The biological effect of cyanoacrylate combined calcium phosphate in rabbit calvarial defect

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감사의 글

이 논문의 연구계획에서부터 완성에 이르기까지 학문적 기틀을 잡아 주시고, 논문이 완성되기까지 부족한 저를 항상 격려해 주시고 아버지와 같은 사랑과 관심으로 이끌어 주신 채중규 교수님께 깊은 감사를 드립니다. 그리고 언제나 따뜻한 관심과 조언을 아끼지 않으셨던 김종관 교수님, 조규성 교수님, 최성호 교수님, 김창성 교수님, 정의원 교수님께도 감사 드립니다.

연구와 실험 과정 내내 많은 도움을 주고 3년간 동고동락한 동기 김진우, 손주연, 장용주와 치주과 모든 의국원들에게도 감사를 드립니다.

그리고 무엇보다도 언제나 저에게 아낌없는 사랑을 주시고 힘들 때 마다 기도와 충고를 아끼지 않으신 사랑하는 부모님, 동생에게 진정으로 사랑과 고마움의 마음을 전합니다. 오늘의 작은 결실에 자만하지 않고 항상 겸손한 자세로 꾸준히 노력하는 좋은 모습을 보이도록 하겠습니다.

모든 것을 계획하시고 이끌어 주시는 하나님 감사합니다.

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ABSTRACT

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Bone grafting techniques have been used extensively to restore maxillofacial osseous defects. Many researchers have attempted to develop the ideal synthetic material as a substitute for autogenous bone, the most recent of which is cyanoacrylate-combined calcium phosphate (CCP). CCP has several physical and mechanical advantages over conventional bone substitutes, such as its plasticity, adhesiveness, and antibacterial properties. The purpose of this study was to determine the biological effects of CCP, and in particular its potential to act as a physical barrier—functioning like a membrane—in rabbit calvarial defects. Male New Zealand White rabbits were used (n = 12). In each animal, four circular calvarial defects with a diameter of 8 mm were prepared and then filled with either nothing (control group) or one of three different experimental materials. In the control condition, the defects were filled only with blood clots (control group); in the experimental conditions, they were filled with CCP alone (CCP group), biphasic calcium phosphate (BCP) and then

covered with an absorbable collagen sponge (ACS; BCP/ACS group), or with BCP and then covered by CCP (BCP/CCP group). Animals were sacrificed after either 4 weeks (six animals) or 8 weeks (six animals) of healing, and radiographic and histomorphometric analyses were performed. After 4 and 8 weeks of healing, new bone formation appeared to be lower in the CCP group than in the control group, but the difference was not statistically significant. The amount of new bone formation was highest in the BCP/ACS group, and appeared to be lower in the BCP/CCP group, although the difference was not statistically significant. In both the CCP and BCP/CCP groups, inflammatory cells could be seen after 4 and 8 weeks of healing.

Within the limits of this study, CCP exhibited limited osteoconductivity in rabbit calvarial defects and was associated with the presence of inflammatory cells histologically. However, CCP appeared to be well tolerated by the host tissue and demonstrated potential as an effective defect filler in bone augmentation, and thus may be appropriate for implantation clinically, *in vivo*.

Key Words: Cyanoacrylate; biphasic calcium phosphate; rabbit calvarial defect; bone regeneration

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I. INTRODUCTION

Bone-grafting techniques have become essential in the restoration of both function and esthetics in the treatment of maxillofacial osseous defects. In dentistry, it has been used widely to treat periodontal osseous defects and to regenerate the bone necessary to permit placement of implants, such as sinus grafts and guided bone regeneration.(Chiapasco and Zaniboni, 2009; Nkenke and Stelzle, 2009; Sculean, Nikolidakis, and Schwarz, 2008) Although autogenous bone has excellent osteogenic properties and elicits no immune response, it has several disadvantages and limitations with regard to patient morbidity, harvest quantity, and complications such

as paresthesia and infection. Many researchers have been working to develop the ideal bone substitute for autogenous bone. Synthetic materials that have been suggested as alternatives have long been investigated in the search for a candidate with adequate osteoconductive properties.

Cyanoacrylates have been used successfully as a tissue adhesive in various surgical applications.(Brown et al., 2009; A. J. Singer and Thode, 2004) It has also been reported that cyanoacrylate has hemostatic and antibacterial properties(Al-Belasy and Amer, 2003; Quinn et al., 1997) when used instead of traditional suture materials to close surgical wounds. Many recent investigations have found that cyanoacrylate does not induce tissue toxicity when it is used as a wound dressing for the treatment of open wounds as well as wound closure.(Eaglstein and Sullivan, 2005; A. Singer, Thode, and McClain, 2001; A. J. Singer et al., 2003) Kutcher reported that devices utilizing cyanoacrylate were safe and effective for pain relief in oral ulcerations.(Kutcher, 2001) According to Bhaskar et al., the application of cyanoacrylate spray to the oral mucosa did not induce any adverse effects in the surrounding tissues.(Inal et al., 2006)

It has recently been suggested that synthetic materials produced using cyanoacrylate can be used as a bone substitute for the restoration of osseous defects. Lee et al. reported that rat calvarial defects reconstructed with cyanoacrylate-combined calcium phosphate (CCP) demonstrated new bone formation,(Lee et al.,

2006) and Park et al. revealed that CCP could be considered as a candidate for osseous healing in bone defects.(Park et al., 2005) CCP is prepared by mixing liquid cyanoacrylate and inorganic bioceramic powders. This material has unique and interesting properties that are different to those of conventional bone substitutes. Granular-type bone substitutes may be lost and are difficult to manipulate when applied to osseous defects that are especially large or that have a limited bony wall for supporting the graft materials. Conversely, because of its plasticity, adhesiveness, and rapid hardening properties (hardens within 3–5 min), CCP can prevent such loss of graft particles and is easily manipulated within osseous defects. In addition, when it is used in combination with different kinds of alloplast or allograft, CCP is able to bind to and immobilize other graft materials within the defect. It is thus possible to consider CCP to be a physical binder that can prevent the loss of graft particles, like a plastic membrane. CCP is also advantageous as a block-type bone substitute, which is difficult to plasticize in nonstandardized osseous defects. CCP has physical and mechanical benefits; however, clinical and histologic evaluations of this material as a bone-graft material are lacking. Furthermore, although cyanoacrylate has been used effectively and reliably for the closure of superficial wounds and lacerations, the biocompatibility of cyanoacrylate as an implant material *in vivo* has not yet been established.

The purposes of this study were to determine histologically the biologic effects of a novel CCP material and its potential as a membrane in surgically prepared rabbit calvarial defects.

Ⅱ. MATERIALS & METHODS

1. Animals

Twelve adult male New Zealand white rabbits weighing 2.5~3.0 kg were used. The animal selection and management, surgical protocols, and preparation followed routines approved by the Institutional Animal Care and Use Committee, Yonsei Medical Center, Seoul, Korea.

2. Graft materials

CCP was prepared by mixing two pastes: one containing 0.1 g of liquid cyanoacrylate and solid inorganic materials, the other containing 0.22 g of osteoconductive β-tricalcium phosphate (β-TCP) with a particle size of 10~50 μm and 0.14 g of glycerin. Inorganic materials in the first paste comprised 0.23 g of monocalcium phosphate (particle size 50~100 μm) and 0.03 g of dicalcium phosphate (particle size 10~20 μm).

Biphasic calcium phosphate (BCP, Osteon^{TM}; Genoss, Suwon, Korea) with a hydroxyapatite (HA)/β-TCP ratio of 70/30, a porosity of 77%, and a pore size of 300~500 μm was used in this study. The HA in this BCP is coated with β-TCP. An

absorbable collagen sponge (ACS, Collatape®, Zimmer Dental, Carlsbad, CA, USA) was used to cover the bone substitute in some cases.

3. Study design

Four circular defects, each with a diameter of 8 mm, were prepared in each rabbit calvarium (Figure 1). Each of the four defects in each animal was immediately filled with different graft materials according to the experimental condition, as follows (the location of the implant material in each animal was assigned randomly).

1. Control group (12 defects): defects were left unfilled, to serve as the surgical control.
2. CCP group (12 defects): defects were filled with only CCP.
3. BCP/ACS group (12 defects): defects were filled with BCP and then covered by ACS.
4. BCP/CCP group (12 defects): defects were filled with BCP and then covered by CCP.

The animals underwent a healing period of either 4 or 8 weeks (six animals for each period per group).

4. Surgical procedures

All animals were anesthetized using an intramuscular injection of a mixture of ketamine hydrochloride (Ketar®, Yuhan, Seoul, Korea) and xylazine (Rumpun®, Bayer Korea, Seoul, Korea). The head of the rabbit was shaved and disinfected with povidone iodine. An incision was made along the midline of the parietal bone from the frontal bone to the occipital bone. A full-thickness flap was elevated. Under copious saline irrigation, four standardized round defects, each 8 mm in diameter, were created using a trephine bur (Figure 1). The resected bones were removed carefully to avoid injury to the underlying brain tissue. The interdefect distance was more than 4 mm, allowing normal healing and easy harvest of the specimens for histologic analysis. The defects were filled with different experimental materials, depending on the study group (see above). The flaps were repositioned and sutured with resorbable suture material (Polyglactin 910, braided absorbable suture, Ethicon, Johnson & Johnson, Edinburgh, UK). The animals were sacrificed at either 4 or 8 weeks postsurgery. The skin flaps were then reflected and the entire calvarium was harvested from each animal using a small sharp fissure bur.

5. Histological processing

Block sections of the surgical sites were fixed in 10% formalin for 10 days. The fixed specimens were decalcified in 5% formic acid for 14 days and then embedded in paraffin. Serial, 5-μm-thick sections were cut along the midline of the calvarial defects. Only sections located at the middle of the defect were selected, and these were stained with hematoxylin-eosin for histologic and histometric analysis.

6. Analysis

(1) Clinical observation

Visual observations were performed after 4 and 8 weeks of healing for clinical evaluation.

(2) Radiologic analysis

After sacrificing the animals, all specimens were radiographed using a X-ray machine for descriptive radiographic analysis.

(3) Histologic analysis

Histologic slides were examined with the aid of a binocular microscope (Leica DM LB, Leica Microsystems, Wetzlat, Germany) equipped with a camera (Leica

DC300F, Leica Microsystems, Heerbrugg, Switzerland). The slides were photographed and the obtained images saved as JPEG files.

(4) Histometric analysis

Histometric measurement was performed using an automated image-analysis computer program (Image-Pro Plus, Media Cybermetics, Sliver Spring, MD, USA). The augmented area (all tissue within boundaries of the defect: newly formed bone, residual graft material, connective tissue, bone marrow) and new bone area (mm^2; Figure 2) were measured.

7. Statistics

The mean and standard deviation of values for each group were calculated. The significance of differences between groups was determined using the Kruskal-Wallis test ($p < 0.05$). The Mann-Whitney test was used to analyze the differences between values at 4 and 8 weeks. The Bonferroni test was used to analyze differences that were significant at the 5% level ($p < 0.05$).

Ⅲ. RESULTS

1. Clinical observations

Healing was uneventful for all animals during the postoperative period. None of the animals exhibited any complications such as infection or exposure of the graft material after surgery.

2. Radiologic observations

In the control group, a small radiopaque area was observed from the defect border after 4 weeks of healing; this area had increased after 8 weeks of healing. In the CCP group, a large radiopaque area surrounded by a radiolucent rim and a slightly greater radiopaque area than the surrounding bone was observed after 4 weeks of healing. There was an overall decrease in the radiopaque area at 8 weeks. In the BCP/ACS group, radiopaque graft particles were densely packed and there was no significant difference between the findings after 4 and 8 weeks of healing. In addition, the radiographic appearance of the BCP/CCP-filled defects was very similar to that of the BCP/ACS-filled defects, except that it was slightly more radiopaque (Figure 3).

3. Histologic analysis

1) Control group

A slight bony ingrowth was observed in the control group from the border of the defects that appeared to proceed to the central portion. Most of the area in the defects was filled with fibrous connective tissue that interconnected with both of the defect margins. The space observed within the defect did not persist, collapsing during the healing period. Some specimens exhibited bony islands within the defects. The amount of new bone observed was greater after 8 weeks than after 4 weeks of healing (Figure 4).

2) CCP group

There was a minimal amount of newly formed bone in the CCP group, and an inflammatory response was detected within the defects. When viewed at a higher magnification, inflammatory cells such as multinucleated giant cells, neutrophils, and lymphocytes were detected. The inflammatory reaction persisted at the 8-week follow-up (Figures 5 and 6).

3) BCP/ACS group

A bony ingrowth originating from the periphery of the defect was observed in

the BCP/ACS group, with immature woven bone in close contact with the graft particles. The regenerated bone contained many osteocytes, and osteoblastic cells surrounded the graft materials. The amount of new bone formation was greater after 8 weeks than after 4 weeks of healing (Figures 7 and 8).

4) BCP/CCP group

Histologic findings of the BCP/CCP group were very similar to those of the CCP group. Many inflammatory cells were seen, and there was limited bone formation, which was seen only at the defect margin. Moreover, immature woven bone was only barely observed around the BCP particles, contrary to the case for the BCP/ACS group (see above). Comparison of the specimens after 4 and 8 weeks of healing revealed them to be distinguishable from each other histologically (Figures 9 and 10).

4. Histometric analysis

The results of the histometric analysis are presented in Table I. The augmented area in the control group was relatively smaller to that in the experimental groups, with a new bone area of $1.04 \pm 0.69\ mm^2$ after 4 weeks and $2.29 \pm 0.86\ mm^2$ after 8 weeks of healing. Although the amount of bone appeared to increase with healing time (i.e., 4 and 8 weeks), the difference was not statistically significant. The mean

bone regeneration in the CCP group was lower than in the control group after both 4 and 8 weeks of healing. After 8 weeks of healing in the CCP group, an increase in the area of new bone was identified, but again this change was minimal and not statistically significant. Meanwhile, a significant increase in the area of new bone was observed in the BCP/ACS group, from 2.10 ± 0.38 mm^2 after 4 weeks of healing to 2.84 ± 1.24 mm^2 after 8 weeks. The amount of new bone found in the BCP/CCP group was 1.26 ± 0.93 mm^2 after 4 weeks of healing, but this diminished to 0.64 ± 0.31 mm^2 after 8 weeks. Furthermore, the mean bone regeneration in the CCP group was lower than in the BCP/ACS group after both 4 and 8 weeks of healing. A statistically significant difference in new bone formation was found between the BCP/CCP and BCP/ACS groups after 8 weeks of healing.

IV. DISCUSSION

This study evaluated the biological effect of CCP in the treatment of rabbit calvarial defects. Various homologues of cyanoacrylate compounds exist, such as methylcyanoacrylate, ethylcyanoacrylate, butylcyanoacrylate, and octylcyanoacrylate. Cyanoacrylate with a longer carbon side chain has a slower the degradation rate and hence also a lower toxicity.(Leggat, Smith, and Kedjarune, 2007) Only butylcyanoacrylate and octylcyanoacrylate have been used thus far in medical and dental applications. In particular, 2-octylcyanoacrylate was approved by the Food and Drug Administration in 1998 and was reported to be a well-established tissue adhesive for surgical wound closure.(Eaglstein and Sullivan, 2005) The CCP used in this study also contained liquid 2-octylcyanoacrylate and was manufactured by combining 2-octylcyanoacrylate with several inorganic calcium phosphates. The monocalcium phosphate in this particular CCP controls the velocity of polymerization. This was necessary, since cyanoacrylate rapidly polymerizes and hardens when it is exposed to moisture at room temperature. The addition of monocalcium phosphate extends the working time necessary to manipulate the CCP and fill the defects with it. The polymerization and hardening of CCP takes about 3 minutes. Among the several other calcium phosphates in CCP, dicalcium phosphate serves as a filler, and β-TCP, which is a well-established osteoconductive synthetic biomaterial that has been

scientifically proven to be absorbed *in vivo* and replaced with new bone, (Bowers et al., 1986; Jensen et al., 2006) is also added to CCP.

Our CCP group exhibited a limited amount of new bone formation compared to the control group after both 4 and 8 weeks of healing; a slight increase was observed at 8 weeks, but it was not statistically significant. Inflammatory infiltrates with numerous multinucleated giant cells, lymphocytes, and neutrophils were observed in the histologic specimens. Although healing progressed to 8 weeks, the extent of inflammation was constant.

A recent study that investigated the same material in a canine model found similar results to the present study, wherein CCP induced slight bone and cementum regeneration in periodontal one-wall intrabony defects.(Im et al., 2009) Conversely, Lee et al. reported no inflammatory response in a defect filled with a cyanoacrylate-based filling material, and further, new bone formation was observed in rat calvarial defects.(Lee et al., 2006) These inconsistent findings are presumably due to differences in the experimental materials, namely N-butyl-2-cyanoacrylate and β-TCP used in the study of Lee et al.(Lee et al., 2006) According to those authors,(Lee et al., 2006) when this compound was mixed, the temperature generated during the polymerization did not increase significantly relative to that generated during the polymerization of N-butyl-2-cyanoacrylate alone. It has been reported that the polymerization process of cyanoacrylate generates heat that could damage the cells

and surrounding tissues, ultimately accounting, at least in part, for the cytotoxicity of cyanoacrylate. (Leggat, Smith, and Kedjarune, 2007) The exothermic properties of CCP *in vivo* have not yet been verified. However, it is possible that the heat released during the polymerization of CCP is associated with the inflammatory response observed in our histologic analysis. Another possible explanation for this finding is a foreign-body reaction to the 2-octylcyanoacrylate itself, when it is implanted in vivo. Dragu et al. reported a foreign-body reaction when a tissue adhesive composed of 2-octylcyanoacrylate was applied to a wrist laceration wound, and identified inflammatory histopathologic results.(Dragu et al., 2009)

The CCP particles used in this study were too small, ranging from 50 to 100 μm. Although an optimal pore or particle size has yet to be determined, it has been reported that particles that are too small induce an inflammatory response or low rate of cell migration, ingrowth, and subsequently less bone regeneration.(Nasr, Aichelmann-Reidy, and Yukna, 1999) Shetty & Han(Shetty and Han, 1991; Zaner and Yukna, 1984) and Zaner et al.(Shetty and Han, 1991; Zaner and Yukna, 1984) reported that macropores larger than 100 μm are recommended to provide space for cell ingrowth and proliferation. It seems that the structural characteristics of CCP might also be associated with the inflammatory response or limited new bone formation.

On the other hand, it has been reported that cyanoacrylate has hemostatic properties and could be considered to be a therapeutic option for the prevention of microvascular bleeding and postoperative hemorrhage in surgical procedures.(Losanoff, Richman, and Jones, 2002; Rengstorff and Binmoeller, 2004; Zhang et al., 2008) However, this means that the hemostatic effect of cyanoacrylate might ironically reduce the osteoconductivity of CCP. New bone formation is achieved by providing the synthetic material with a sufficient blood supply, and so this hemostatic effect may in some way be responsible for the minimal new bone formation found in the CCP group. However, further investigation is necessary to verify whether the hemostatic effects of cyanoacrylate can adversely influence the osteoconductivity of CCP.

The defects reconstructed with BCP and ACS exhibited some regenerated bone after both 4 and 8 weeks of healing, although it was not statistically significantly different to that observed in the control group. Histologically, grafts exhibited many osteoblasts surrounding the graft material, and immature woven bone. The maturity and quantity of new bone increased with the healing time. These histologic and histometric results concur with those of previous studies demonstrating the osteoconductive effects of BCP in both clinical and animal experiments.(Fleckenstein et al., 2006; Kim et al., 2008; Um et al., 2008)

The ACS that was applied to cover the BCP was completely biodegraded within 10–14 days. During this period it was possible to separate the bone graft material

from the cutaneous flap and prevent graft particles escaping from the defects. In our previous study, which is yet to be published, we confirmed that placement of ACS over the particles was an effective method of accelerating bone regeneration in canine one-wall periodontal intrabony defects. Moreira-Gonzalez et al. indicated the importance of maintaining graft particles, finding that the migration of particles into the surrounding tissue results in limited bone regeneration.(Moreira-Gonzalez et al., 2005) The ability of CCP to act as a mechanical binder and physical barrier to maintain the graft materials within the defect was also evaluated by comparing it with and without ACS with regard to bone regeneration. New bone formation was observed in the BCP/CCP group, but it was not significantly greater than that observed in the BCP/ACS group after either 4 or 8 weeks of healing. Histologic specimens from the BCP/CCP group appeared similar to those from defects filled with only CCP. In the former there were multinucleated giant cells and inflammatory cells around BCP particles, as well as a minimal amount of immature woven bone.

Although the BCP/CCP groups exhibited limited new bone formation compared to the BCP/ACS group, it was found that the augmented areas of the former were higher than in all of the other groups. Histologic observations of the BCP/CCP groups showed that the BCP granules located under CCP were stably maintained without soft-tissue collapse. This indicates that the plasticity and adhesiveness of CCP may help to stabilize graft particles, functioning like a membrane or fixation screw in

defects, preventing soft-tissue collapse. In addition, the augmented area in all CCP and BCP/CCP groups was well maintained over the entire healing period, again without soft-tissue collapse, suggesting that CCP is an effective defect filler for an atrophied alveolar ridge, or for large osseous defects such as cystic cavities.

V. CONCLUSION

In conclusion, CCP induced limited new bone formation in rabbit calvarial defects throughout the healing period, attracting inflammatory cells that were observed histologically. However, its placement into bone defects appears to be well tolerated clinically, and demonstrating its ability to stabilize graft particles and to maintain augmented areas. Future investigations should attempt to improve the biocompatibility and osteoconductivity of CCP.

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LEGENDS

Figure 1. Clinical photographs of defect preparation (A) and application of the experimental materials (B)

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Figure 2. Schematic diagram of a calvarial osteotomy defect showing the histometric analysis. New bone area (mm^2) = *n*; residual biomaterial, fibrovascular tissue, bone marrow = *m*; augmented area (mm^2) = *n* + *m*

Figure 3. Radiologic presentation of calvarial defects after 4 weeks (A) and 8 weeks (B) of healing

Figure 4. Histologic presentation of a specimen from the control group after 4 weeks (A) and 8 weeks (B) of healing. Slight bony ingrowth can be seen from the border of defects, along with collapse of the connective tissue. Hematoxylin-eosin (H-E) staining; arrowheads, defect margin; A: original magnification ×10; B: original magnification ×10

Figure 5. Histologic presentation of the CCP group after 4 weeks of healing. A limited amount of new bone formation and inflammatory infiltration can be seen. H-E staining; arrowheads, defect margin; (A) original magnification ×10; (B) original magnification ×100

Figure 6. Histologic presentation of the CCP group after 8 weeks of healing. H-E staining; arrowheads, defect margin; NB, new bone; (A) original magnification ×10; (B) original magnification ×100

Figure 7. Histologic presentation of the BCP/ACS group after 4 weeks of healing. New bone is seen in close contact with the graft material. H-E staining; arrowheads, defect margin; NB, new bone; BCP, BCP material; (A) original magnification ×10; (B) original magnification ×100

Figure 8. Histologic presentation of the BCP/ACS group after 8 weeks of healing. Enhanced and mature bone surrounds the graft materials. H-E staining; arrowheads, defect margin; NB, new bone; BCP, BCP material; (A) original magnification ×10; (B) original magnification ×100

Figure 9. Histologic presentation of the BCP/CCP group after 4 weeks of healing. Limited bone formation is observed at the defect margin and in contact with the BCP materials. H-E staining; arrowheads, defect margin; NB, new bone; BCP, BCP material; arrow, inflammatory infiltrate; (A) original magnification ×10; (B) original magnification ×100

Figure 10. Histologic presentation of the BCP/CCP group after 8 weeks of healing. The connective tissue is infiltrated with inflammatory cells. H-E staining; arrowheads, defect margin; BCP, BCP material; (A) original magnification ×10; (B) original magnification ×100

TABLES

Table 1. Histometric results at 4 weeks and 8 weeks. All parameters is expressed as mm^2 (group mean ±SD mm^2; n=number of specimens)

	Parameters	Control	CCP	BCP/ACS	BCP/CCP
4 weeks	Augmented area	5.07±1.25	15.30±5.13∗	11.11±0.96	19.09±3.85∗¶
(n=6)	New bone area	1.04±0.69	0.4±0.17¶	2.10±0.38	1.26±0.93
8 weeks	Augmented area	5.52±1.87	12.24±1.88∗	10.50±1.81∗	14.43±1.89∗†
(n=6)	New bone area	2.29±0.86	0.75±0.58¶	2.84±1.24	0.64±0.31¶

∗ Significant statistical difference compared to control group at each week ($p<0.05$)

¶ Significant statistical difference compared to BCP/ACS at each week ($p<0.05$)

† Significant statistical difference compared to 4 weeks ($p<0.05$)

FIGURES

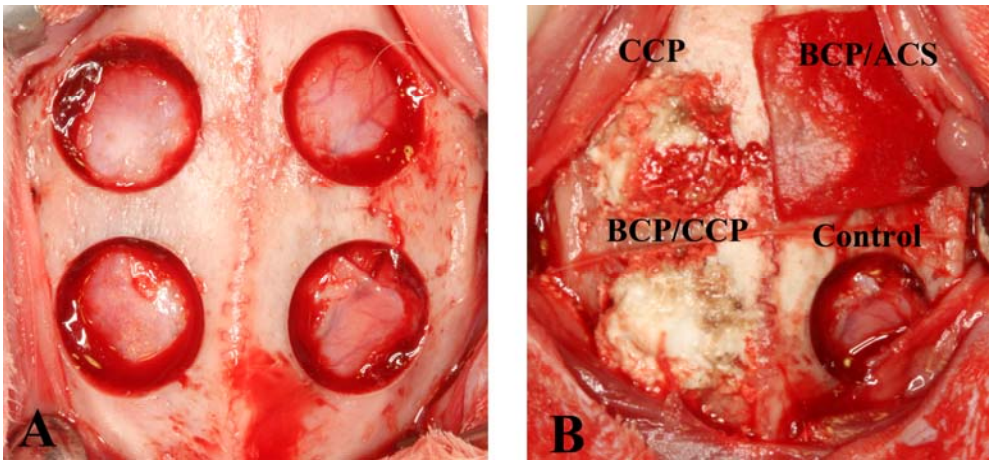
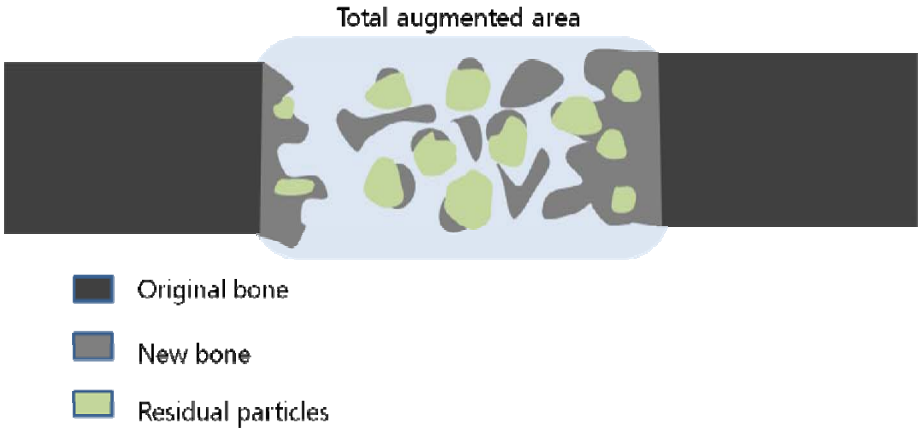


Figure 1



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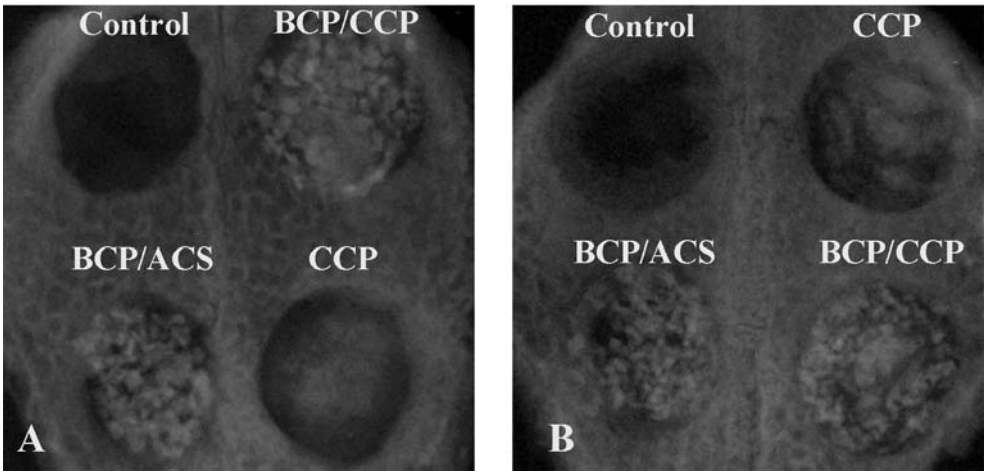

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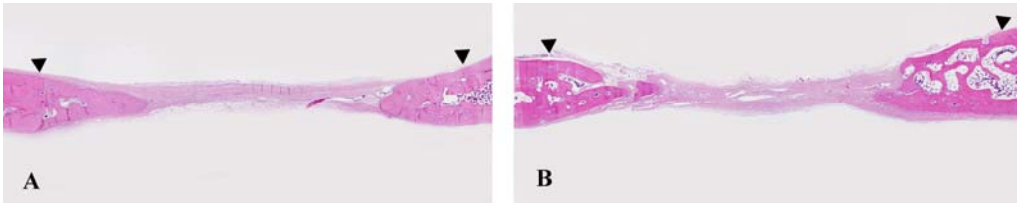

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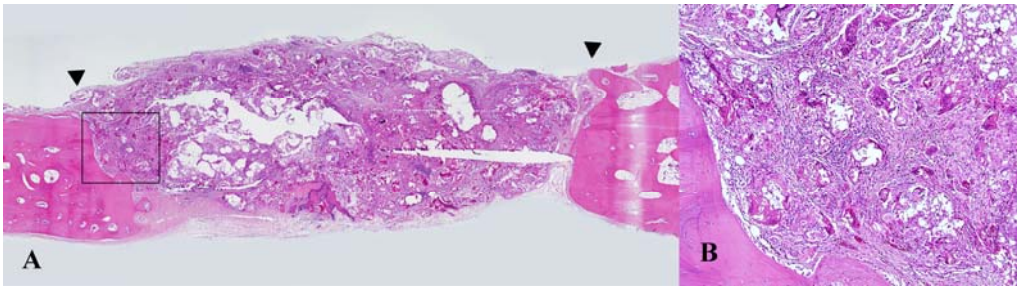

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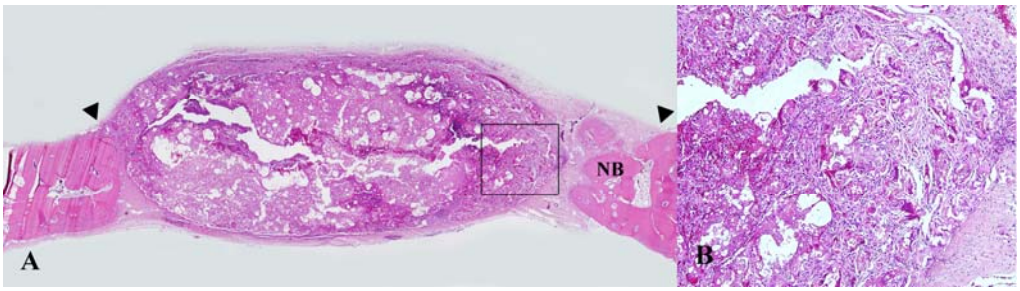

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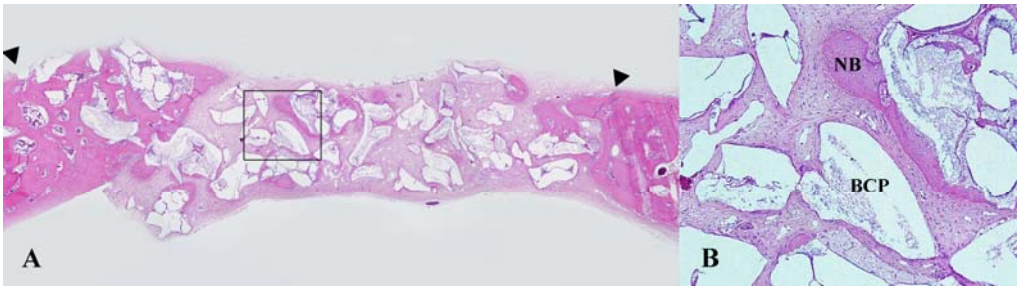

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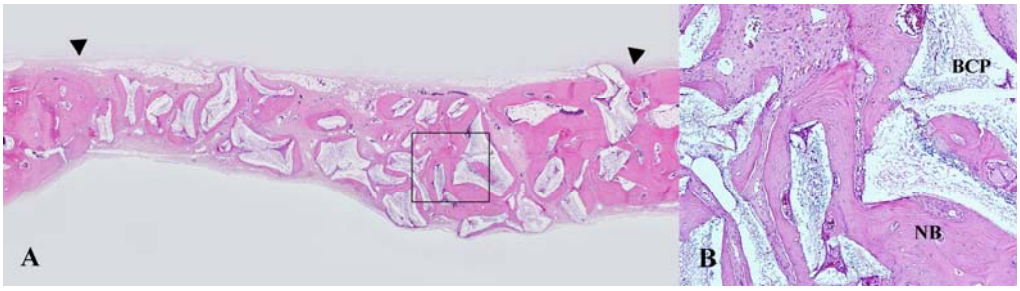

Figure 8

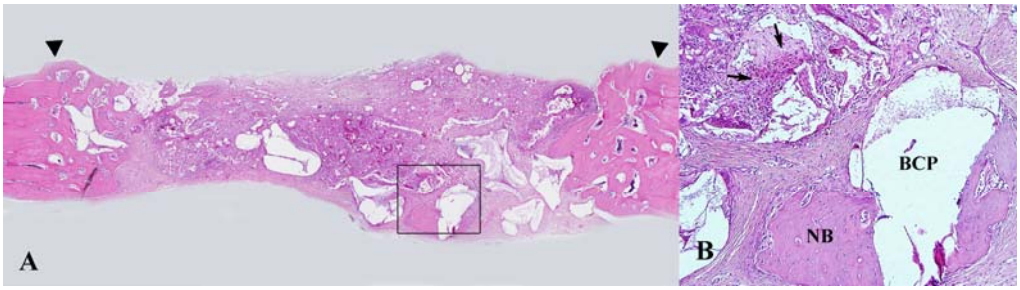

Figure 9

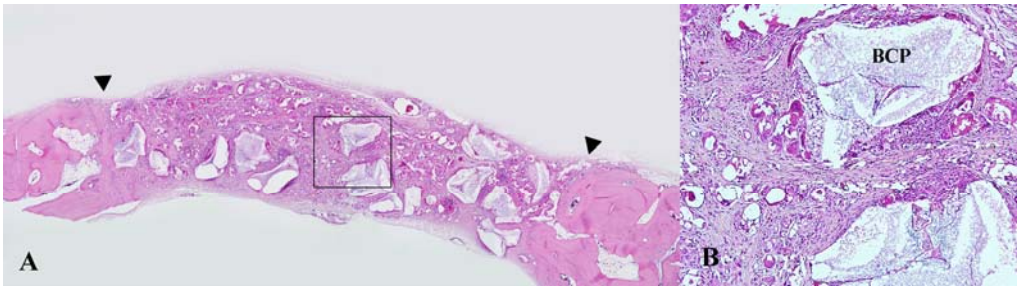

Figure 10

국문요약

가토 두개골 결손부에서 시아노아크릴레이트 결합 칼슘포스페이트의 생물학적 효과

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장 윤 영

골이식술은 구강 악안면 영역에서 골결손부위의 기능적, 심미적 수복을 위해 광범위하게 이용되어왔다. 많은 연구자들은 이런 골이식술에 이용될 이상적인 골이식재 개발을 위해 노력해왔으며 최근에는 Cyanoacrylate combined calciumphosphate (CCP) 가 새로운 골이식재로서 제시되었다. CCP 는 기존 골이식재와는 다르게 접착성, 가소성과 같은 고유의 물리적, 기계적 장점을 가지고 있으며 항세균효과도 가지고 있다고 보고되었다. 본 연구에서는 가토 두개골 결손부에서 CCP 의 생물학적 효과를 평가하고 골 재생과 관계하여 물리적 차단막의 가능성 여부 또한 분석하고자 하였다.

총 12 마리의 NewZealand white rabbit 을 사용하였으며 두개부에 4 개의 8mm, 원형 결손부를 형성하였다. 각각의 결손부를 1) Control, 2) CCP

이식군 3) Biphasic calcium phosphate(BCP)을 이식후 흡수성 콜라겐 막으로 피개한 군 4) BCP 을 이식후 CCP 로 피개한 군으로 분류하여 각각의 실험재료들을 이식하였다. 이식후 6 마리씩 4 주와 8 주의 치유기간을 가진 후 희생하여 평가하였다.

CCP 을 이식한 군은 control 에 비하여 4 주 경과시 제한된 골재생을 보였으며 염증세포또한 발견되었다. 8 주경과시에도 유사한 결과를 보여주었다. BCP 을 이식하고 흡수성 콜라겐 막으로 피개한 군은 비록 control 과 비교시 통계적 유의성은 없었지만 우수한 골재생을 보였으며 8 주 경과시 성숙된 골조직을 보였다. BCP 이식후 CCP 로 피개한 군은 BCP 이식후 흡수성 콜라겐 막으로 피개한 군과 비교시 제한된 골재생을 보였으며 염증세포가 발견되었다.

결론적으로 CCP 는 가토 두개골 결손부에서 제한된 골전도능과 조직학적으로 염증세포의 분포를 보였다. 그렇지만 임상적으로 정상적인 치유양상을 보였으며 다른 골이식재의 손실을 막아 골결손부내에 유지시킬 수 있는 기계적인 장점과 우수한 공간유지능력을 보였다.

핵심되는 말 : Cyanoacrylate; Biphasic calcium phosphate (BCP); 토끼 두개골 결손부; 골재생