Comparative study of hydroxyapatite block bone and bovine hydroxyapatite incorporated with collagen on the healing of 1-wall intrabony defects in dogs

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Comparative study of hydroxyapatite block bone and bovine hydroxyapatite incorporated with collagen on the healing of 1-wall intrabony defects in dogs

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감사의 글

이 논문이 완성되기까지 부족한 저를 지도해주시고 따뜻한 격려로 이끌어주신 최성호 교수님께 깊은 감사를 드립니다. 그리고 많은 조언과 관심을 주신 김종관 교수님, 조규성 교수님, 이용근 교수님께도 진심으로 감사 드립니다.

연구 내내 많은 도움을 주신 정의원 교수님, 이중석 교수님과 차재국 선생님께도 특별한 감사를 드립니다.

그 동안 정이 많이 든 치주과 의국원들에게도 고마운 마음을 전합니다.

힘든 시기에 묵묵히 병원을 잘 지켜준, 자랑스러운 청아치과 가족들에게도 이 글을 빌어 진심으로 고맙다는 말을 하고 싶습니다.

마지막으로, 이 자리에 오기까지 늘 아낌없는 사랑을 주시고 든든한 기도의 후원자가 되어주신 부모님과, 사랑하는 아내 연교, 그리고 성준, 성민, 서연에게도 사랑과 고마움의 마음을 전합니다.

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ABSTRACT

Comparative study of hydroxyapatite block bone and bovine hydroxyapatite incorporated with collagen on the healing of 1-wall intrabony defects in dogs

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Bone grafts are often used as part of a surgical protocol to regenerate periodontal structures. HA and Bio-oss are used as bone graft materials for periodontal regeneration, and some studies using them in periodontal defects showed good results. But, due to the limitation of particulated bone grafts, periodontal regeneration was not enough in critical periodontal defects such as 1 wall defects. Therefore block type bone graft like HA block or Bio-oss collagen are being developed to enhance the early period wound stability and easy manipulation.

We evaluated the periodontal regenerative potential of HA block bone and Bio-oss collagen for clinical applications. In five male beagle dogs, we bilaterally created 4x5 mm one-wall intrabony defects at the distal aspect of the second mandibular premolars, and at the mesial aspect of the fourth mandibular premolars. These defects were either experimentally treated with HA block bone, Bio-oss collagen or surgery with no filling material as a control group. The dogs were sacrificed eight weeks after surgery, analyzed using micro CT, and block sections of the defects were collected for histologic and histometric analysis.

Postoperative healing was uneventful. On micro CT analysis, HA block showed greater ability of space maintenance than control group, and Bio-oss collagen has irregular results. But, histological analysis revealed that HA block showed relatively small amount of new bone formation, and cementum formation was not different from contol.

In this study, we expected that HA block preserve the clot and enhance bone formation because of the space maintaining and wound stabilizing ability, however, the bone formation was limited compared to prominent space maintenance.

Key Words : bovine hydroxyapatite, bio-oss collagen, hydroxyapatite, block bone, periodontal 1 wall defect, periodontal regeneration

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I. Introduction

One objective of periodontal therapy is regeneration of the periodontal attachment including cementum, a functionally oriented periodontal ligament, and alveolar bone. To achive this goal, the most important factor is providing a space, in which neighboring cells can grow [1]. In order to make a space within a periodontal defect, various bone grafts have been applied with or without occlusive membrane. Almost all the previous studies used particulated [2,3] or moldable type [4,5] of bone graft materials for the periodontal regeneration, because of an irregularity of the periodontal defect morphology. However, the ideal graft material still remains elusive. Caton et al. reported that particulated bone graft alone in a periodontal defect resulted in long junctional epithelium rather than periodontal new attachment [6].

Regeneration of periodontal tissues is hardly achieved because of the biological peculiarities of periodontal defects. First of all, many kinds of resident bacteria can hinder the regenerative process, and poor initial sealing between the epithelium and the tooth is hard to protect the wound site from the oral environment [1]. Finally, tooth mobility produced by the destruction of the periodontal support can bring down the wound stability [7]. In this unstable situation, every bone graft particle can have both macro- and micro-movement, so that the early healing process may be cut off and shifted into the other direction. Previous studies [3,8], which grafted materials were covered with a membrane for the sake of the stability, reported more increased periodontal attachment formation.

Advance of computed tomography imaging and CAD/CAM system brought the defect-driven customized block bone fabrication for various bone defects [9-11]. If this trial is widely used, a block-typed bone graft material for the irregular periodontal defect can be made and applied. Because of their interconnected skeletal structure, block-typed bone graft material would provide more strong mechanical stability compared with particulated type. Additionally, wound stability in early healing phase may increase by fittingness of customized bone graft into the defect. However, there have been a few studies utilized block-type graft within a periodontal defect.

The choice of proper material for a scaffold is the most important step of the tissue engineering, because the properties of the applied material may affect the other critical point of tissue engineering. Among the biomaterials, hydroxyapatite (HA) is one of the most widely used graft material in research and clinical fields. HA has a similar composition and structure with the natural bone mineral [12], and is known to bond chemically directly to bone when implanted [13,14]. Therefore HA has been received considerable attention as a scaffold for bone tissue engineering, however, its poor performance of mechanical stability and inconsistent cell reaction according to the surface properties limit its clinical use for various situations of bone defects [12,15]. To overcome these limitations, newly developed HA of nano-particles was introduced and was reported increased mechanical properties and improved protein adsorption capacity [16].

Bovine hydroxyapatite (BH) has been widely used for correction of periodontal osseous defects and augmentation of the resorbed alveolar rigdes around dental implants [17-21]. Similarities to human bone in porosity and microstructure provide excellent osteoconductive environment within the osseous defects[22].

It is known that BH is categorized into almost nonresorbable bone substitutes, and occupies its space in the defect while embedded with the newly formed bone [23-25].

It was reported that tight filling of the BH particles itself at the intrabony defects can protect the epithelial cells from migration without a barrier membrane[21]. Therefore, it is assumed that bone grafting alone can act as a barrier membrane as well as a scaffold, if the grafted materials are well localized and maintained within the defect. It might be true at the contained type such as the extraction sockets or three wall intrabony defects. However, particles would be dispersed in large or noncontained defects without segregation by a membrane[26].

The BH particles incorporated with a porcine type-I collagen matrix (BHC) can be stabilized without dissipation like a hard sponge, which allow to adapt and condense into the irregular defects. When it gets wet, it is softened and has favorable manageability.

A number of preclinical and clinical studies indicated that BHC grafting enhanced periodontal regeneration in periodontal intrabony defects [20,27-29].

The BHC, which is a form of block bound collagen matrix, is expected to hold the dimension during healing phase even in the noncontained type such as one-wall intrabony defect.

In a dog experiment by Stavropoulos and Wikesjo, BHC was grafted at either 4X4 mm or 6X6mm intrabony defect and was covered by a collagen membrane[30]. Following 18 months of healing period, it revealed periodontal regeneration almost similar to the original level. In spite of the excellent histologic results, it is wondered whether use of a barrier membrane would act an important role to improve the healing potential or not.

The aim of this study was to evaluate the regenerative capacity of newly developed HA block bone and BHC in 1-wall intrabony defect in dogs.

II. Materials and Methods

1. Animals

Five male beagle dogs, approximately 15 months old, weight 9–13 kg, bred exclusively for biomedical research purposes, were used. The animals exhibited an intact dentition with a healthy periodontium. Animal selection and management, surgical protocol, and preparation followed routines approved by the Institutional Animal Care and Use Committee, Yonsei Medical Center, Seoul, Korea. The animals had an ad libitum access to water and a pelleted laboratory diet with the exception of 8 weeks immediately post-surgery when they were fed a canned soft-dog-food diet (Prescription Diet Canine i/d, Hill's Pet Nutrition Inc., Topeka, KS, USA).

2. HA block

A. Preparation of nano-hydroxyapatite (n-HA) powder

Hydroxyapatite nanoparticles were prepared using the sol-gel process according to the previous published methods[31]. In brief, $Ca(NO_3)_2$-$4H_2O$ (99%; Sigma-Aldrich Co., St. Louis, MO, USA) and $(OC_2H_5)_3P$ (97%; Sigma-Aldrich Co.) were used as precursors of the HA sol. The hydroxyapatite sol was prepared by the reaction of the two precursors at a stoichiometric Ca:P ratio of 1.67, and then dried at 950°C.

B. Preparation of porous n-HA block

Porous n-HA block was prepared using prefabricated n-HA powders and a polymeric sponge according to the previous published methods[32]. Reticulated polyurethane ester sponge (Regicell, Jehil Urethane Co., Korea), which dimension is 7*7*9mm, was used in this experiment. This sponge has 500 three-dimensionally interconnected open pores per each linear mm. First, n-HA slurry was prepared by dispersing the prepared n-HA powders into distilled water with organic additives such as binder, dispersant and a drying chemical control additive (DCCA). Second process was infiltration, which the porous sponge was immersed into the n-HA slurry and several times, followed by rolling it through the teflon twin rollers whose spacing was controlled to compress and shrink the sponge up to75% in thickness. Finally, heat-treatment was applied up to 600◦C for 2 hours in a kanthal furnace, in order to burn out the sponge entirely and to volatilize the organic additives. Then the remaining HA was sintered for 2 h at various temperatures from 650 to 850◦C. The full procedure listed above was repeated twice to thicken the framework of the porous block. The finished block was trimmed into 4*4*5mm of the same size with the periodontal defect by low speed saw (Isomet®, Buehler, USA).

3. Bio-oss collagen

A block type BHC (4*4*5) was prepared from Bio-oss collagen (Geistlich Pharma AB, Wolhusen, Switzerland). The size of Bio-oss particle was 0.25~1mm, and the weight ratio between Bio-oss and collagen was 9:1.

4. Surgical procedures

The surgical protocol and post-surgery procedures followed established routines (Kim et al. 2004, 2005). Briefly, with minor modifications, food was withheld the night preceding surgery. The surgical procedures were performed under general anaesthesia induced by a subcutaneous injection of atropin (0.05 mg/kg; Kwangmyung Pharmaceutical Ind. Co. Ltd., Seoul, Korea) and an intra-venous injection of a combination of xylazine (Rompun, Bayer Korea Co., Seoul, Korea) and Zoletil (Virbac SA, Carros, France) followed by inhalation anaesthesia (Gerolan, Choongwae Pharmaceutical Co., Seoul, Korea). Routine dental infiltration anaesthesia was used at the surgical sites.

An experienced surgeon performed all surgeries. The mandibular first and third pre-molars were surgically extracted before the experimental surgery and the extraction sites were allowed to heal for 8 weeks. The remaining dentition received oral prophylaxis in conjunction with the extractions.

Experimental surgeries were performed following the 8-week healing interval. Using 5 animals, buccal and lingual mucoperiosteal flaps were elevated to create critical-size, “box-type”, 4 × 5 mm (width × height), one-wall intrabony defects at the distal aspect of the second and the mesial aspect of the fourth mandibular pre-molar teeth in right and left jaw quadrants (Fig. 1) [33]. Following root planing to remove the root cementum, a reference notch was made into the root surface at the base of the defects.

Unilateral P2 & P4 defect sites received a customized HA block or Bio-oss collagen in random manner, which just fitted the sites to the level of the alveolar crest. Contralateral sites served as sham surgery control.

The mucogingival flaps were advanced, adapted, and sutured using 4-0 absorbable suture (Monosyn®. 4.0 glyconate monofilament, B.Braun, Tuttlingen, Germany).

The animals received an intramuscular administration of a broad-spectrum antibiotic (Cefazoline Sodium 20 mg/kg, Yuhan Co., Seoul, Korea) and daily topical application of a 0.2% chlorhexidine solution (Hexamedins, Bukwang Pharmaceutical Co., Seoul, Korea) for infection control. Observations of experimental sites with regard to gingival health, maintenance of suture line closure, oedema, and evidence of tissue necrosis or infection were made daily until suture removal, and at least twice weekly thereafter. The animals were euthanized at 8 weeks post-surgery using an overdose of pentobarbital sodium (90–120 mg/kg; i.v.). Block sections including defect sites and surrounding alveolar bone and mucosal tissues were then collected. Photographic and radiographic recordings were completed intrasurgery, immediately post-surgery, and at 8 weeks post-surgery.

The block specimens were rinsed in sterile saline and immersed in 10% neutral buffered formalin at a volume 10 times that of the tissue block for 10 days. After rinsing in sterile water, the sections were decalcified in 5% formic acid for 14 days, trimmed, dehydrated in a graded ethanol series, and embedded in paraffin. Step-serial sections, 5 μm thick, were cut in a mesial–distal vertical plane, at approximately 80 μm intervals. The sections were stained using haematoxylin/eosin. The four most central sections of each defect site selected based on the width of the root canal were used for the histological and histometric analysis.

5. Evaluation methods

1) Clinical and Micro CT evaluation

The fixed specimens were scanned in a micro CT (SkyScan 1072®, SkyScan, Aartselaar, Belgium) at a resolution of 35 μm (100 kV, 100 μA).

2) Histological observations

One experienced masked examiner performed the histopathologic evaluation using incandescent and polarized light microscopy (Olympus Multi-view microscope BH2, Tokyo, Japan) including observations of bone regeneration (lamellar and woven bone), residual biomaterial and associated tissue reaction(s), cementum regeneration (cellular/acellular cementum; cementoid/cementum-like layer; intrinsic/extrinsic/ mixed fibre cementum), PDL orientation/density (0: no PDL fibres; 1: low-density PDL fibres; 2: moderate-density PDL fibres; 3: high-density PDL fibres, or same as the native adjoining PDL), ankylosis, and undermining root resorption.

3) Histometric analysis

One calibrated masked examiner performed the histometric analysis using a PC-based image analysis system (Image-Pro Plus™, Media Cybernetic, Silver Spring, MD, USA) and incandescent and polarized light microscopy (Olympus Multi-view microscope BH2). The parameters in Fig.2 were analysed for the four central sections.

6. Statistical analysis

Summary statistics (mean ± SD) based on animal means for the experimental treatments were calculated using the four central sections from each defect; defects being averaged for each site. Animal means were used to test for differences between experimental conditions using Mann-Whitney U test. The level of significance was set at 5%.

III. Results

1. Clinical and Micro CT observations

All defect sites healed uneventfully with minimal signs of inflammation, except one site of control group showed gingival recession.

The Micro CT evaluation showed variable new bone formation; however, sites received HA block appeared more bone formation compared with that observed for the sham-surgery control. In one site that HA block had placed overtopped compared to the height of contacting alveolar bone, micro CT images showed overtopped and unchanged shape of HA block still at the 8 weeks after surgery (Figure 6).

In bio-oss collagen group, 3 out of 5 dogs failed to maintain the space and most of the graft was lost. So, it showed no difference compared to control on average (Table 2).

2. Histological observations

Only one site of control showed a bit severe root resortion.

Bio-oss collagen maintained the shape in 2 sites out of 5, and new bone formation was observed between grafts, but in the other 3 sites most of the grafts were lost and bone formation was minimal.

HA showed minimal inflammation and bone formation was limited in all specimen.

However, HA still remained within the defect while the block shape was unchanged. PDL-like space with regenerated cementum was observed between root dentin surface and HA, although they were still immature state. In addition, new blood vessel formation was observed in the HA scaffold and only polymorphonuclear cells infiltrated minimally into residual biomaterials.

3. Histometric analysis

There was no significant difference between three groups only except that HA showed better results in bone height (space maintenance) than control in histometric and micro CT analysis. (2.47 ± 0.37 vs. 1.27 ± 0.42 for HA versus control group).

Cementum regeneration, connective tissue adhesion, and junctional epithelium were indistinguishable between two groups (Table 1).

In Bio-oss collagen group, there were no statistically significant differences in all parameters from those of control groups.

IV. Discussion

Hydroxyapatite (HA) block and Bio-oss collagen are being evaluated to support periodontal regeneration.

Evaluation of candidate technologies for periodontal regeneration ultimately commands analysing all components of the periodontal attachment. The canine one-wall intrabony defect model used herein allows an evaluation of the alveolar bone, cementum, PDL, and gingival tissues. Previous studies have used this defect model for the evaluation of a variety of biomaterials and regenerative techniques [33-38].

Histological analysis has been referred as a solid methodology to identify clearly each tissue components. However, it is not enough to understand 3 dimensional comprehensive wound healing, since histologic slide just provides a representative central cross-sectional view. In this study, overall healing pattern was observed through 3-dimensionally reformatted micro CT.

Most of previous studies for the periodontal regeneration have focused on particulated bone graft, because of clinical applicability into a periodontal defect of an irregular shape. In addition, several studies reported greater bone regeneration in bone defects received particulated bone graft material compared with block type one [39,40]. However in a recent study[41], hydroxyapatite block was suggested as a prefabricated scaffold of combining cell transplantion for the periodontal regeneration. Because of mechanical stability, block bone graft can be more suitable scaffold for periodontal tissue engineering, if it is possible to produce the defect-driven customized block bone graft for an irregular shape of periodontal defect. Indeed, block type graft resulted in a resolution of the defect in some situations like a case of vertical augmentation, which could not have been solved using particulated bone graft materials [42,43].

In a radiographic evaluation using a micro CT, sites received HA block showed statistically significant increase of bone regeneration compared to sham control sites. Whereas, histology revealed just minimal bone growth into the grafted HA block. Radiographic measurements would overestimate the result, due to a radiographic illusion including residual biomaterials into the regenerated bone. Even though minimal bone regeneration within HA block, grafted block bone still remained with an unchanged shape in both radiographic and histologic observations. These are different from the other study of 1-wall defect model received particulated bone graft [44].In sites received particulated bone graft, scattered biomaterials could be observed in a periodontal defect and supracrestal connective tissue area, and newly formed woven bone were shown around the biomaterials intact from the native bone [44]. These differences are in accordance with the previous studies [39,40], which reported inferior bone density with block bone graft in lateral defects and calvarial defects. In calvarial defect received particulated bone, new bone formation was occurred onto the surface of individual particles of biomaterials, and grew into the space between the particles at longer healing period. Whereas in sites of block bone graft, smaller bone formation started from the surface of the grafted block bone, and grew into the deeper area at longer healing period[39].

Recent study reported bone formation from the core of HA block using a combination with cell transplantation directly into the block graft [31,41]. In addition, many growth factors were reported enhancing bone regeneration within block type biomaterial[39,40,45]. These technologies of tissue engineering can improve the shortcomings of block bone graft as a periodontal scaffold.

Remarkably, new attachment formation including PDL space and cementum was observed between the well-maintained HA block and the denuded root surface. At the base of the defect, new attachment included thick CMSC and many inserting fibers into the newly formed cementum. At the upper area of the defect, however, cementum was gradually getting thinner, and most of all area showed phase I or II (early healing phase) of Araujö's classification of cementum regeneration[46]. In addition, collagen fibers originated from the pore space of the grafted HA block ran into the PDL space perpendicularly, like Sharpey's fibers of alveolar bone. These are important compositions of periodontal attachment, although they were in an immature state. And, considering multinuclear osteoclast-like cells around the residual biomaterials and scattered blood vessels all over the space, test sites could be on a process of ongoing degradation and remodeling.

Another remarkable phenomenon of the HA sites is minimal inflammation around the biomaterials and within connective tissue area. On the contrary, previous study using calcium phosphate particles in a same model, reported that residual particles were observed within connective tissue area, and associated extension of junctional epithelium. Although greater alveolar bone formation, epithelial attachment extended significantly more apical, and smaller cementum formation was occurred in sites received particulated bone graft compared to sham surgery control [44]. These differences would be caused by mechanical stability of block bone graft own and via fittingness into the defect. Indeed, Bartold et al. suggested that wound stability in early healing phase of periodontal regeneration would affect the regenerative potentiality[1].

Bone grafting of BHC in one wall periodontal defect showed inconsistent results according to the extent of localization and maintenance of the grafted material within the defects. Two samples of five animals showed almost complete regeneration of new cementum and moderate new bone formation while the graft materials were maintained and integrated within the defect. However, 3 samples failed to localize and remaining materials was hardly find in histologic slide. The outcomes from histometric measurements were similar to the sham surgery control.

Stavropoulos and Wikesjo (2010) evaluated the long-term effect of GTR procedure by using BHC with collagen membrane in two defect dimensions (4X4mm, and 6X6mm) of box-type one-wall intrabony defects in dogs. In the results of 18 months of healing period, almost complete periodontal regeneration was histometrically observed, irrespective to the difference of defect dimensions. However, it is unclear if the combination of BHC and collagen membrane would contribute to the best result, since sham surgery control, BHC alone, and collagen membrane alone groups was not included in the study design.

Box type one-wall intrabony defect model in dogs has been used to evaluate the effect of a certain biomaterial on the periodontal regeneration as a well established model. In the present study, the distal side of the mandibular second premolars the mesial side of the mandibular fourth premolars was used. The other studies that reported enhanced periodontal regeneration compared to the control, used the mesial side of the first molars to prepare the periodontal intrabony defects. [47] There is big defference between the molar and the premolar in the area and width of the alveolar bone surrounding the defect. Major source of the regenerative precursor cells is originated for the neighboring bony wall including the buccal and lingual plate adjacent to the exposed root surface and bony base of the defect [39]. Therefore, the first molar area having larger surface of bony wall would be more favorable in regenerative potential than the fourth premolar area.

The proportion of the remaining graft material was quite lower compared to the original amount of the graft at surgery, even if the heterogeneity of the healing response was allowed. Dissipation or exfoliation of the graft particles from the defect site might be considered as a main reason. BHC is comprised of 90% of BH and 10% of porcine type I collagen in weight. Since the BHC was not condensed, but just be placed at the defects, space occupied by collagen matrix might make the density of the BH particles loose. In Araujo's experiments, most of collagen matrix was resorbed to disappear in 1 to 2 weeks following grafting. Therefore, early loss of the collagen matrix might be responsible to the instability of the loosely embedded particles in the defects. Buccoligually opened one-wall defect would facilitate loss of the graft. Although BH is categorized into a slow or non-resorbable bone substitute, the possibility of biodegradation by osteoclasts has been reported. [48-51] In the present study, osteoclast like multinucleated giant cells were observed surrounding some BH particles. Lack of the remaining materials might be influenced also by osteoclastic resorption.

Presence of the condensed graft materials themselves at the coronal entry of the defect can play a role of a barrier block the epithelial downgrowth. On the other hand, some studies demonstrated that high density of the non-resorbable bone substitute may obstruct formation of provisional matrix and in consequence, retard overall healing and maturation.

V. Conclusion

When grafted to 1 wall intrabony defects, Bio-oss collagen shows similar space maintenance and bone regeneration to that of control. On the contrary, Newly developed HA blocks maintain the space better than control ($p<0.05$), but HA block showed minimal bone regeneration, and failed to show significant difference to control & Bio-oss collagen group.

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Legends

Table 1. Histometric analysis : Defect height (CEJ to apical extension of ro instrumentation), epithelium attachment, connective tissue attachment, new cementu and bone height in millimeter (Mean values and SD).

Table 2. Micro CT measurements : Defect height (CEJ to apical extension of ro instrumentation) and bone height in millimeter (Mean values and SD).

Figure 1. Surgical procedures. Surgically created, critical-size, one-wall, intrabon periodontal defect at the distal aspect of the mandibular 2nd and the mesial aspect the mandibular 4th premolar teeth (a). After placement of grafts (b), mucoperioste flaps are adapted and sutured for primary intention healing (c). The right panel shov healing at week 8 postsurgery (d).

Figure 2. Landmarks/parameters used in the histometric analysis. CEJ, cementoenam junction; JE, junctional epithelium; aJE, apical extension of junctional epithelium; C connective tissue; cNC, coronal extension of new cementum; cMT, coronal extensi‹ of mineralized tissue; BH, height of mineralized tissue; DH, defect height; NC, heig of new cementum.

Figure 3. Histolgical view of control (flap-only) site. Base of junctional epitheliu (white), top of cementum (black) and new bone crest (yellow) are indicated by tl arrowhead. A small amount of bone fill can be seen. H&E stain, scale bar: 1 mm (a) 100 μm (b & c).

Figure 4. Histolgical view of HA block experiemental site. Base of junction epithelium (white), top of cementum (black) and new bone crest (yellow) are indicat by the arrowhead. H&E stain, scale bar: 1 mm (a) & 100 μm (b & c).

Figure 5. Histolgical view of Bio-oss collagen experiemental site. Base of junction epithelium (white), top of cementum (black) and new bone crest (yellow) are indicat by the arrowhead. Asterisks show residual grafts. H&E stain, scale bar: 1 mm (a) 100 μ m (b & c).

Figure 6. Micro CT view. HA remained overtopped compared to the height of contacting alveolar bone with unchanged shape (a). Bio-oss collagen maintained the shape in 2 sites (c) out of 5, but in the other 3 sites most of the grafts were lost and bone formation was minimal. (b) & (d) is the view of contol sites.

Tables

Table 1. Histometric analysis. (N=5; mm; mean ± standard deviation)

	Experiment 1		Experiment 2	
	HA block	Control (HA block)	BHC	Control (BHC)
LJE	1.22 ± 0.40	1.24 ± 0.42	1.73 ± 0.49	1.40 ± 0.66
CTA	0.87 ± 0.62	0.64 ± 0.68	0.55 ± 0.69	1.61 ± 1.33
CR	2.75 ± 0.38	3.08 ± 0.85	2.74 ± 0.85	2.46 ± 0.81
BH	2.47 ± 0.37 §	1.27 ± 0.42 §	1.71 ± 1.24	1.31 ± 1.15
DH	5.05 ± 0.61	4.96 ± 0.22	5.01 ± 0.43	5.48 ± 0.70

LJE: Long junctional epithelium; CTA: Connective tissue attachment;
CR: Cementum regeneration; BH: Bone height; DH: Defect height

§ Significant statistical difference between groups ($p < 0.05$)

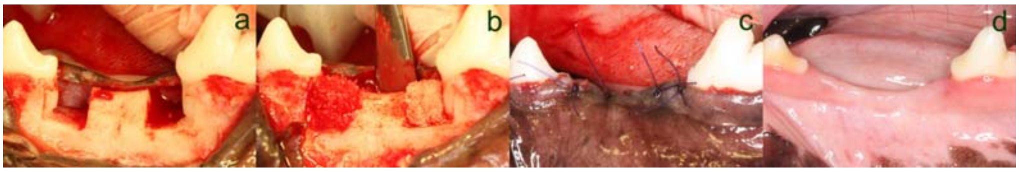
Table 2. Micro CT measurements. (N=5; mm; mean ± standard deviation)

	Experiment 1		Experiment 2	
	HA block	Control (HA block)	BHC	Control (BHC)
BH	2.27 ± 0.38 §	1.06 ± 0.63 §	1.36 ± 0.97	0.85 ± 0.67
DH	5.43 ± 0.31	5.13 ± 0.16	5.67 ± 0.24	6.02 ± 0.57

BH: Bone height; DH: Defect height

§ Significant statistical difference between groups ($p < 0.05$)

Figures



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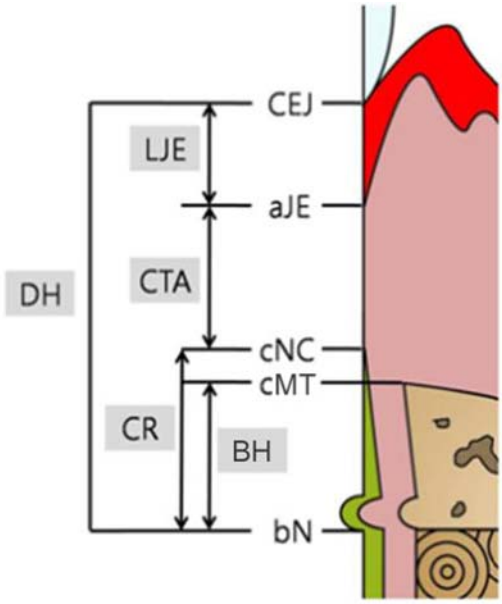

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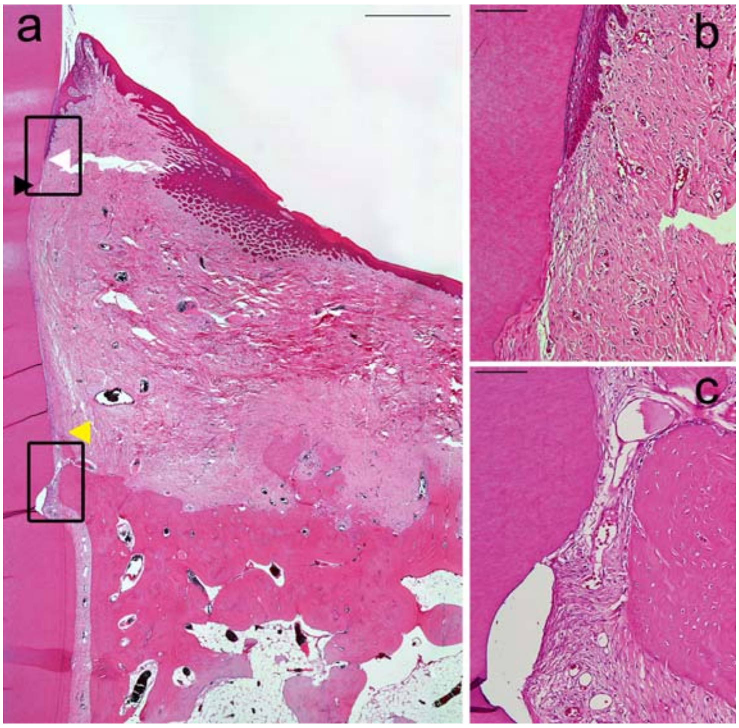

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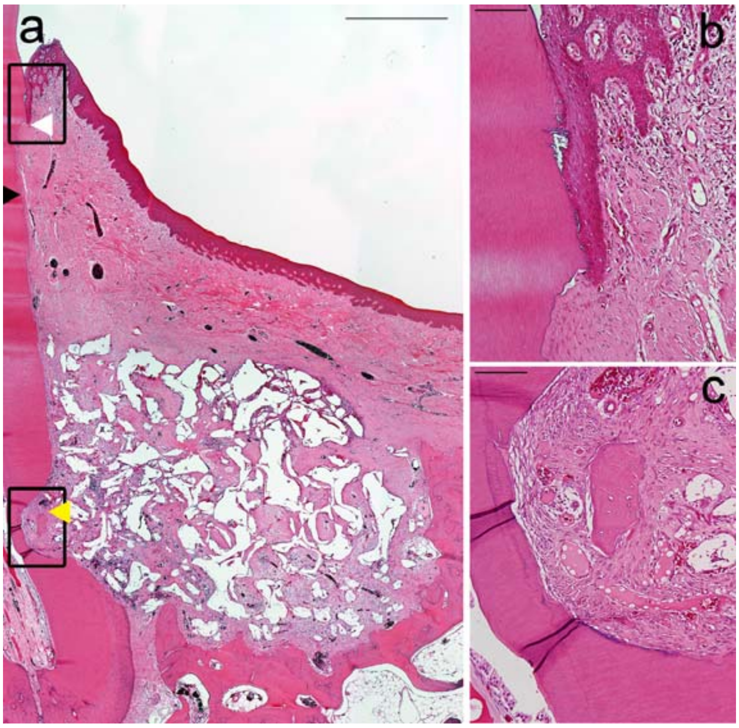

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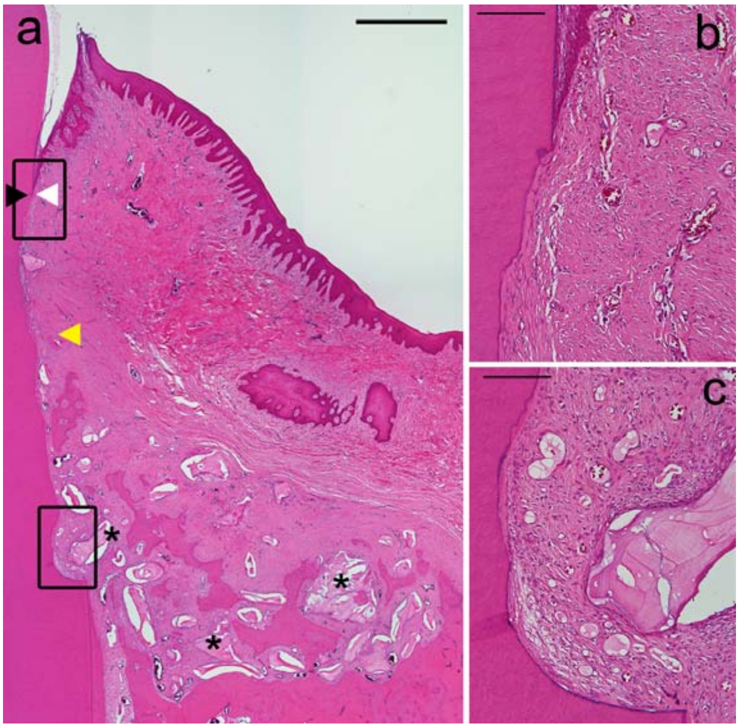

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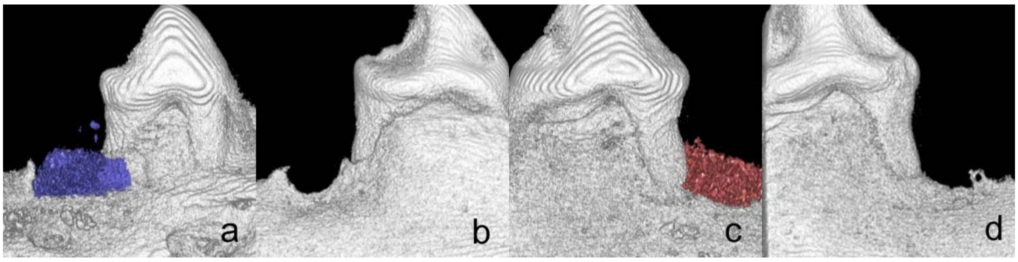

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국문요약

성견 1 벽성 골결손부에서 hydroxyapatite block bone 과 bovine hydroxyapatite incorporated with collagen 이 치주조직 재생에 미치는 영향

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(지도 최성호 교수)

박 원 영

골이식은 치주 조직의 재생을 위한 외과적 처치로서 흔히 이용된다. HA 와 Bio-oss 는 골이식에 사용되는 대표적 재료로, 좋은 결과를 보고한 연구들이 많으나 입자형 골이식재의 한계점으로 인해 1 벽성 골견손부 등의 critical defect 에서는 그 재생 효과가 제한적이다. 따라서 치주치유에서 초기 창상안정성과 조작성을 위해 block type 의 골이식재가 개발되고 있는데, 대표적인 것이 HA block 과 Bio-oss collagen 이다.

본 연구에서는 상기 재료들의 임상적 적용을 위해, 새롭게 개발된 HA block 과 Bio-oss collagen 의 치주조직 재생력을 평가하였다. 5 마리의 수컷 beagle 견에서, 하악 제 2 소구치의 원심면과 하악 제 4 소구치의 근심면에 양측성으로 4x5mm 의 일벽성 골결손부를 생성시켰다. 결손부는 HA block, Bio-oss collagen 으로 채워지거나 sham surgery 가

시행되었다. 개들은 수술 후 8 주 뒤에 희생되었고, micre CT 분석을 시행하였으며, 조직학적 계측을 위해 결손부의 block sections 을 수집했다. 술후 치유는 특이 사항이 없었다. Micro CT 분석에서 HA block 은 Bio-oss collagen 이나 control 에 비해 공간을 잘 유지하고 있었으며, Bio-oss collagen 은 일정치 않은 결과를 보였다. 반면 조직학적 관찰에서는 Bio-oss collagen 이 더 나은 골형성을 보였으며, HA block 주변에서는 골형성이 제한적이었다.

실험의 한계 내에서 보면, HA block 은 non-contained defect 에서 창상을 안정시키고 공간을 유지하는데 우수함을 보였고, 반면 신생골 형성은 8 주 기간중에 제한적이었다.

Bio-oss collagen 은 1 벽성 골결손부에서는 공간유지능이 다소 떨어졌고, 신생골 형성에 있어서는 HA 보다 우수하였다.

핵심되는 말 : bovine hydroxyapatite, bio-oss collagen, hydroxyapatite, 블록형 골이식재, 1 벽성 치주골결손부, 치주재생