# Ridge Preservation Using Demineralized Bone Matrix Gel with Recombinant Human Bone Morphogenetic Protein-2 After Tooth Extraction: A Randomized Controlled Clinical Trial



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Directed by Professor Kyoo-Sung Cho

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# 감사의 글

이 논문이 완성되기까지 부족한 저를 이끌어 주시고, 연구에 매진할 수 있도록 아낌없는 격려와 지도를 해주신 조규성 교수님, 박정철 교수님께 깊은 감사를 드립니다. 그리고 언제나 따뜻한 관심과 조언을 아끼지 않으셨던 김종관 교수님, 채중규 교수님, 최성호 교수님, 김창성 교수님, 정의원 교수님, 이중석 교수님께 감사드립니다. 또한 바쁘신 와중에도 심사를 맡아주시고 많은 조언과 격려로 지도해주신 이근우 교수님께도 감사드립니다.

저의 연구가 무사히 진행되고 완료될 수 있도록 도움을 준 김재신, 신현기 선생님을 비롯한 치주과 모든 의국원들과 연구원들께도 감사의 말씀을 전합니다.

그리고 무엇보다도 언제나 저를 위해 기도해주시고, 힘들 때마다 따뜻한 위로와 충고를 아끼지 않으신 사랑하는 부모님, 늘 웃음과 행복을 주는 저의 소중한 가족분들께 고마움의 마음을 전합니다.

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## Abstract

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The aim of the present randomized controlled trial was to determine the safety and efficacy of injectable demineralized bone matrix (DBM) gel combined with recombinant human bone morphogenetic protein-2 (rhBMP-2) on alveolar ridge preservation after tooth extraction.

A total of 69 patients were randomly assigned to either a test group (n = 35) or a control group (n = 34). In the test group, DBM, together with rhBMP-2 (0.05 mg/mL; rhBMP-2/DBM) was transplanted into the extraction sockets.

The control group received DBM alone. The safety of rhBMP-2/DBM was evaluated by oral examination, serum chemistry, and hematologic examination. The radiographic changes in alveolar bone height and width were measured using computed tomography scans performed immediately after transplant and again 3 months thereafter.

Healing was uneventful in all subjects, with no anticipated adverse events and no clinically significant changes in the serum chemistry and hematologic findings. No meaningful immune response was found among the study groups. No significant difference was found in the radiographic changes of alveolar bone height and width ($P > .05$).

This new injectable biomaterial can be used easily and safely in clinical applications.

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**Keywords:** rhBMP-2, Demineralized Bone Matrix, bone regeneration, human, RCT

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## I. Introduction

Demineralized bone matrix (DBM) is made from donated human bone from which the inorganic mineral has been removed, leaving behind the organic collagen matrix.[1] During this process, a group of proteins becomes sequestered in the residual inorganic bone matrix; these proteins have been termed “bone morphogenetic proteins” (BMPs) by Urist.[2] Owing to the osteogenetic characteristics of native BMPs, DBM has been classified as an

osteoinductive material,[3] and it has been routinely used to promote bone regeneration, not only in orthopedic surgery, but also in dental implant surgery.[4,5]

However, controversy exists regarding the osteoinductive potential of DBM. Although it has been shown in animal studies that DBM implants placed in mid-diaphyseal defects and extraction sockets have failed to induce new bone formation,[6,7] Landsberg et al[8] found that DBM did promote bone formation in defects adjacent to dental implants. Even the results of meta-analyses of previous clinical trials have been controversial. Reynolds et al[9] reported a beneficial effect of DBM, and Laurell et al[10] stated that its use might not be beneficial. This apparent lack of consistency in the ability of DBM to induce bone regeneration could be attributable to variations in the donor characteristics. A few studies have found that donor age, physiology, and pharmacologic status[11,12] could be contributing factors to the variable osteoinductive capacity of DBM. Furthermore, the processing and sterilization protocols used have differed according to the bone bank used, which might have influenced the quality of the final product by affecting the DBM particle size,[13] just as would the acid exposure times during the demineralization procedure. Therefore, the use of DBM in clinics, with the associated beneficial release of native BMPs, has been limited owing to their variable concentration

within, or inadequate recovery from bone.

Recombinant technologies have been used to provide controlled concentrations of BMPs, resulting in the development of recombinant human BMP (rhBMP), which expresses osteoinductive properties.[14-16] It has been shown that when rhBMP-2 is successfully loaded into inactive DBM, the addition of rhBMP-2 directly to inactive DBM provides consistent bone induction.[17] Furthermore, a few other studies have found that DBM is a suitable carrier for rhBMP-2.[18] The mechanism underlying these useful effects of DBM as a carrier for rhBMP-2 is not clear; however, it seems that the collagenous substrate that remains after hydrochloric acid extraction of the mineral fraction might provide a sustained pattern of release of the osteoinductive protein[19] and serve as a scaffold for the proliferation and differentiation of osteoprogenitor cells.[20] Moreover, the manufacture of DBM into a putty- or paste-type form provides easy handling without scattering, which might facilitate its retention in the grafted area.

To the best of our knowledge, no well-controlled, randomized clinical trials (RCTs) of the utility of DBM combined with rhBMP-2 and modified into an injectable gel form for ridge preservation after tooth extraction have been performed. Hence, the present study was designed to determine the effect of DBM combined with rhBMP-2 in injectable gel form (rhBMP-2/DBM) for

alveolar ridge preservation after exodontia. The aims of our RCT were to assess the safety of rhBMP-2/DBM in human subjects and to evaluate the radiographic changes in the alveolar ridge after transplantation of either DBM alone or rhBMP-2/DBM gel into extraction sockets.

# II. Materials and methods

## STUDY POPULATION AND DESIGN

The present single-blind, prospective, and parallel-arm RCT was conducted at 2 centers in the Republic of Korea from April 2011 to March 2013, and the study protocol was approved by the institutional review board at each of the 2 study centers (approval nos. 2-2010-0004, MD09019). The present study was conducted with the approval of the Korean Food and Drug Association. This clinical trial was registered at (http://cris.nih.go.kr/cris/index.jsp).

All patients aged 20 to 70 years, who required single tooth extraction in the anterior region and alveolar ridge preservation were candidates for the present study. At the first visit, the patients were asked for their informed consent before enrollment in our study.

The inclusion criteria were systemically healthy subjects who required extraction of a single-rooted nonmolar tooth and residual extraction sockets with less than 50% bone loss in all dimensions. The exclusion criteria were the presence of severe periodontitis or acute infections at tooth extraction; pregnancy or planning to become pregnant within 1 year of the experiment; recent myocardial infarction or uncontrolled bleeding disorders; the presence

of mental illnesses or suspected mental illnesses; hypersensitivity to bone graft materials; and the presence of clinically significant or unstable systemic diseases affecting bone or soft tissue growth, or other renal, hepatic, endocrine, hematologic, and autoimmune diseases.

Randomization was performed using a computer-generated randomization list. The randomization code was opened only at surgery (visit 2), and the patients were randomly allocated to either the test group or the control group. The test group received rhBMP-2/DBM (Rafugen DBM Gel plus rhBMP-2, 0.05 mg/ml; Korea Bone Bank, Seoul, Korea). The control group received DBM alone into the extraction socket immediately after tooth removal.

**PREPARATION OF rhBMP-2/DBM**

After cleaning the cortical bones with distilled water and grinding them to a particle size of 0.5–1.0 mm, the lipid and fat were removed in 70% ethanol and 3% hydrogen peroxide for 2 hours. The bone specimens were decalcified in 0.6 N hydrochloric acid for 72 hours, lyophilized at –70ºC under vacuum conditions, and then stored at room temperature.

A 1-ml volume of Chinese hamster ovary cells expressing rhBMP-2

(0.05 mg/ml) was dispersed in 1 ml of DBM and stored at –70ºC overnight. It was then freeze dried at –70ºC under vacuum conditions. The freeze-dried powder was stored at 4ºC until clinical use.

To facilitate the handling and reliable delivery of DBM,[21] porcine collagen gel and carboxy-methyl-cellulose (CMC) were applied to the matrix. Both DBM alone and rhBMP-2/DBM were mixed with 3% porcine collagen type I gel and 5.7% CMC. The mixture of DBM and porcine collagen gel (Rafugen DBM Gel, Korea Bone Bank, Seoul, Korea) and the mixture of rhBMP-2 coated DBM, collagen gel, and CMC (Rafugen BMP-2 DBM Gel, Korea Bone Bank Co. Ltd.) were injectable using a syringe. Both types of gel were stored at 4ºC until clinical use.

## SURGICAL TREATMENT

After administration of local anesthesia, crestal and intrasulcular incisions were made to the adjacent teeth in all patients to expose the involved teeth and alveolar crest. Extractions were performed as atraumatically as possible. The teeth were sectioned if necessary to preserve all of the socket's bony walls. The extraction sockets were thoroughly debrided to remove all soft tissue. The test material was delivered through a syringe and packed into the socket by 1 designated dentist at each of the 2 centers. It was passively packed after the careful bleeding control with gauze. A collagen membrane (Bio-Gide; Geistlich Biomaterials, Wolhusen, Switzerland) was tucked under the flaps and sutured over the materials using mattress suture technique. Primary closure was obtained using periosteal releasing incisions, if possible; minor exposure was accepted (Fig 1).

The medication prescribed to all subjects included antibiotics (500 mg of amoxicillin 3 times daily for 5 days) and analgesics (200 mg of Ibuprofen 3 times daily for 5 days). The patients wore temporary prostheses after the surgery for esthetic reasons, taking care to avoid pressure on the wound area. The sutures were removed after 7 days, and the subjects were followed up 1 and 3 months thereafter.

## SAFETY ASSESSMENT

The oral wounds at the treated sites were examined at each visit, including at baseline and days 2 and 14 and 1 and 3 months postoperatively, to monitor the occurrence of any of the commonly seen postoperative complications associated with the augmentation procedure (ie. pain, discomfort, swelling, fever, and wound dehiscence). Serum chemistry and hematology tests were performed at the screening and final visits, and the formation of antibodies to rhBMP-2 was evaluated using an enzyme-linked immunosorbent assay (Automatic Microplate reader, VERSAmax; Molecular Devices, Sunnyvale, CA).

## RADIOGRAPHIC ANALYSIS

Computed tomography (CT; HiSpeed Advantage; GE Medical Systems, Milwaukee, WI; and SOMATOM Sensation 16; Siemens, Erlangen, Germany) was used to investigate the following parameters: alveolar bone height (1 measurement) and bone width (3 measurements at 1, 3, and 5 mm below the superior point of the lingual alveolar bone of the extraction sockets. These measurements were taken from the baseline CT scans (ie, within 4 days

after transplantation) and at 3 months thereafter. The data were processed in Digital Imaging and Communications in Medicine (DICOM) format, and the area of interest was reconstructed using the OnDemand 3-dimensional (3D) software (Cybermed, Seoul, Korea). The OnDemand "fusion" function, a visualization tool that uses a registration technique to combine and display the image data, was implemented to superimpose the original DICOM data of the 2 CT scans. The 2 data sets were thus aligned and then manually checked to confirm a perfect match (Fig 2). Subsequently, the bone height and bone width responses (3-month value minus the baseline value for both; Fig 3) were calculated using the same reference points and lines.

**STATISTICAL ANALYSIS**

The major effects of the bone graft materials were assessed by comparing the alveolar bone height at baseline and 3 months after transplantation between the control and experimental groups. Furthermore, the minor effects of the bone graft materials, and changes in alveolar bone width at 1, 3, and 5 mm below the superior point of the lingual alveolar bone immediately after ridge preservation and at 3 months after transplantation were compared between the control and experimental groups.

The mean ± standard deviation values of the test parameters was calculated using Statistical Analysis System, version 9.1.3 (SAS Institute, Cary, NC, USA). For each parameter, the difference between the 2 groups was compared using the Wilcoxon rank sum test. The paired t test was used to determine the significance of the changes. $P < .05$ was considered statistically significant.

# III. Results

Patient flow through the study is shown in Figure 4. A total of 78 patients were initially screened, and 69 eligible patients were randomly allocated at surgery (visit 2) into the test group ($n$ = 35) or the control group ($n$ = 34). Six subjects were withdrawn or lost during follow-up period(Table 1). Although the radiologic data of another 6 patients were not of diagnostic quality, their clinical parameters were included in the safety assessment.

**SAFETY ASSESSMENT**

Healing was uneventful in all subjects, with no severe adverse events. No clinically significant changes were found in blood count, blood chemistry, or urinalysis results. The presence of antibodies to DBM alone and the rhBMP-2/DBM gel was found in 34 experimental patients and 32 control patients receiving bone graft material into extraction sockets. Of the 34 patients receiving the rhBMP-2/DBM gel, 2 (5.88%) developed antibodies, compared to 0 of 32 (0%) in the control group; the difference was not statistically significant ($P$ = .4965; Table 2).

## RADIOGRAPHIC ANALYSIS

Representative cross-sectional CT images of both experimental groups are shown in Figure 5. The mean change in alveolar bone height, which was evaluated by comparing the CT scans taken immediately and 3 months after transplantation, was –1.50 ± 1.07 mm in the control group and –1.17 ± 0.82 mm in the experimental group. Both groups exhibited a significant vertical height reduction from baseline to the final examination, and no statistically significant difference between the 2 groups ($P > .05$; Table 3).

Changes in the alveolar bone width were also measured to determine the minor effects of the bone grafts on the preservation of alveolar bone. At 1 mm below the baseline, there was a –1.21 ± 1.31 mm change was seen in the bone width of the control group and –1.06 ± 1.26 mm in the experimental group. The corresponding values were –0.58 ± 0.68 and –0.43 ± 0.71 mm at 3 mm below the baseline and –0.37 ± 0.61 and –0.23 ± 0.45 mm at 5 mm below the baseline. Therefore, both groups exhibited significant horizontal width reduction between the baseline and the final examination, with no statistically significant difference between the 2 groups ($P > .05$; Table 4).

# IV. Discussion

In the present study, the application of rhBMP-2 using injectable DBM gel into the extraction socket successfully preserved the volume of the alveolar ridge, and its clinical safety was well demonstrated. In addition, no adverse reactions to the graft material, including rhBMP-2 were observed.

The experimental model in the ridge preservation procedure after extraction is a well established study design and has been used in a number of studies.[22] In the present study, the extraction sockets with buccal bone loss less than 50% were included, and Fiorellini et al[23] included the sockets with more than 50% of buccal bone loss, termed the "postextraction buccal wall defect model". Both study models are well established; however, the latter is more focused on the evaluation of efficacy than the former. The primary aim of the present study was to evaluate the local and systemic safety and the efficacy of the rhBMP-2/DBM gel. However, the evaluation of the efficacy of rhBMP-2/DBM gel using the aforementioned buccal wall defect model could be investigated in future studies.

The rhBMP-2/DBM gel did not show a significant difference from the DBM alone in terms of alveolar bone width and height. We hypothesized that this phenomenon could be attributed to the relatively lower dosages of

rhBMP-2 than those in the previous studies. [23,24] Controversies regarding the proper dosage of rhBMP-2 for maxillofacial application and uncertainty of possible adverse events from the higher dosage application still exist.[25] In the present study, we used a lower dosage of rhBMP-2 than used in previous studies and maximum precaution was undertaken to ensure the safety of the materials. The results from the current study have shown that rhBMP-2/DBM gel and DBM alone were well tolerated both locally and systemically, with no adverse events, and we have shown that the resorption of the alveolar ridge was successfully prevented. Furthermore, the technical feasibility of device implantation was also achieved.

During the 3-month follow-up period, the patients experienced neither unexpected adverse events nor clinically significant changes in blood count, blood chemistry, or urinalysis results. Moreover, no significant immune response to rhBMP-2 was seen. Of the 34 patients receiving the rhBMP-2/DBM gel, 2 (5.88%) developed antibodies. Antibody formation can have the potential to affect the safety or efficacy of the rhBMP-2. In some studies, no difference was observed in the adverse event rates between antibody-positive patients and antibody negative patients, including adverse events.[26] These findings are similar to those of previous studies using rhBMP-2/absorbable collagen sponge,[27,28] suggesting that no specific toxicity is related to this study

device. However, several reports have been published of complications occurring after the application of rhBMP-2. Therefore, additional evaluation of changes in antibody titer should be conducted to monitor the long-term safety of this product.

The major limitation of the present study was the lack of a negative control group in which patients received no graft after extraction. However, the original purpose of our clinical trial was to compare the clinical and radiographic changes of the 2 transplanted materials within the extraction socket and to investigate their safety and efficacy using an injectable application. Therefore, it was beyond the scope of our study to ascertain the effect of the DBM applications compared with the outcomes for an untreated extraction socket. The results from the present study have substantially shown that both materials are equally safe.

# V. Conclusion

The results from this randomized, controlled, multicenter clinical study have shown that the application of rhBMP-2/DBM or DBM gel is safe to use clinically for preservation of the alveolar ridge, and no difference in dimensional change was observed between the 2 groups.

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# Legends

**Figure 1.** Clinical photographs of the surgical procedure.

(A) Residual root of the mandibular second premolar. (B) Extraction site after atraumatic exodontia. (C) Placement of rhBMP-2/DBM into the socket (which was ultimately covered with a collagen membrane). (D) Primary coverage was achieved.

**Figure 2.** (A) Superimposition of the DICOM data of 2 CT images at (B), baseline and (C), 3 months after transplantation of maxillary left canine to determine whether any changes had occurred in the measurement parameters between the 2 points.

**Figure 3.** Radiographic, computed tomography (CT) measurements of the cross-sectional area, height, and width of alveolar bone at baseline(within 4 days after transplantation or demineralized bone matrix (DBM) or recombinant human bone morphogenetic protein-2/DBM) and 3 months later. (A) First, point d was marked at the same point of the apex of the extraction socket on the representative CT scans taken at baseline and 3 months after transplantation. Second, line a' connected points a and d, taking into

consideration the axis of the extraction socket. Third, points b and c were marked at the same distance from line a'. Fourth, line b' connected points b and c. Fifth, line c' was drawn perpendicular to line a' from the most superior point of the buccal alveolar bone. Finally, the bone height was defined as the distance between point a and line c'. (B) First, line g was drawn perpendicular to line a' from the most superior point of the lingual alveolar bone. Second, the alveolar bone width was measured at 1, 3, and 5 mm below line g.

**Figure 4.** Patient flow diagram.

**Figure 5.** Cross-sectional images of the grafted areas. CT scans made at baseline (A, C) and at 3 months after transplantation (B, D) for the DBM-only (maxillary right second premolar) and rhBMP-2/DBM (maxillary left canine) groups.

# Tables

TABLE 1. AGE AND SEX DISTRIBUTIONS IN BOTH GROUPS.

| Item | Classification | Control group | Experiment group | All |
|---|---|---|---|---|
| Patients | | 34 | 35 | 69 |
| Gender | Male | 19 | 15 | 34 |
| | Female | 15 | 20 | 35 |
| Age group | Mean age(yr) | 51.18 ± 10.14 | 50.37 ± 13.45 | |
| | <50 yr | 13 | 14 | 27 |
| | 50−59 yr | 15 | 12 | 27 |
| | >60 yr | 6 | 9 | 15 |

TABLE 2. EVALUATIONS OF THE SAFETY OF RHBMP-2/DBM

(IE, THE IMMUNE RESPONSE).

| 3 month | Experimental group | | Control group | | *P* value* |
|---|---|---|---|---|---|
| | Negative,*n* (%) | Positive,*n* (%) | Negative,*n* (%) | Positive,*n* (%) | |
| Baseline | | | | | |
| Negative | 31 (91.18) | 2 (5.88) | 29 (90.63) | 0 (0.00) | .4965 |
| Positive | 0 (0.00) | 1 (2.94) | 0 (0.00) | 3 (9.38) | |

*P* < .05, *Fisher's exact test

TABLE 3. RADIOGRAPHIC EVALUATION OF CHANGES IN ALVEOLAR BONE HEIGHT IN THE BOTH GROUPS

| Alveolar bone height | Baseline | | | 3 months | | | Height change | | | *P* value |
|---|---|---|---|---|---|---|---|---|---|---|
| | Mean ± SD | Median | Min, Max | Mean ± SD | Median | Min, Max | Mean ± SD | Median | Min, Max | |
| Experimental group (*n* = 29) | 20.98 ± 7.74 | 21.14 | 9.54 39.58 | 19.81 ± 7.73 | 19.03 | 7.29 37.17 | –1.17 ± 0.82 | –1.19 | –2.71, 0.00 | .1844* |
| Control group (*n* = 30) | 21.83 ± 6.89 | 22.12 | 11.79 35.75 | 20.32 ± 6.92 | 20.29 | 10.14 35.75 | –1.50 ± 1.07 | –1.41 | –4.45, 0.00 | |

*P* < .05, *Wilcoxon rank sum test

TABLE 4. RADIOGRAPHIC EVALUATION OF CHANGES IN ALVEOLAR BONE WIDTH IN BOTH GROUPS.

| Alveolar bone width | | Baseline | | | 3 months | | | Width change | | | *P* value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Mean ± SD | Median | Min, Max | Mean ± SD | Median | Min, Max | Mean ± SD | Median | Min, Max | |
| At 1 mm | Experimental group (*n* = 29) | 7.61 ±2.71 | 7.78 | 1.49 12.25 | 6.56 ±2.73 | 6.28 | 1.10 11.32 | –1.06 ±1.26 | –0.57 | –5.58, 0.00 | .4574* |
| | Control group (*n* = 30) | 8.39 ±2.00 | 8.29 | 5.50 13.01 | 7.18 ±2.04 | 7.51 | 4.29 12.76 | –1.21 ±1.31 | –0.94 | –6.78, 0.00 | |
| At 3 mm | Experimental group (*n* = 29) | 8.06 ±2.22 | 7.66 | 4.63 12.30 | 7.63 ±2.22 | 6.96 | 4.49 11.38 | –0.43 ±0.71 | –0.16 | –3.28, 0.00 | .1758* |
| | Control group (*n* = 30) | 8.57 ±2.44 | 8.36 | 4.97 14.16 | 7.98 ±2.34 | 7.68 | 4.30 14.04 | –0.58 ±0.68 | –0.34 | –2.67, 0.00 | |
| At 5 mm | Experimental group (*n* = 29) | 8.31 ±2.42 | 7.70 | 4.28 13.15 | 8.08 ±2.41 | 7.41 | 4.28 12.57 | –0.23 ±0.45 | 0.00 | –2.23, 0.00 | .6939* |
| | Control group (*n* = 30) | 8.56 ±2.59 | 8.45 | 4.65 15.31 | 8.19 ±2.49 | 7.76 | 4.25 14.74 | –0.37 ±0.61 | 0.00 | –2.24, 0.00 | |

*P* < .05, *Wilcoxon rank sum test.

# Figures

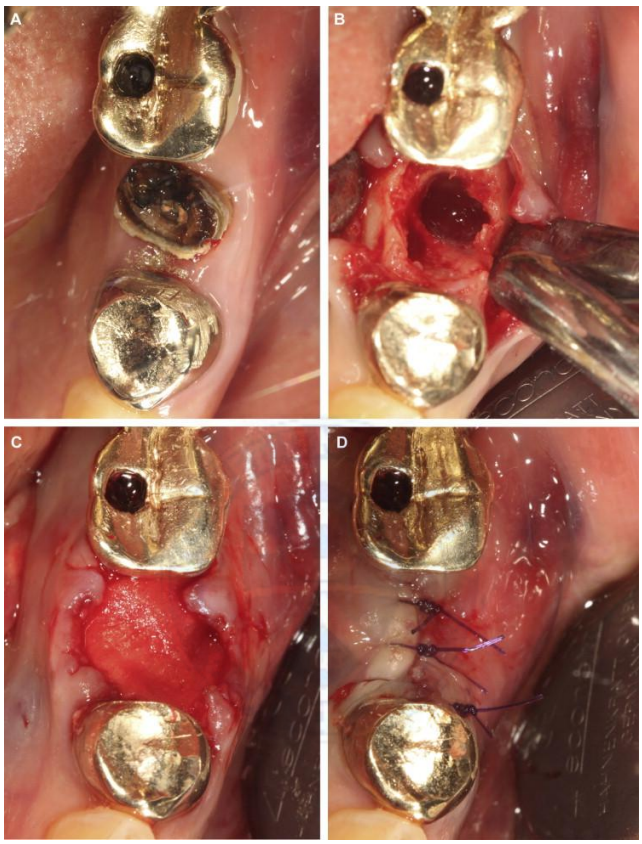


**Figure 1**

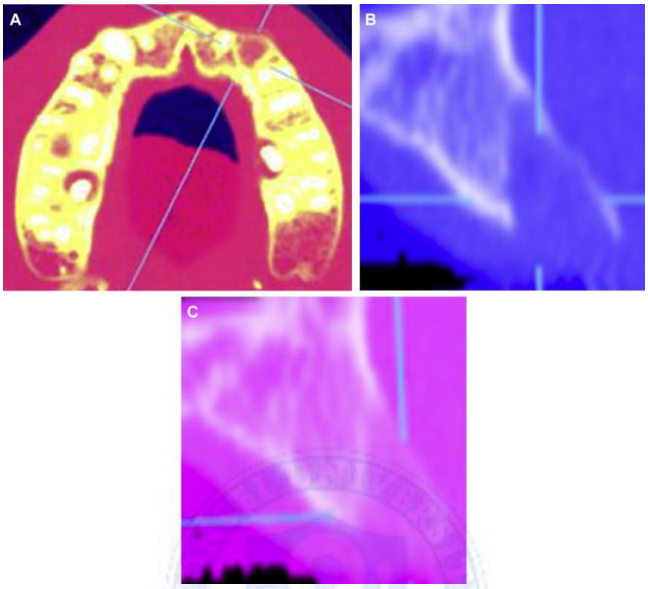


**Figure 2**

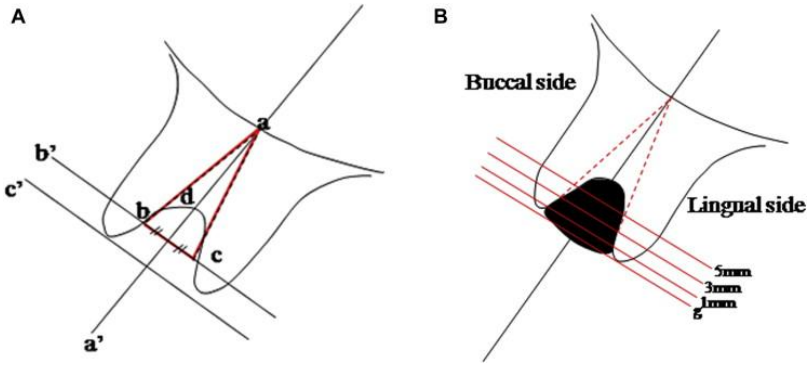


**Figure 3**

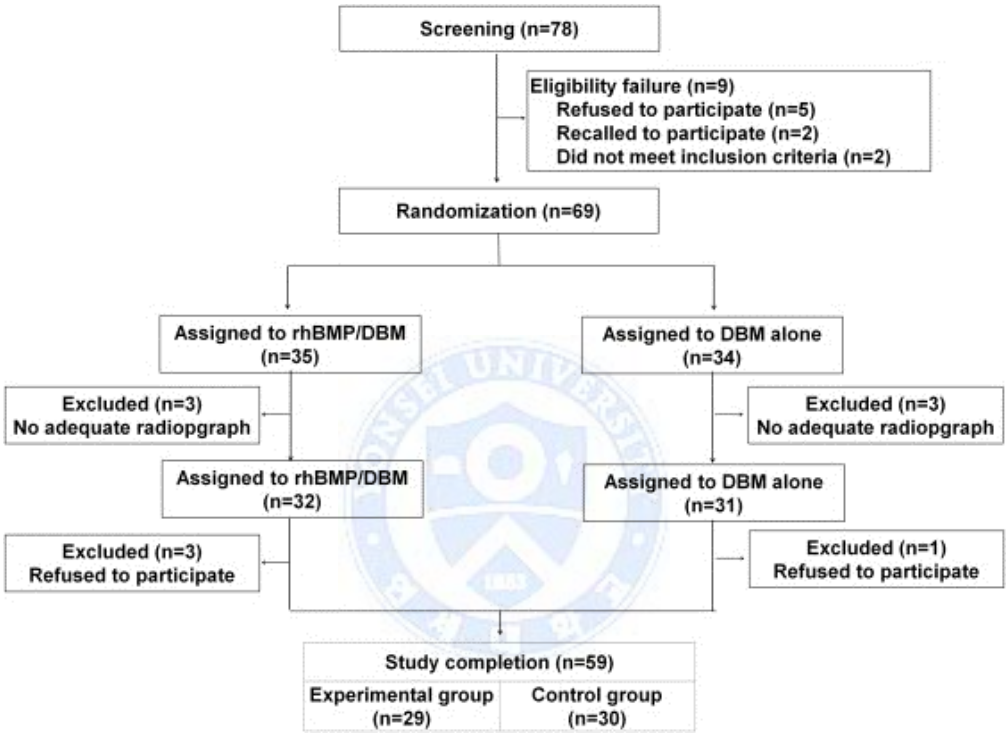
Screening (n=78)
Eligibility failure (n=9)
Refused to participate (n=5)
Recalled to participate (n=2)
Did not meet inclusion criteria (n=2)
Randomization (n=69)
Assigned to rhBMP/DBM (n=35)
Assigned to DBM alone (n=34)
Excluded (n=3) No adequate radiopgraph
Excluded (n=3) No adequate radiopgraph
Assigned to rhBMP/DBM (n=32)
Assigned to DBM alone (n=31)
Excluded (n=3) Refused to participate
Excluded (n=1) Refused to participate
Study completion (n=59)
Experimental group (n=29)
Control group (n=30)

**Figure 4**

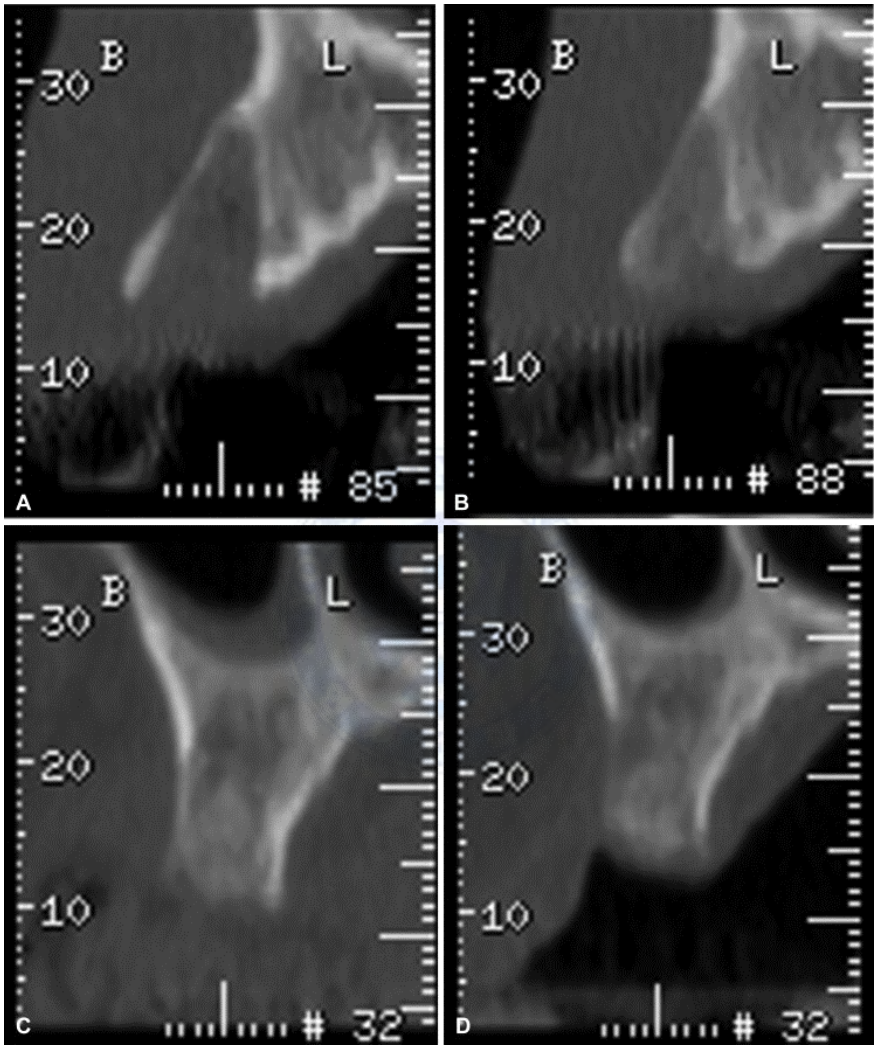


**Figure 5**

국문요약

# 제 2 형 재조합 인간 골형성 단백질을 포함한 탈무기화 골 기질(demineralized bone matrix, DBM)을 이용한 치조제 보존술에 대한 무작위 배정 임상 연구

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김 유 진

본 연구는 국내에서 생산된 재조합 인간 골형성 단백질-2 (recombinant human bone morphogenetic protein-2; rhBMP-2)이 함유된 탈무기화 골기질 골이식재 (Demineralized Bone Matrix; DBM)의 안정성과 골재생의 효과 및 치조골의 보존 효과를 평가하는 것을 목적으로 한다.

본 연구는 69 명의 환자들을 실험군과 대조군으로 무작위 선정 및 배정한 후 조작이 편리하게 주입식으로 만든 골이식재를 단근치 발치후 발치와에 이식하였다. 실험군에 배정된 35 명의 환자에게는 단근치 발치후 발치와에 재조합 인간 골형성 단백질-2 (rhBMP-2)이 함유된 탈무기화 골기질 골이식재 (DBM)를, 대조군에 배정된 34 명의 환자에게는 탈무기화 골기질 골이식재 (DBM)를 이식하였다. 3 개월 후 실험군과 대조군의

치조골 보존 효과를 방사선학적으로 평가한 것을 바탕으로 하여 1) 통계적 분석을 시행하여 유효성을 평가하고, 2) 혈청화학 검사와 혈액학적 검사를 시행하고 rhBMP-2 단백질에 대한 항체생성여부를 확인하여 안정성을 평가하였다.

안정성 평가 결과 모든 군에서 특기할 만한 부작용은 없었다. 혈청화학 검사와 혈액학적 검사에서 임상적인 문제는 발견되지 않았으며, 항체 생성 부분에서도 의미 있는 결과를 보이지 않았다. 유효성 평가에서는 이식수술을 한 직후와 3 개월을 비교한 결과 골높이와 폭에서 통계적으로 유의성은 없었다 (P >.05).

이상의 연구를 통해, 새로 계발된 주입식 골이식재는 임상에서 쉽고 안전하게 사용될 수 있음을 확인할 수 있었다.

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**핵심되는 말** : 재조합 인간 골형성 단백질-2, 탈무기화 골기질 골이식재, 골재생, 무작위 배정 임상 연구