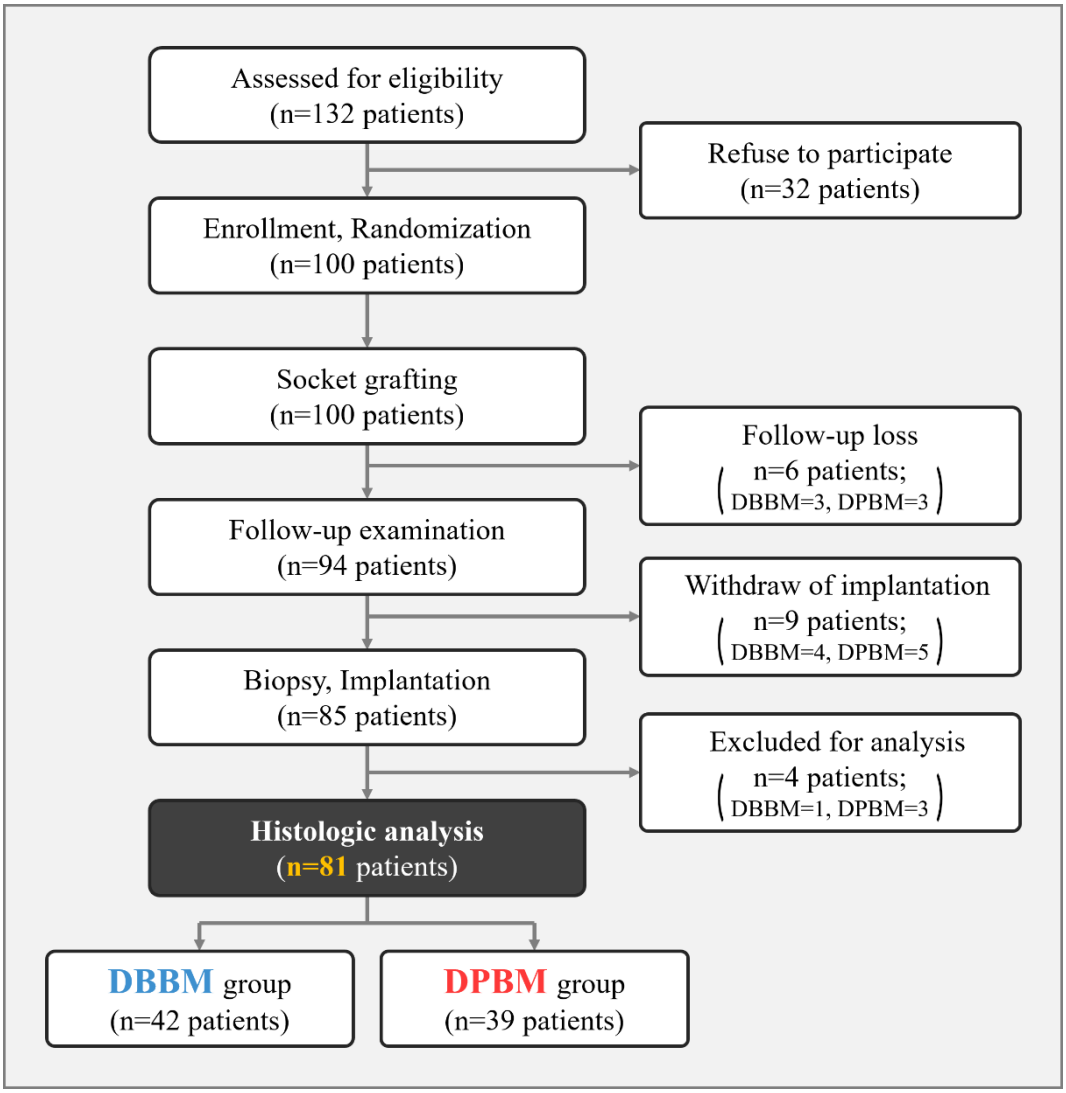


Figure 1

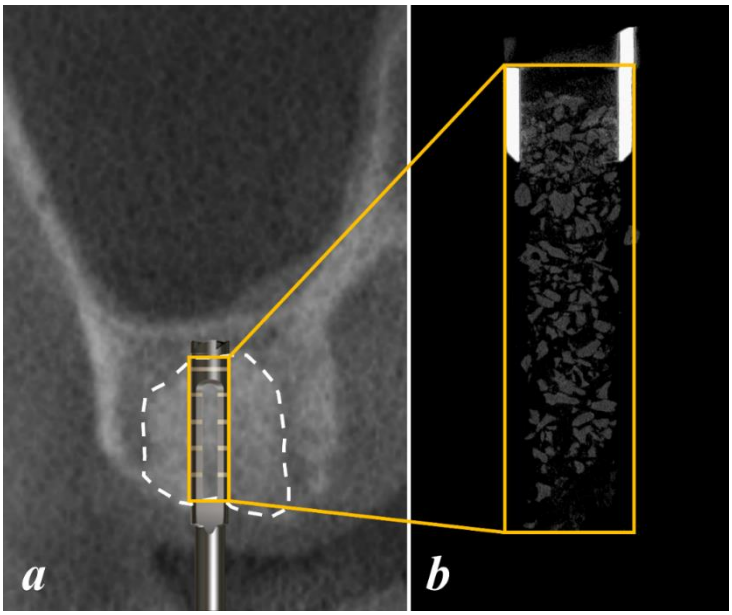
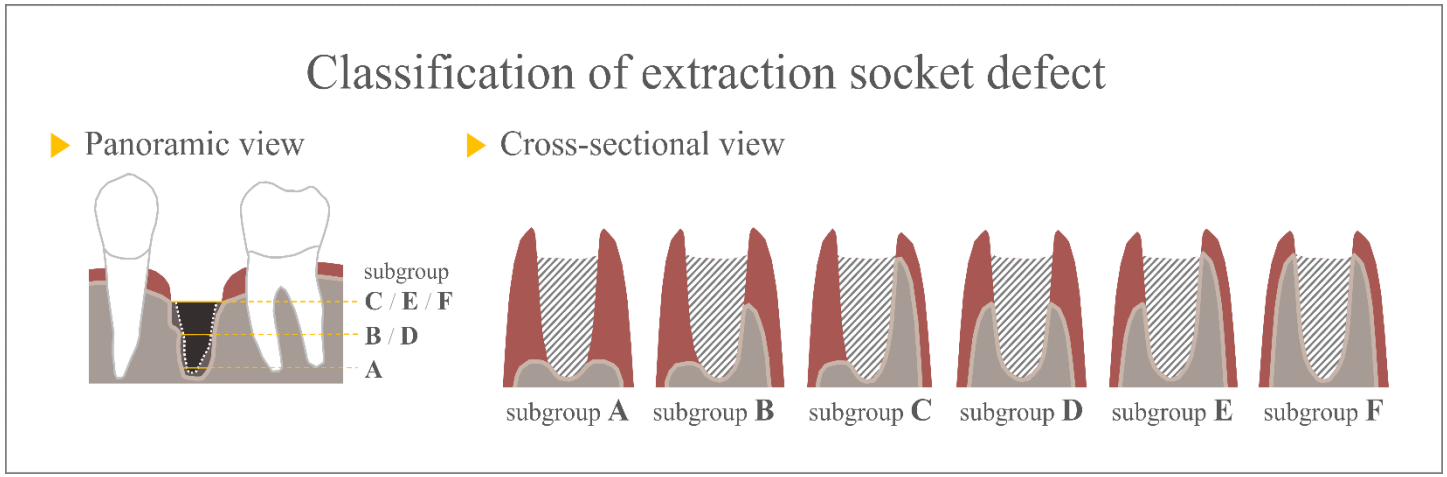


Figure 2



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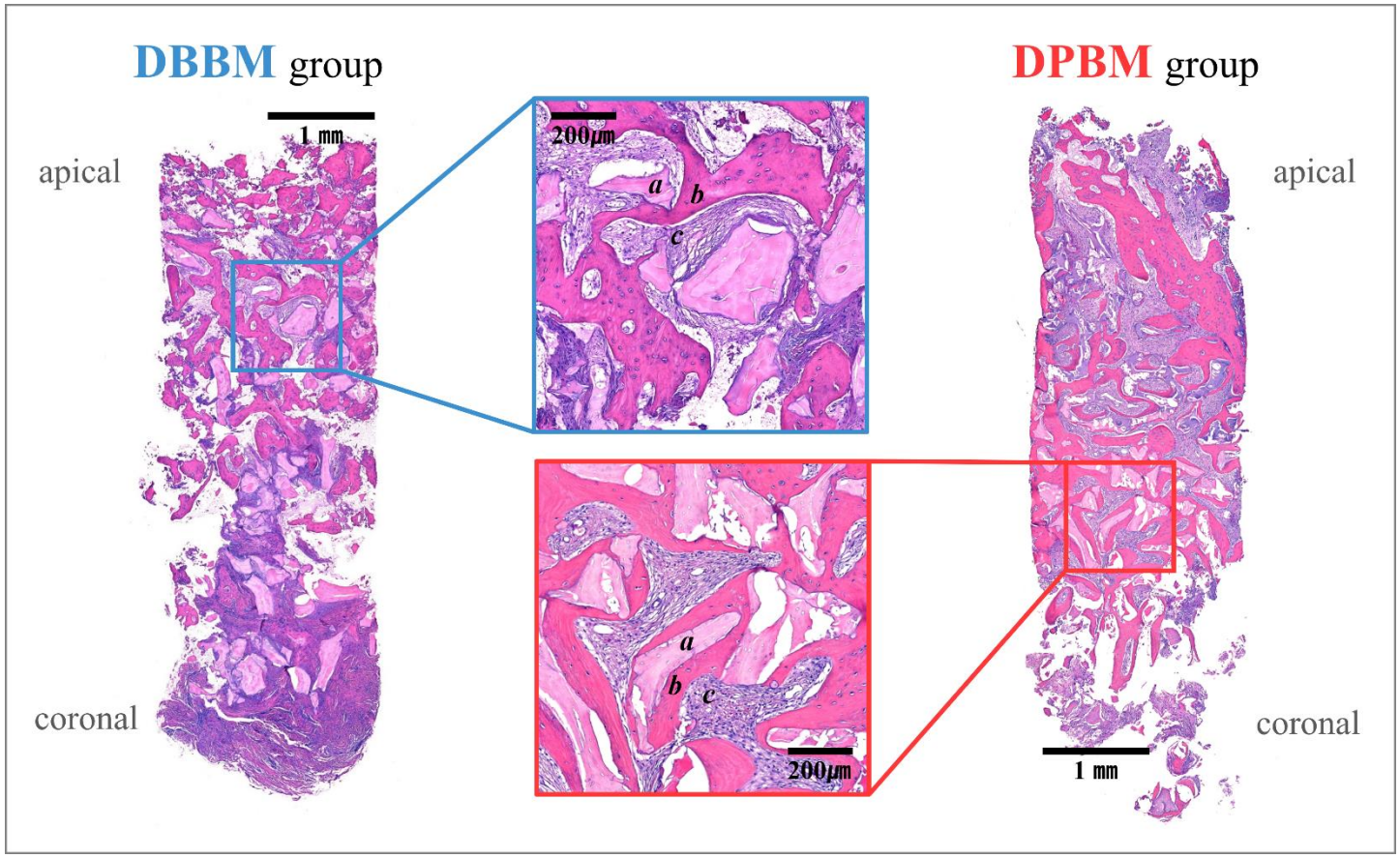

Figure 4

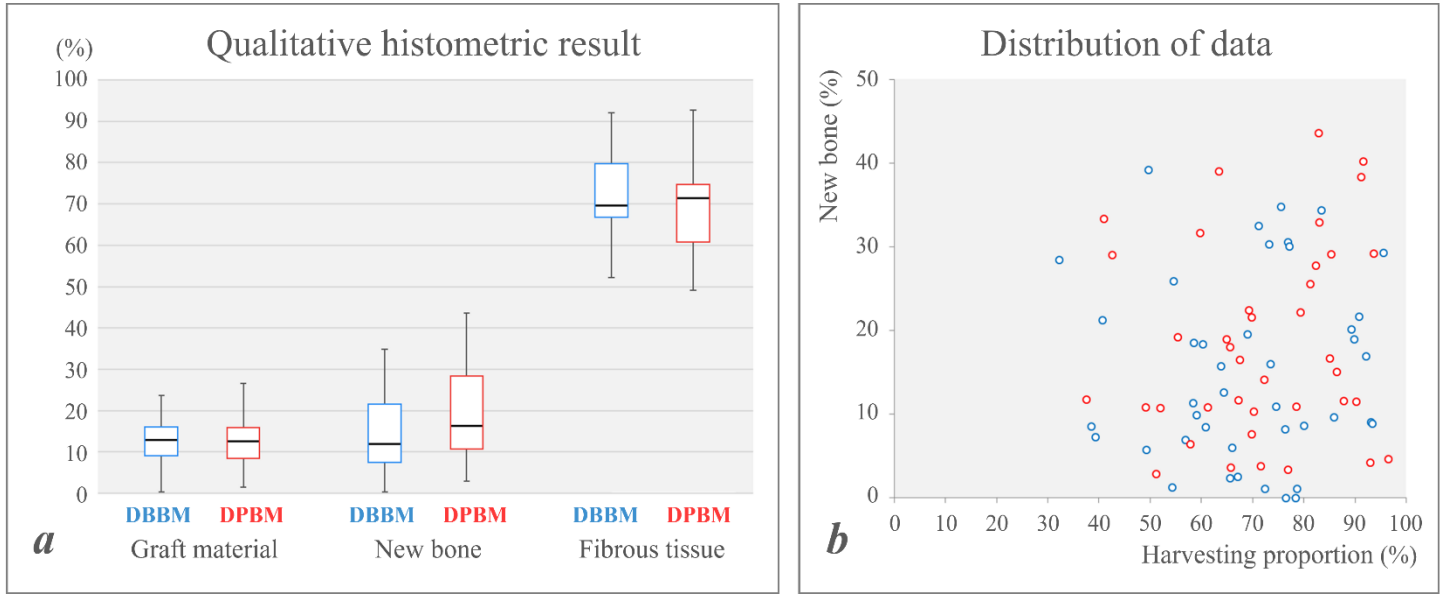

Figure 5

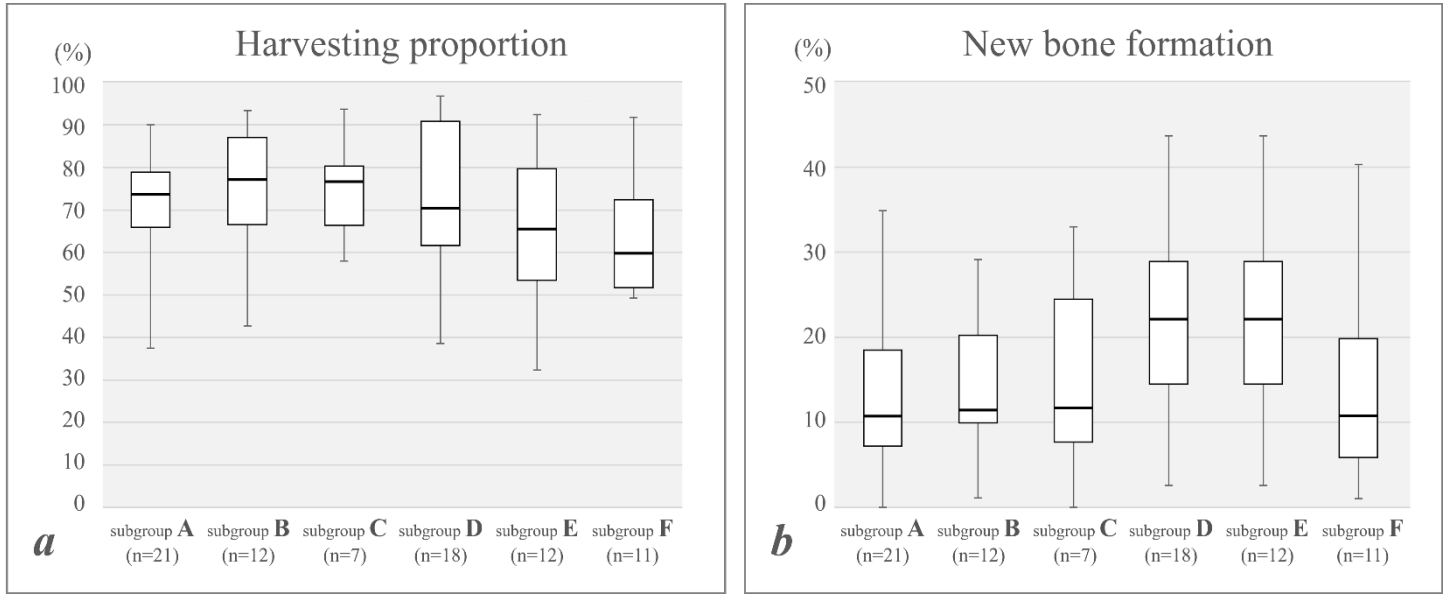

Figure 6

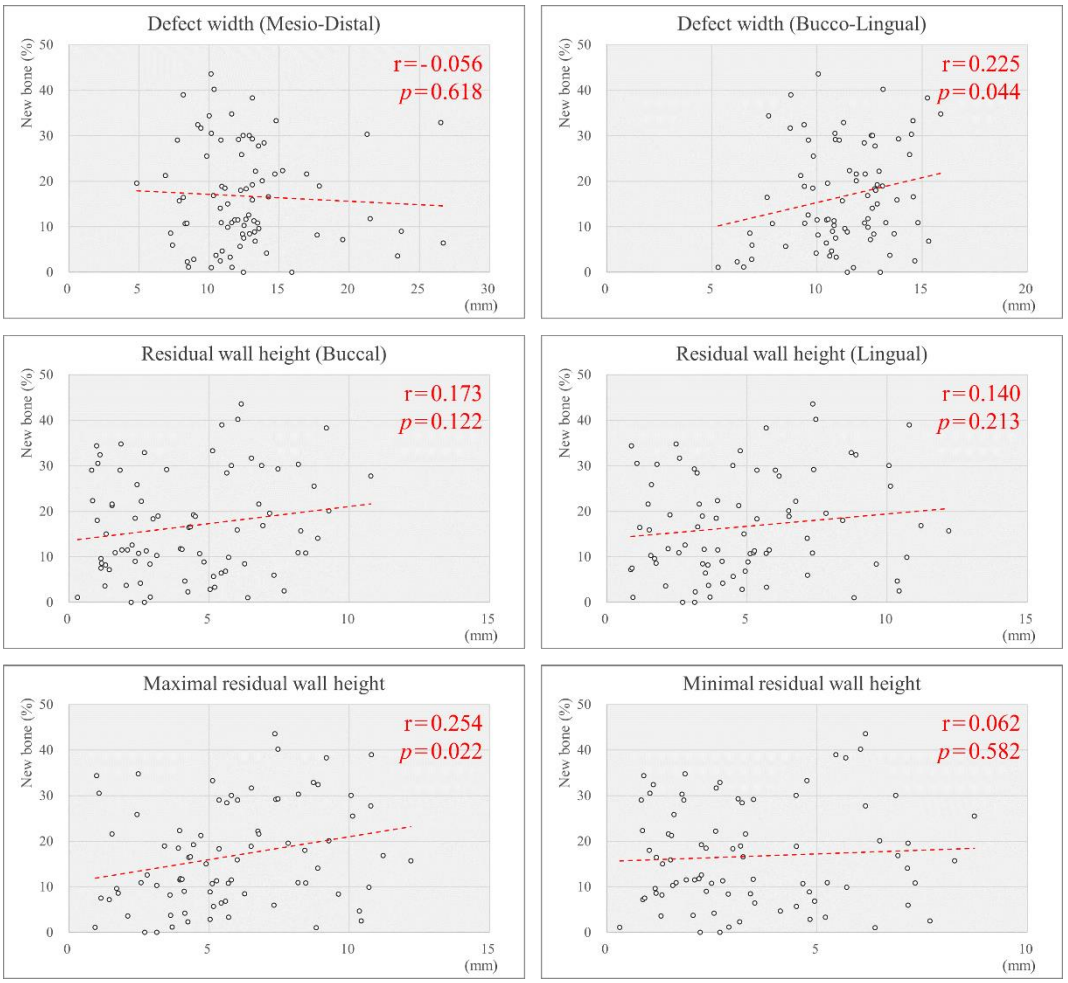

Figure 7

국문요약

파괴된 발치와에서 탈단백 소, 돼지 뼈 기질을 적용한 골이식술의 조직학적 분석: 무작위 배정 임상 연구

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발치 후 치조골은 해부학적 고유 특성으로 상당한 양의 흡수를 동반한다. 이를 최소화하기 위해 개발된 발치와 이식술은 초기에 손상되지 않은 전치부에 국한되어 시행되었지만 최근에는 구치부와 파괴된 발치와까지 적응증이 확장되어졌다.

이 연구의 목적은 파괴된 발치와에서 탈단백 소뼈, 돼지뼈 기질을 적용하고 흡수성 교원질 차폐막으로 피개하여 골이식술을 시행한 후 이식 부위에서 채득한 생검 표본을 조직학적으로 분석하는 것이다.

만성 치주염으로 발치 및 임플란트가 필요한 100명의 성인 환자가 이 연구에 등록되었다. 모든 환자에 대해 눈가림법 무작위 배정을 통해 각 군별로 탈단백 소뼈 기질과 돼지뼈 기질이 각각 적용되어 발치와 골이식을 시행하였다.

추적 관찰 과정에서 15명의 환자가 탈락하였고, 술 후 4개월에 85명 환자의 임플란트 식립 부위에서 트레핀을 사용하여 골편 조직을 채득하였다.

채득한 조직 절편 85개 중 81개가 조직학적 분석에 포함되었다 (소뼈군 42개, 돼지뼈군 39개). 조직계측학적 분석 결과, 잔존 골이식재 (12.37±5.67%, 12.21±5.75%), 신생골 (15.07±10.52%, 18.47±11.47%), 비광화결체 조직 (72.56±10.07%, 71.55±15.47%) 모두 비슷하게 계측되었고 다른 두 군 간에 통계적으로 유의미한 차이는 나타나지 않았다.

치주적으로 손상된 발치와에서 탈단백 소뼈, 돼지뼈 기질을 적용한 골이식술을 시행한 두 군 모두 유사한 조직학적 신생골 형성을 관찰하였다. 협설측에 관계없이 보다 건전한 잔존벽을 가진 발치와에서 더 많은 신생골 형성 경향을 보였다. 그러나 골이식술 시행 4개월 후에 나타난 치유의 광범위한 편차와 제한된 골형성은 임상 적용에 있어 장애가 될 수 있다.

핵심되는 말 : 발치와, 골 재생, 골 대체제, 임상 연구, 조직 유도 재생