# Alveolar ridge preservation versus guided bone regeneration after spontaneous healing on intact and damaged extraction sockets of narrow alveolar ridge: an in vivo experimental study

**Hae Jee Shin**

**Department of Dentistry**

**The Graduate School, Yonsei University**

# Alveolar ridge preservation versus guided bone regeneration after spontaneous healing on intact and damaged extraction sockets of narrow alveolar ridge: an in vivo experimental study

Directed by Professor Jung-Seok Lee

The Master's Thesis
Submitted to the Department of Dentistry
and the Graduate School of Yonsei University
in fulfillment of the requirements for the degree of
Master of Dental Science

Hae Jee Shin

October 2023

This certifies that the Master's Thesis
of Hae Jee Shin is approved.

Thesis Supervisor: Jung-Seok Lee

Jae-Kook Cha

Jin-Young Park

The Graduate School
Yonsei University
November 2023

# TABLE OF CONTENTS

# List of tables

# List of figures

Abstract

# Alveolar ridge preservation versus guided bone regeneration after spontaneous healing on intact and damaged extraction sockets of narrow alveolar ridge: an in vivo experimental study

**Hae Jee Shin, B.S., D.D.S.**

*Department of Dentistry*
*The Graduate School, Yonsei University*

(Directed by Professor Jung-Seok Lee, D.D.S., M.S.D., PhD.)

**Aim:** To compare (1) bone regeneration around the implant, and (2) dimensional alterations of alveolar ridge when early placement is performed into sites that received either alveolar ridge preservation (ARP) or spontaneous healing followed by simultaneous guided bone regeneration (GBR) in narrow ridges with varying extraction socket defect.

**Materials and Methods:** In six beagle dogs, distal roots of three mandibular premolars were extracted bilaterally. On each side, the three types of extraction sockets were either left intact, or surgically manipulated into 1-wall or 2-wall sockets. On one side, ARP was (ARP group) performed, whereas on the other side, spontaneous healing was administered followed by simultaneous GBR (GBR group) with implant placement in both groups after 8 weeks. Animals were killed after another 8 weeks. Quantitative and qualitative analyses were performed based on micro-computed tomography imaging and histological sections.

**Results:** Bone-to-implant contact **(**BIC) revealed no statistically significant differences between the GBR group (40.19 ± 11.88%) and the ARP group (33.79 ± 12.32%; $p>0.05$). The measurement of first-BIC and natural bone support (NBS) revealed that GBR (2.63 ± 0.85mm, 4.09 ± 1.08mm) significantly reduces coronal dehiscence and enhances NBS around the implant compared to ARP (3.90 ± 1.09mm, 2.27 ± 1.45mm; $p<0.05$), regardless of the extraction socket configuration. Radiographically, the ridge dimension increase from the baseline was significantly larger in the GBR group (150.03 ± 22.37%) compared to the ARP group (112.49 ± 10.52%; $p<0.05$). Histologically, the augmented ridge area was significantly larger in the GBR group (36.94 ± 6.46$mm^2$) compared to ARP group (20.16 ± 2.23$mm^2$; $p<0.05$). Similarly, the regenerated ridge area was larger in the GBR group (22.22 ± 4.32$mm^2$) compared to ARP group (17.73 ± 2.04$mm^2$; $p<0.05$).

**Conclusions:** In the narrow alveolar ridge, early implant placement with simultaneous GBR provides the space for enhanced bony support around implant, and bone regeneration by augmenting further alveolar ridge dimensions than ARP. Smaller coronal dehiscence of implant can be obtained by GBR than ARP, regardless of the extraction socket configuration. In addition, the natural bone support around the implant was enhanced following GBR which might be owed to the spontaneous socket healing following extraction.

---

**Keywords:** alveolar ridge augmentation, animal model, bone substitutes, tooth extraction

# Alveolar ridge preservation versus guided bone regeneration after spontaneous healing on intact and damaged extraction sockets of narrow alveolar ridge: an in vivo experimental study

**Hae Jee Shin, B.S., D.D.S.**

*Department of Dentistry*
*The Graduate School, Yonsei University*

(Directed by Professor Jung-Seok Lee, D.D.S., M.S.D., PhD.)

## I. INTRODUCTION

Sufficient alveolar bone width surrounding the dental implant has been considered a prerequisite for clinical success, despite limited evidence and controversy [1, 2]. Alveolar ridge preservation (ARP) and guided bone regeneration (GBR) have emerged as prominent approaches for preserving or augmenting the alveolar ridge dimensions [3, 4]. After tooth extraction, all sites experience dimensional collapse, particularly in the buccal region, regardless of socket wall damage [5, 6]. GBR aims to reconstruct the alveolar ridge following such collapse, whereas ARP focuses on maintaining the original ridge dimensions before the collapse occurs. While GBR is a well-established and documented procedure, ARP is also supported by a growing body of preclinical and clinical data, despite its more recent introduction in dental practice. Moreover, due to its technical simplicity and minimal invasiveness, ARP has been increasingly utilized over the past two decades.

ARP is a clinical procedure initially pioneered through landmark preclinical studies in dogs [7-14]. These studies primarily employed a single intact extraction socket model with a thin buccal bone plate, leading to ARP's initial recommendation for single-site applications in the anterior region. However, indications for ARP have since expanded, encompassing posterior regions [15, 16] as well as damaged sockets [17, 18]. The rationale for ARP's broader application lies in its capacity to mitigate dimensional shrinkage both horizontally and vertically, even in sockets with wall deficiencies [18]. Nevertheless, ARP, like any clinical procedure, presents limitations alongside its advantages. In a recent clinical trial, we observed a wide range of histologic bone regeneration at implant sites within the grafted region, ranging from 0% to 40% [19]. Additionally, ARP does not provide a guarantee against the need for additional grafting procedures at the time of implant placement; recent clinical data indicate that 60% of ARP sites necessitated additional augmentation through the use of supplementary guided bone regeneration procedures [20].

The clinical choice between ARP and GBR should be made with careful consideration. In case of implantation in the narrow alveolar ridge, such as the lower anterior region, unnecessary repetition of two grafting procedures may occur, similar to the aforementioned 60% of ARP sites. However, there is a paucity of studies directly comparing these two clinical approaches. While one preclinical study compared ARP and early implantation with GBR after spontaneous healing, they primarily demonstrated comparable volumetric changes through radiographic and digitally scanned clinical images [21]. Nonetheless, for a comprehensive and well-informed clinical decision-making process, it is imperative to consider not only external volume data but also histologic new bone formation and implant surface area supported by osseointegration.

Therefore, the aim of this preclinical study was to compare bony support around the implant and bone regeneration when early placement is performed into sites that received either ARP or spontaneous healing followed by simultaneous GBR. This investigation specifically encompasses both intact and damaged sockets within the context of narrow alveolar ridges, utilizing an in vivo model.

# II. MATERIALS AND METHODS

## 1. Animals and materials

Six male beagle dogs weighing 25-30kg and aged 18-24 weeks were used in this study. The animals were individually housed at a normal temperature and humidity, and provided a standardized diet. The sample size was determined based on the previous studies [6], [22]. and three Rs principle (replacement, reduction, and refinement) in animal study. The study design was based on the ARRIVE guideline [23], and it protocol was approved by the Institutional Animal Care and Use Committee, Yonsei Medical Center, Seoul, Korea (IRB No. 2020-0250).

Particulate type of deproteinized porcine bone minerals (DPBM; THE Graft, Purgo Biologics, Seongnam, Korea) and non-crosslinked collagen membranes (BioCover, Purgo Biologics) were used for both ARP and GBR [22].

## 2. Study design

The study comprised two primary groups:

- ARP group: ARP was performed after tooth extraction, followed by implant placement at 8 weeks;

- GBR group: Spontaneous healing was allowed after tooth extraction, followed by simultaneous GBR and implant placement at 8 weeks;

A split-mouth design was adopted, with each group being assigned to one unilateral alveolar ridge, while the other group was applied to the contralateral alveolar ridge.

The present study involved three distinct extraction socket models within each unilateral alveolar ridge, categorized as follows: (a) Intact, (b) 1-wall-damaged (buccal wall deficiency), and (c) 2-wall-damaged (buccal- and lingual-wall deficiency). These models were induced following established protocols from previously published studies [6], [10], [22] and implemented on the second (P2), third (P3), and fourth premolars (P4). Each type of extraction socket model was methodically allocated to the sites to ensure even distribution.

## 3. Surgical protocols

*A. Tooth extraction and ridge preservation procedures (Surgery I)*

All surgical procedures were performed under general anesthesia with Alfaxalone (2-3mg/kg, IV; Jurox, Rutherford, NSW, Australia), and inhalation of isoflurane (2-3%, Forane, Choongwae Pharmaceutical, Seoul, South Korea). To place the implant in the same position as the root in a standardized manner at a time of Surgery II, the position and axis of the extraction socket was taken with a prefabricated template and a self-curing acrylic resin (Figure1). These guide templates later made prior to the Surgery II, using a three-dimensional printing technology based on the scanned data pre-taken. Three premolars (P2, P3, and P4) of each unilateral mandible were hemi-sectioned, and the distal roots were removed using a root forcep. In these sites, three types of standardized intact and damaged extraction sockets were induced; a whole length of buccal bone wall or buccal/lingual walls in the sockets were surgically removed using a high-speed rotary engine and a carbide fissure bur for 1-wall- or 2-wall-damaged models. The mesial roots were decoronated at the level of bone crest and were maintained for the use as the pristine control site. In ARP sites, all three types of extraction sockets were filled with DPBM, and covered with the collagen membrane. The periosteal flaps were repositioned and sutured (4/0 Coated Vicryl, Ethicon, U.S). In GBR sites, the periosteal flaps were sutured right after the defect induction. Antibiotic medication and wound dressing with saline irrigation were applied for 1 week, and then, the sutures were removed (Figure1B).

*B. Implant placement and GBR procedures (Surgery II)*

Both ARP and GBR groups received implants (Anyridge ⌀3.5× h8.5, Megagen Implant, Daegu, Korea), after eight weeks of healing. Full-thickness muco-periosteal flaps were elevated and the implants were placed in accordance with the prefabricated surgical guide templates. In ARP sites, no additional bone augmentation was performed even in a case of implant dehiscence. In GBR sites, DPBM was augmented on the exposed implant surface, and covered with the collagen membrane. The periosteal flaps were repositioned and sutured. Oral antibiotics were administered. Wound dressing was performed with saline irrigation for 1 week, then the sutures were removed (Figure1C and 1D).

*C. Post-surgical treatments and sample collection.*

All dogs were sacrificed after eight weeks from the implant placement, and intraoral scan was taken and both alveolar ridges were retrieved for radiographic and histologic analyses. The acquired specimens were fixed in 10% neutral buffered formalin.

## 4. Microcomputed tomography radiographic analysis

Micro-computed tomography scanning (Skyscan 1173, Bruker-microCT) was performed (Number of projections=800, Frame averaging=4) at a resolution of 32μm (achieved using 100kV and 60μm). The micro-CT images were retrieved and converted into DICOM format, transferring the cross-sectional slides for morphometric evaluations on three-dimensional software (On-Demand3D, Cybermed). Coronal sections of the mandibular were captured for the superimposition. The most-central region of both distal experiment site (post-surgery) and mesial dental root (baseline) were superimposed with reference anatomical structures such as the mandibular canal and the lower border of the mandible (Figure 2A). Radiographic analysis was conducted using computer software (Adobe Photoshop CS5, Adobe Systems). The region of interest (ROI) for the micro CT measurements were defined as the area of entire alveolar bone, apex to the most crestal region. The proportion of alveolar preservation (%) was calculated by the ratio of the total alveolar ridge area in an experimental site to the corresponding pristine site.

## 5. Histological preparation and analysis.

The specimen from each unilateral mandible was sectioned into three blocks containing three experimental sites received with dental implants. Bone blocks containing each site were fixed in 10% neutral-buffered formalin solution, and then dehydrated with ethanol solutions and embedded in methyl methacrylate (Technovit 7200, Kulzer, German) for ground section. The most-central bucco-lingual sections were obtained from the sites with dental implants. The ground sections were produced with final thickness of 50μm, and then stained with Goldner's trichrome stain. Histologic slides were digitally scanned at a magnification of ×200 (Panoramic 250 Flash III), and histomorphometric analysis was performed using computer software (Adobe Photoshop CS5, Adobe Systems) by one experienced examiner (HJS). A region of interest (ROI) for the histomorphometric analysis was determined by (i) the outermost margin of total tissue on both buccal and lingual aspects (ii) a perpendicular line drown from the implant apex and implant platform (Figure2B).

The following parameters were measured in the ROI;

- Bone-to-implant contact (BIC): a proportion of the length of bone-contacted implant threads at the buccal aspect among the entire length of the implant threads at the buccal aspects (%)
- First bone-to-implant contact (fBIC): the distance from the implant platform to the first bone-to-implant contact at the buccal aspect of the implant.
- Natural bone support (NBS): the height of the native bone measured from the implant apex at the buccal aspect. (Regenerated bone occupying the interspace of residual biomaterials has been excluded from the measurements)
- Augmented Ridge Area (ARA; $mm^2$): Area demarcated by the outermost line of grafted biomaterials and alveolar bone from the level of the implant apex;

- Regenerated Ridge Area (RRA; $mm^2$): Area demarcated by the outermost margin of the newly formed bone and the alveolar bone from the level of the implant apex. Excluding the bone islanded from the defect margin.

## 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 the Mauchly's sphericity test were applied to evaluate the normality of the data and the sphericity assumption, respectively. Repeated measured ANOVA was used for intergroup analysis between ARP group and GBR group and intragroup analysis among three configuration types of socket models. Bonferroni *p*-value correction was applied to detect significant differences for intragroup analysis among three configuration types of socket models. The cutoff for significance was set as *p*-value of 0.05, and the modified *p*-value of 0.016 was applied on the intragroup analysis.

# III. RESULTS

## 1. Clinical findings

All experimental sites healed uneventfully during the observational periods. Horizontal shrinkage could be seen in the experimental sites after spontaneous healing (GBR group) from the tooth-extraction and defect induction, and the damaged (defect-induced) sites exhibited more pronounced bucco-lingual collapse compared to the intact socket sites. However, sites in ARP group showed reduced dimensional collapse compared to the abovementioned sites in GBR group, regardless of the socket configuration. After flap elevation, ARP sites also had maintained ridge dimension compared to the GBR sites, but some residual biomaterials and the newly formed bone tissue could be found at the internal surface of the flap. Horizontal dehiscence defects occurred in both groups, but the exposed surfaces of the implant were reduced in ARP sites (Figure1).

## 2. Radiographic observations

Radiographs in ARP group revealed some exposure of implant surfaces with buccal dehiscence defect; the largest dehiscence in intact socket, but some radiopaque granules covered partly the implant surface on the dehiscence defect area in both damaged socket sites. On the other hand, all sites in GBR group demonstrated significantly increased area of the augmented alveolar ridge with some scattered radiopaque granules at the outer-most region (Figure3). In addition, there were no clear demarcation between the outer line of the preexisting alveolar bone and the augmented region.

## 3. Histological observations

Newly formed bone contacting the most coronal area of implant positioned higher on GBR sites than ARP sites. The graft particles completely covered whole the implant surfaces in GBR sites, but ARP sites had dehiscence defects exposing the implant surfaces directly to a surrounding connective tissue. In addition, a larger area of the regenerated alveolar ridge within the augmented area were shown in the GBR sites than the ARP sites.

At the buccal aspect, unintegrated graft particles could be seen scattered over the regenerated alveolar ridge on both ARP and GBR groups. Contrary to the buccal region, lingual bone walls of three extraction socket models seemed less compromised than buccal bone walls regardless of treatment type (ARP or GBR), even in the 2-wall-damaged sites.

Highly magnified views demonstrated that the outermost margin of newly formed bone in the ARP sites appeared mature with lamellar bone formation and fibrous-encapsulated biomaterials beyond the regenerated alveolar ridge. On the other hand, GBR groups revealed unclear margin of the newly formed bone with few evidences of osteogenesis around the residual particles of biomaterials, indicating on-going phase of bone formation and remodeling process (Figure4).

### 4. Quantitative measurement of superimposed micro-CT images and histologic slides

On radiographic analysis, ARP group (112.49 ± 10.52%) showed significantly less dimensional increase from the baseline compared to GBR group (150.03 ± 22.37%; $p$=0.001), regardless of the extraction socket configuration. According to the types of damaged extraction socket models, dimensional alteration of ARP vs GBR group were: intact (110.33 ± 10.63% vs. 142.92 ± 7.50%), 1-wall-damaged (111.39 ± 11.37% vs. 159.62 ± 28.02%), and 2-wall-damaged (115.77 ± 8.56% vs. 147.52 ±22.60%; $p$=0.316) (Figure5).

On histologic analysis, ARP group (20.16 ± 2.23mm$^2$) showed less augmented ridge dimension compared to GBR group (36.94 ± 6.46mm$^2$; $p$<0.001). In addition, ARP group showed less regenerated ridge dimension (17.73 ± 2.04mm$^2$) compared to GBR group (22.22 ± 4.32mm$^2$; $p$=0.009), regardless of the extraction socket configuration. According to the types of damaged extraction socket models, the augmented and the regenerated ridge areas of ARP vs GBR are: Intact (19.38 ± 1.80mm$^2$ and 18.78 ± 2.05 mm$^2$ vs. 33.56 ± 6.07mm$^2$ and 21.94 ± 3.55 mm$^2$, respectively), 1-wall-damaged (19.17 ± 1.38mm$^2$ and 17.07 ± 1.28 mm$^2$ vs. 39.49 ± 6.14mm$^2$ and 20.32 ± 1.40 mm$^2$), and 2-wall-damaged (21.93 ± 2.25mm$^2$, 17.35 ± 2.24 mm$^2$ vs. 37.77 ± 5.66mm$^2$, 24.40 ± 5.74 mm$^2$; $p$=0.189 and $p$=0.216) (Figure5).

BIC result of ARP group (33.79 ± 12.32%) was slightly less than that of GBR group (40.19 ± 11.88%; $p$=0.118), but no statistical difference. According to the types of damaged extraction socket models, ARP vs GBR group were : Intact (29.49 ± 12.82% vs. 32.48 ± 10.89%), 1-wall-damaged (30.58 ± 4.55% vs. 37.85 ± 7.71%), and 2-wall-damaged (41.31 ± 13.59% vs. 50.23 ± 8.91%; $p$=0.801). Regardless of treatment group, statistical significance among three types of socket models was found in serial order of: Intact (30.98 ± 11.99%) < 1-wall-damaged (34.21 ± 7.30%) < 2-wall-damaged (45.77 ± 12.33%; $p$=0.010) (Table1).

ARP group (3.90 ± 1.09mm, 2.27 ± 1.45mm) showed significantly increased fBIC and less NBS compared to GBR group (2.63 ± 0.85mm, 4.09 ± 1.08mm; $p$=0.012 and $p$=0.003), regardless of the extraction socket configuration. According to the types of damaged extraction socket models, the corresponding values in ARP vs GBR group are respectively; Intact (3.90 ± 1.08mm, 3.61 ± 1.04mm vs. 2.72 ± 0.71mm, 4.21 ± 0.74mm), 1-wall-damaged (4.58 ± 0.57mm, 1.73 ± 0.98mm vs. 3.21±0.71mm, 3.31±0.89mm) and 2-wall-damaged (3.23±1.09mm, 1.47±1.23mm vs. 1.97±0.64mm, 4.76±1.05mm; $p$=0.939 and p=0.005) (Table1).

# IV. DISCUSSION

The present preclinical study compared 'ARP' vs. 'GBR after the spontaneous healing' at a narrow type alveolar ridge, in the aspect of alveolar ridge augmentation and bone regeneration around the dental implant. The main findings were (1) bony support by both the newly formed and natural bone tissue were increased by GBR with spontaneous healing compared to ARP; (2) ARP maintained the preexisting alveolar ridge dimension, but implant surfaces were partly exposed to the lining mucosa on a narrow alveolar ridge; (3) GBR augmented the alveolar ridge dimension, and the whole implant surface surrounded by the augmented tissue volume.

The ARP is a well-documented technique with tremendous scientific evidences at both the preclinical and clinical level [7-14], [24] and the present result of ARP group was in line with the previous studies that the alveolar ridge was maintained its dimension comparably in all intact and damaged extraction sockets [16, 17], [22], [25-27]. However, the dental roots are at buccally-biased positions in the beagle dog model, and the implant was designed to be placed in the middle of the preexisting extraction socket with the aid of the surgical guide system in the present study. Consequently, unresolved dehiscence defect was left at a bucco-coronal region of the dental implant in ARP site. This can be one of the reasons why the additional augmentation procedure should have been done in some cases from the previous clinical data [28-31], while these cases are inevitable at narrow alveolar ridges or buccally-positioning sites. Therefore, it is imperative to diagnose preexisting condition of the alveolar ridge before planning ARP to reduce the unnecessarily repeated surgical interventions.

GBR is also a well-documented technique, especially for a horizontal defect [32]. A previous systematic review provided evidences for successful clinical results of GBR in specific indications of fenestration or dehiscence defect sites [33, 34] and recent clinical and preclinical studies also revealed a volume stability and substantial bone formation within the extensively and horizontally augmented sites even by the use of a collagen membrane [35-37]. In the present results, GBR sites also showed well maintained volume of augmentation surrounding a dental implant. These spaces provided a space for new bone formation enhancing the regenerated ridge area, and the most-coronal point of first bone-to-implant contact (fBIC) could be found at the higher level than the ARP sites.

The present histologic results of GBR sites demonstrated limited bone formation at the outermost region of the augmented area. This is on the contrary to the previous preclinical study resulting regeneration of alveolar ridge within the bony envelope, while they also showed residual biomaterials encapsulated with connective tissue at the outermost region beyond the bony envelope in the augmented area [36]. These differences might be caused by disparate observational period from two experiments; 8 and 16 weeks for the present and the previous study, respectively. The other preclinical study on the horizontal augmentation of the dog model demonstrated significantly enhanced bone formation over 10 weeks [38]. The highly magnified views of the present histologic slides in GBR sites also showed the evidence of osteogenesis in a space between the biomaterial granules or on to their surfaces (Figure4), which we can extrapolate further bony regeneration in the coronal region of augmented area. Therefore, the single chance of surgical approach by GBR provides both enhanced augmentation and bony regeneration than the sites received ARP in a narrow type of alveolar ridge, as well as the full coverage of implant surface [32].

In addition, GBR sites were permitted with spontaneous healing to be filled with natural bone at all the intact and the damaged extraction sockets. The histologic findings from previous ARP studies revealed a wide range of histologic bone regeneration in a clinical data from the conventional ARP [39] and the ARP in the damaged socket sites [19]. Even though the other clinical data showed the feasibility of the regenerated bone tissue to support the dental implant favorably [40, 41], heterogenic bone regeneration in the ARP sites should be interpreted carefully since healing period allowed has differential effect on natural bone support [42].

Bone regeneration is influenced significantly from the defect configuration type in the surgical sites [43]. Not only the presence of wall defect increases dimensional shrinkage or pronounced collapse [6], [44-46], but also prospectively affects bone quality after the treatment. Natural bone support differed also in accordance with the number of residual walls of the experimental model on ARP group. Intact sockets undergone ARP showed more favorable natural bone support than 1-wall- or 2-wall-damaged sockets. This pattern resembles the dimensional healing being affected by the range of periodontally compromised extraction sockets which can be confirming previous findings [43].

This study was subjected to some limitations. Firstly, ARP sites had received one more surgical intervention with the elevation of the flap for implant placement, which might cause more loss of augmented biomaterials compared to the GBR sites. Second, radiographic and histologic analysis regarding the area of augmentation and regeneration was conducted planimetrically, rather than 3D volumetric analyses, and these should be interpreted with caution. Third, the appropriate amount of augmentation for each types of damaged extraction socket models on the present study was determined differentially according to the defect morphology; each experimental site was grafted with biomaterials in accordance to the pristine alveolar ridge shape from the adjacent bone tissues.

# V. CONCLUSION

In the narrow alveolar ridge, early implant placement with simultaneous GBR provides the space for enhanced bony support around implant, and bone regeneration by augmenting further alveolar ridge dimensions than ARP. Smaller coronal dehiscence of implant can be obtained by GBR than ARP, regardless of the extraction socket configuration. In addition, the natural bone support around the implant was enhanced following GBR which might be owed to the spontaneous socket healing following extraction.

# Reference

1. Spray JR, Black CG, Morris HF, Ochi S. The influence of bone thickness on facial marginal bone response: stage 1 placement through stage 2 uncovering. Ann Periodontol 2000;5(1):119-28.
2. Waller T, Herzog M, Thoma DS, Hüsler J, Hämmerle CHF, Jung RE. Long-term clinical and radiographic results after treatment or no treatment of small buccal bone dehiscences at posterior dental implants: A randomized, controlled clinical trial. Clin Oral Implants Res 2020;31(6):517-25.
3. Avila-Ortiz G, Chambrone L, Vignoletti F. Effect of alveolar ridge preservation interventions following tooth extraction: A systematic review and meta-analysis. J Clin Periodontol 2019;46 Suppl 21:195-223.
4. Benic GI, Hämmerle CH. Horizontal bone augmentation by means of guided bone regeneration. Periodontol 2000 2014;66(1):13-40.
5. Cardaropoli G, Araújo M, Lindhe J. Dynamics of bone tissue formation in tooth extraction sites. An experimental study in dogs. J Clin Periodontol 2003;30(9):809-18.
6. Lee JS, Choe SH, Cha JK, Seo GY, Kim CS. Radiographic and histologic observations of sequential healing processes following ridge augmentation after tooth extraction in buccal-bone-deficient extraction sockets in beagle dogs. J Clin Periodontol 2018;45(11):1388-97.
7. Araújo MG, Lindhe J. Dimensional ridge alterations following tooth extraction. An experimental study in the dog. J Clin Periodontol 2005;32(2):212-8.
8. Cardaropoli G, Araújo M, Hayacibara R, Sukekava F, Lindhe J. Healing of extraction sockets and surgically produced - augmented and non-augmented - defects in the alveolar ridge. An experimental study in the dog. J Clin Periodontol 2005;32(5):435-40.
9. Araújo MG, Sukekava F, Wennström JL, Lindhe J. Tissue modeling following implant placement in fresh extraction sockets. Clin Oral Implants Res 2006;17(6):615-24.
10. Araújo M, Linder E, Wennström J, Lindhe J. The influence of Bio-Oss Collagen on healing of an extraction socket: an experimental study in the dog. Int J Periodontics Restorative Dent 2008;28(2):123-35.
11. Araújo MG, Lindhe J. Ridge preservation with the use of Bio-Oss collagen: A 6-month study in the dog. Clin Oral Implants Res 2009;20(5):433-40.
12. Araújo M, Linder E, Lindhe J. Effect of a xenograft on early bone formation in extraction sockets: an experimental study in dog. Clin Oral Implants Res 2009;20(1):1-6.
13. Araújo MG, Liljenberg B, Lindhe J. Dynamics of Bio-Oss Collagen incorporation

in fresh extraction wounds: an experimental study in the dog. Clin Oral Implants Res 2010;21(1):55-64.

14. Lindhe J, Cecchinato D, Donati M, Tomasi C, Liljenberg B. Ridge preservation with the use of deproteinized bovine bone mineral. Clin Oral Implants Res 2014;25(7):786-90.
15. Walker CJ, Prihoda TJ, Mealey BL, Lasho DJ, Noujeim M, Huynh-Ba G. Evaluation of Healing at Molar Extraction Sites With and Without Ridge Preservation: A Randomized Controlled Clinical Trial. J Periodontol 2017;88(3):241-9.
16. Cha JK, Song YW, Park SH, Jung RE, Jung UW, Thoma DS. Alveolar ridge preservation in the posterior maxilla reduces vertical dimensional change: A randomized controlled clinical trial. Clin Oral Implants Res 2019;30(6):515-23.
17. Lee JS, Jung JS, Im GI, Kim BS, Cho KS, Kim CS. Ridge regeneration of damaged extraction sockets using rhBMP-2: an experimental study in canine. J Clin Periodontol 2015;42(7):678-87.
18. Lee JS, Cha JK, Kim CS. Alveolar ridge regeneration of damaged extraction sockets using deproteinized porcine versus bovine bone minerals: A randomized clinical trial. Clin Implant Dent Relat Res 2018;20(5):729-37.
19. Koo TH, Song YW, Cha JK, Jung UW, Kim CS, Lee JS. Histologic analysis following grafting of damaged extraction sockets using deproteinized bovine or porcine bone mineral: A randomized clinical trial. Clin Oral Implants Res 2020;31(1):93-102.
20. Park SH, Song YW, Sanz-Martín I, Cha JK, Lee JS, Jung UW. Clinical benefits of ridge preservation for implant placement compared to natural healing in maxillary teeth: A retrospective study. J Clin Periodontol 2020;47(3):382-91.
21. Naenni N, Bienz SP, Muñoz F, Hämmerle CHF, Jung RE, Thoma DS. Volumetric changes following ridge preservation or spontaneous healing and early implant placement with simultaneous guided bone regeneration. J Clin Periodontol 2018;45(4):484-94.
22. Tien HK, Lee WH, Kim CS, Choi SH, Gruber R, Lee JS. Alveolar ridge regeneration in two-wall-damaged extraction sockets of an in vivo experimental model. Clin Oral Implants Res 2021;32(8):971-9.
23. Percie du Sert N, Hurst V, Ahluwalia A, Alam S, Avey MT, Baker M, et al. The ARRIVE guidelines 2.0: Updated guidelines for reporting animal research. PLoS Biol 2020;18(7):e3000410.
24. Barone A, Aldini NN, Fini M, Giardino R, Calvo Guirado JL, Covani U. Xenograft versus extraction alone for ridge preservation after tooth removal: a clinical and histomorphometric study. J Periodontol 2008;79(8):1370-7.
25. Aimetti M, Manavella V, Corano L, Ercoli E, Bignardi C, Romano F. Three-dimensional analysis of bone remodeling following ridge augmentation of compromised extraction sockets in periodontitis patients: A randomized controlled study. Clin Oral Implants Res 2018;29(2):202-14.

26. Lim HC, Seo S, Thoma DS, Park JC, Hong JY, Shin SY. Late implant placement following ridge preservation versus early implant placement: A pilot randomized clinical trial for periodontally compromised non-molar extraction sites. J Clin Periodontol 2020;47(2):247-56.
27. Nunes FAS, Pignaton TB, Novaes AB, Jr., Taba M, Jr., Messora MR, Palioto DB, et al. Evaluation of a bone substitute covered with a collagen membrane for ridge preservation after tooth extraction. Clinical and tomographic randomized controlled study in humans. Clin Oral Implants Res 2018;29(4):424-33.
28. Couso-Queiruga E, Mansouri CJ, Alade AA, Allareddy TV, Galindo-Moreno P, Avila-Ortiz G. Alveolar ridge preservation reduces the need for ancillary bone augmentation in the context of implant therapy. J Periodontol 2022;93(6):847-56.
29. Fischer KR, Solderer A, Arlt K, Heumann C, Liu CC, Schmidlin PR. Bone envelope for implant placement after alveolar ridge preservation: a systematic review and meta-analysis. Int J Implant Dent 2022;8(1):56.
30. Atieh MA, Alsabeeha NH, Payne AG, Ali S, Faggion CMJ, Esposito M. Interventions for replacing missing teeth: alveolar ridge preservation techniques for dental implant site development. Cochrane Database Syst Rev 2021;4(4):Cd010176.
31. Park JY, Song YW, Ko KA, Strauss FJ, Thoma DS, Lee JS. Effect of collagen membrane fixation on ridge volume stability and new bone formation following guided bone regeneration. J Clin Periodontol 2022;49(7):684-93.
32. Schwarz F, Schmucker A, Becker J. Long-term outcomes of simultaneous guided bone regeneration using native and cross-linked collagen membranes after 8 years. Clin Oral Implants Res 2017;28(7):779-84.
33. Milinkovic I, Cordaro L. Are there specific indications for the different alveolar bone augmentation procedures for implant placement? A systematic review. Int J Oral Maxillofac Surg 2014;43(5):606-25.
34. Retzepi M, Donos N. Guided Bone Regeneration: biological principle and therapeutic applications. Clin Oral Implants Res 2010;21(6):567-76.
35. Arnal HM, Angioni CD, Gaultier F, Urbinelli R, Urban IA. Horizontal guided bone regeneration on knife-edge ridges: A retrospective case-control pilot study comparing two surgical techniques. Clin Implant Dent Relat Res 2022;24(2):211-21.
36. Song YW, Jung HJ, An YZ, Jung UW, Lee JS. Addition of autogenous bone chips to deproteinized bovine bone mineral does not have additional benefit in lateral ridge augmentation-A preclinical in vivo experimental study. Clin Oral Implants Res 2021;32(9):1105-14.
37. Park JY, Chung HM, Strauss FJ, Lee JS. Dimensional changes after horizontal and vertical guided bone regeneration without membrane fixation using the retentive flap technique: A 1-year retrospective study. Clin Implant Dent Relat Res 2023;25(5):871-80.
38. Aludden H, Mordenfeld A, Dahlin C, Hallman M, Starch-Jensen T. Histological

and histomorphometrical outcome after lateral guided bone regeneration augmentation of the mandible with different ratios of deproteinized bovine bone mineral and autogenous bone. A preclinical in vivo study. Clin Oral Implants Res 2020;31(10):1025-36.
39. De Risi V, Clementini M, Vittorini G, Mannocci A, De Sanctis M. Alveolar ridge preservation techniques: a systematic review and meta-analysis of histological and histomorphometrical data. Clin Oral Implants Res 2015;26(1):50-68.
40. Mordenfeld A, Hallman M, Johansson CB, Albrektsson T. Histological and histomorphometrical analyses of biopsies harvested 11 years after maxillary sinus floor augmentation with deproteinized bovine and autogenous bone. Clin Oral Implants Res 2010;21(9):961-70.
41. Lee JS, Cha JK, Thoma DS, Jung UW. Report of a human autopsy case in maxillary sinuses augmented using a synthetic bone substitute: Micro-computed tomographic and histologic observations. Clin Oral Implants Res 2018;29(3):339-45.
42. Yu X, Teng F, Zhao A, Wu Y, Yu D. EFFECTS OF POST-EXTRACTION ALVEOLAR RIDGE PRESERVATION VERSUS IMMEDIATE IMPLANT PLACEMENT: A SYSTEMATIC REVIEW AND META-ANALYSIS. J Evid Based Dent Pract 2022;22(3):101734.
43. Kim CS, Choi SH, Chai JK, Cho KS, Moon IS, Wikesjö UM, et al. Periodontal repair in surgically created intrabony defects in dogs: influence of the number of bone walls on healing response. J Periodontol 2004;75(2):229-35.
44. Jovanovic SA, Hunt DR, Bernard GW, Spiekermann H, Wozney JM, Wikesjö UM. Bone reconstruction following implantation of rhBMP-2 and guided bone regeneration in canine alveolar ridge defects. Clin Oral Implants Res 2007;18(2):224-30.
45. Schenk RK, Buser D, Hardwick WR, Dahlin C. Healing pattern of bone regeneration in membrane-protected defects: a histologic study in the canine mandible. Int J Oral Maxillofac Implants 1994;9(1):13-29.
46. Kaushal S, Kumar A, Khan MA, Lal N. Comparative study of nonabsorbable and absorbable barrier membranes in periodontal osseous defects by guided tissue regeneration. J Oral Biol Craniofac Res 2016;6(2):111-7.

**Table 1.** Results of linear measurement related with osseointegration.

| | | ARP | GBR | *p*-value |
|---|---|---|---|---|
| BIC [+] | Intact | 29.49±12.82 | 32.48±10.89 | 0.699 |
| | 1-wall-D | 30.58±4.55 | 37.85±7.71 | 0.100 |
| | 2-wall-D | 41.31±13.59 | 50.23±8.91 | 0.248 |
| | Average | 33.79±12.32 | 40.19±11.88 | 0.118 |
| fBIC [*,+] | Intact | 3.90±1.08 | 2.72±0.71 | 0.067 |
| | 1-wall-D | 4.58±0.57 | 3.21±0.71 | 0.007* |
| | 2-wall-D | 3.23±1.09 | 1.97±0.64 | 0.050 |
| | Average | 3.90±1.09 | 2.63±0.85 | 0.012* |
| NBS [*,+,#] | Intact | 3.61±1.04 | 4.21±0.74 | 0.320 |
| | 1-wall-D | 1.73±0.98 | 3.31±0.89 | 0.023 |
| | 2-wall-D | 1.47±1.23 | 4.76±1.05 | 0.001* |
| | Average | 2.27±1.45 | 4.09±1.08 | 0.003* |

*Statistical significance between two groups was found regardless of extraction socket models (Average) or regarding each extraction socket models (Intact, 1-wall-, and 2-wall-damaged model) through RM Anova (cutoff $p$ value = 0.05) and Bonferroni t-test post-work analysis (cutoff $p$ value = 0.016)

+Statistical significance among three socket models was found through RM Anova (cutoff $p$ value = 0.05)

#Statistical significance between two groups and three socket models has been found through RM Anova (cutoff $p$ value = 0.05)

## Figures

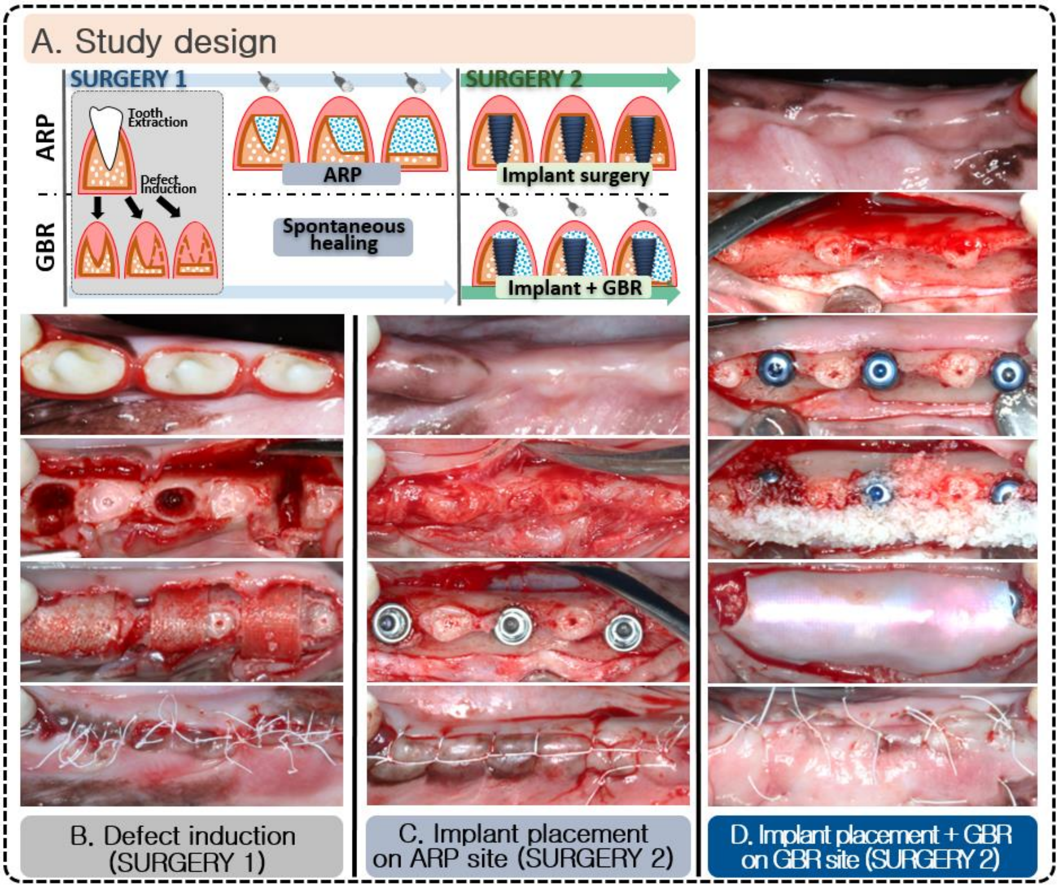


**Figure 1. Experimental study design and clinical photographs of surgical procedures**

Timeline showing the study protocols including respective treatment procedures and healing phases of both ARP and GBR groups (A). Mesial roots kept for reference and distal roots extracted for experimental purpose. Three types of extraction socket models (Intact, 1-wall-, and 2-wall-damaged) induced were treated with ARP and sutured with modified horizontal mattress techniques (B). After 8 weeks of healing period, ARP group had undergone implant placement, then sutured with single interrupted techniques (C). GBR group had undergone 8 weeks of spontaneous healing after the tooth extraction, implant was placed, simultaneous GBR was performed, and sutured with single interrupted techniques (D).

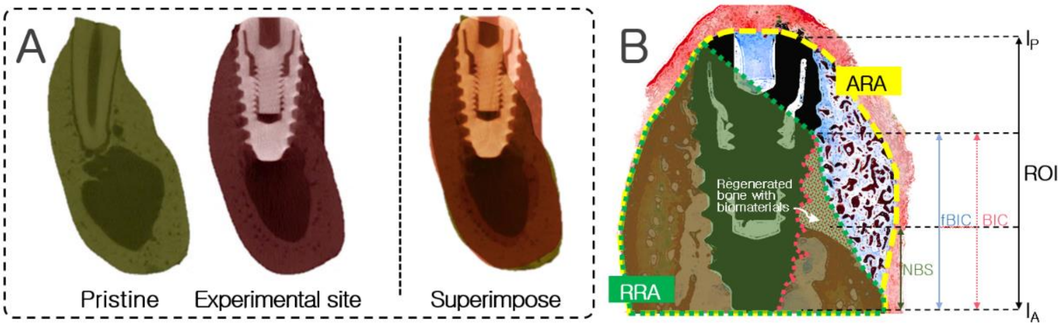


**Figure 2. Description of radiographic and histomorphometric measurements**

Superimposition of micro-CT images. The proportion of alveolar preservation (%) was calculated through pristine mesial root (baseline) to the experimental site (post-surgery) (A). Schematic diagram of evaluation method on the histological analysis, augmented ridge area (ARA) and regenerated ridge area (RRA) was measured upon histologic slides (B). Linear measurements regarding osseointegration, bone-to-implant contact (BIC), first-bone-to-implant contact (fBIC) and natural bone support (NBS) was measured upon histologic slides (B).

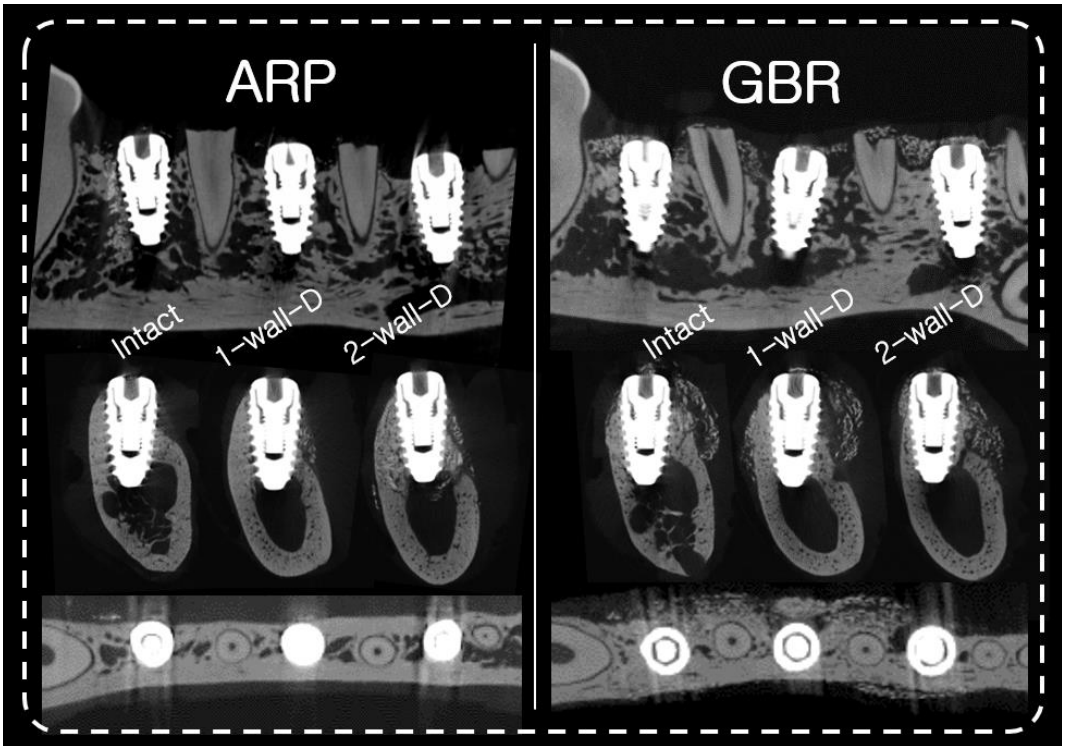


**Figure 3. Radiographic results with micro-CT images of ARP and GBR groups on three types of extraction socket configuration.**

Radiographic images showing panoramic and axial view on micro-CT showing three types of extraction socket configuration allocated at each distal site. Cross-sectional micro-CT images with two experimental groups aligned in accordance with the extent of extraction socket damage. GBR group shows larger augmented dimension and higher radiopacity next to the implant fixture than ARP group.

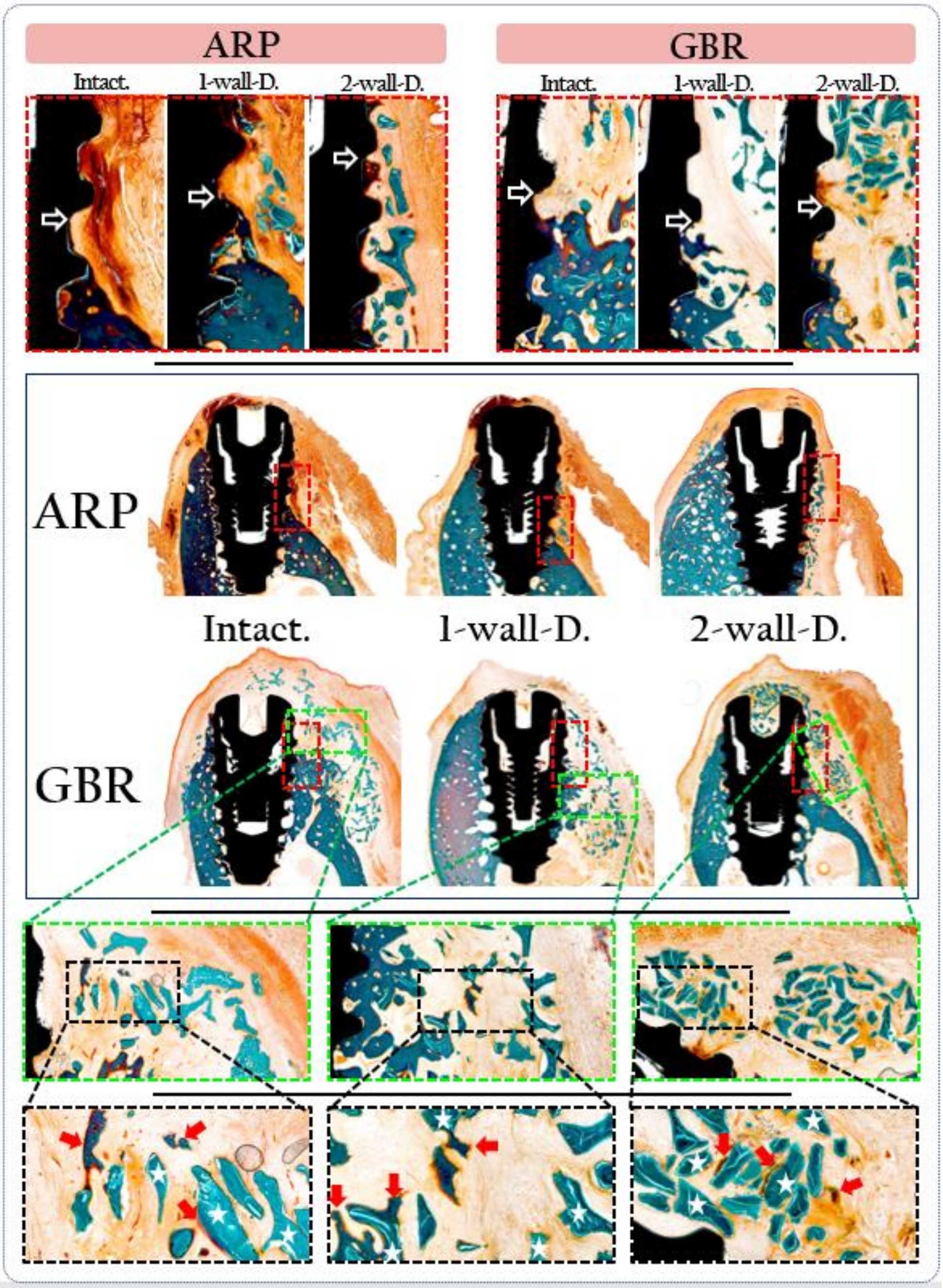


**Figure 4. Histologic results of ARP and GBR groups on three types of extraction socket configuration.**

Magnified view obtained from histologic sections of ARP vs GBR groups. Intact, 1-wall-, and 2-wall- damaged socket models shown from the left to right. ARP group shows fibrous incapsulation underneath the graft materials. On the other hands, GBR group shows evidences of osteogenesis in spaces between the biomaterial granules or on to their surfaces, indicating bone-regenerative potential within augmented area is present on buccal aspects of each damaged extraction socket models.

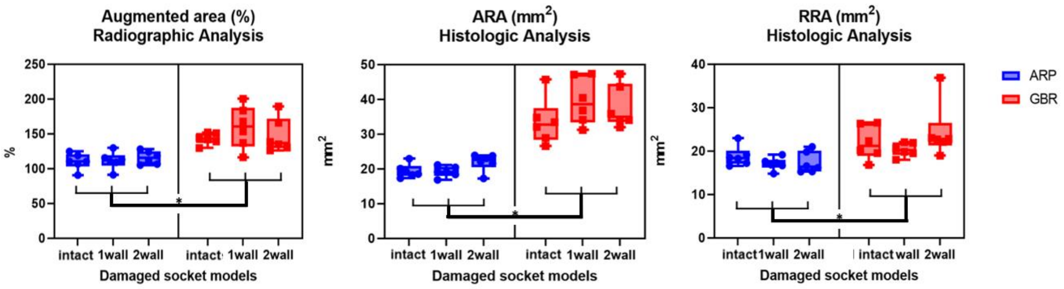


**Figure 5. Radiographic and histomorphometric results on dimensional alteration of augmented and regenerated alveolar ridge.**

Dimensional preservation (%) on radiographic analysis and the dimensional measurements ($mm^2$) of ARA and RRA on histological analysis. Statistical significances found between two groups, regardless of the extraction socket configuration (denoted by asterisk*).

국문요약

# 건전하거나 손상된 발치와에서의 치조제보존술과 골유도재생술의 비교에 관한 전 임상 연구

<지도교수 **이 중 석**>

연세대학교 대학원 치의학과

**신 해 지**

성견의 하악치조골을 대상으로 한 치조제보존술 또는 골유도재생술을 비교하는 본 전 임상연구의 목적은 다음에 있다. (1) 치아 임플란트 주변부의 골유착 및 자연 골 지지 정도, (2)수술 후 치조골 의 크기 변화 (3) 증대된 치조제 내 조직학적 구성을 영상 의학적, 조직학적으로 평가하여 건전하거나 손상되지 않은 발치와 에서의 치조제보존술 또는 골유도재생술의 효과를 비교하였다.

6 마리의 성견에서 하악 소구치 3 개의 원심 치근을 발치하고 근심 치근을 보존하여 세 가지 유형의 발치와 모델을 수술적으로 유도하였다. (a) 손상되지 않은 온전한 소켓 (b) 1-벽 손상된 소켓(협벽 제거) (c) 2-벽 손상된 소켓(협측 및 설측벽 제거). 두 개의 실험군이 양측 하악에 각각 적용되는 실험 디자인으로 설정되었으며, 하악의 양쪽 측면에 각각의 치료 프로토콜이 적용되었다. (제 1 군) 발치 직후 치조골보존술 + 임플란트 식립, (제 2 군) 치아 발치 + 임플란트 식립에 이은 동시적인 골유도재생술. 정량적 및 정성적 분석은 마이크로 컴퓨터 단층 촬영 및 조직학을 통해 수행되었다.

골유도재생술 시행군(150.03 ± 22.37%)은 수술 전과 수술 후의 증강된 치조제 면적의 크기가 치조제보존술 시행군(112.49 ± 10.52%)에 비해 크기가 유의하게 증가하였다. 골유도재생술 시행군(36.94 ± 6.46mm$^2$)은 치조제보존술 시행군(20.16 ± 2.23mm$^2$)에 비해 증강된 영역이 유의하게 큰 것으로 나타났다($p<0.05$). 또한, 골유도재생술 시행군(22.22 ± 4.32mm$^2$)은 치조제보존술 시행군(17.73 ± 2.04mm$^2$)에 비해 재생된 골 면적이 유의하게 크다($p<0.05$). 골유도재생술 시행군의 치료 부위(2.63 ± 0.85mm)는 치조제보존술 시행군의 치료 부위(3.90 ± 1.09mm)에 비해 임플란트 고정체 주변부의 골 열개 적은 길이로 나타났으며($p<0.05$), 골유도재생술 시행군의 치료 부위(4.09 ± 1.08mm)에서는 임플란트 고정체 주변부의 자연골 지지가 치조제보존술 시행군의 치료 부위(2.27 ± 1.45mm)에 비해 더 큰 것으로 나타났다($p<0.05$).

결론적으로 파괴된 발치와의 유형에 관계없이 골유도재생술은 골 열개의 유발을 감소시키며, 임플란트 식립에 불충분한 좁은 치조제에서의 치조제증강술을 시행할 때 치조제보존술에 비해 임플란트 고정체 주위의 골 유착 및 자연적인 골 지지량을 크게 향상시키며, 안정적인 치조제 증강의 결과를 기대해 볼 수 있겠다.

---

**핵심되는 말:** 치조제보존술, 파괴된 발치와, 발치, 골유도재생술