The Effect of Calcium Sulfate with Alloplast on the Periodontal Regeneration in One-wall Intrabony Defect of Beagle Dogs

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감사의 글

본 논문이 완성되기까지 학위 과정뿐 아니라 여러 면에서 이끌어 주시고 조언해 주신 김종관 지도 교수님께 깊은 감사를 드립니다. 그리고 항상 관심 가져주시고 진행 과정을 꼼꼼히 챙겨주신 최성호 과장님께도 진심으로 감사 드립니다. 논문 준비로 병원에 갈 때마다 항상 웃음으로 맞이 해주시는 채중규 병원장님, 꼼꼼한 지적과 완성하기 힘들었던 점을 잘 이해해 주신 조규성 교수님께 감사의 말씀 드립니다. 바쁘신 일정에 시간을 내 주시어 부족한 논문에 여러 지적을 주신 김경남 교수님, 이용근 교수님께도 감사 드립니다.

연구 기간 내내 도움을 주었던 경준이, 영택이, 정철이, 유정이 그리고 잔심부름 마다 않고 해준 용주, 그 외 모든 의국원 수련의 후배님들께 고맙단 말을 전합니다.

논문 준비하느라 병원 업무를 다소 소홀함이 있었겠지만 옆에서 싫은 소리 않고 격려 해 주었던 우리 고운미소 원장들과 실장 이하 직원 모두에게도 고마움을 전합니다.

가정을 꾸리고 새 일을 시작하는 자식 걱정에 항상 노심초사 하시는 부모님께 이제는 한시름 놓으시고 건강 살피면서 편히 즐기며 지내시라는 말과 함께 감사하단 말씀 드립니다.

무엇보다도 병원 일, 네트워크 업무, 논문 준비 등을 하느라 많은 시간을 밖에서 보내야 해서 같이 있어 줄 시간이 부족했던 나의 생활에도 아랑곳 하지 않고, 곁에서 사랑하는 나의 분신 은찬이를 건강하게 출산 해 준 나의 부인 전경선에게도 감사하고 고맙고 사랑한다고 지면을 빌어 이야기하고 싶습니다.

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Abstract

The Effect of Calcium Sulfate with Alloplast on the Periodontal Regeneration in One-wall Intrabony Defect of Beagle Dogs

In periodontal treatment, the goal of bone augmentation procedures is to stimulate the new bone growth into the defect site damaged by destructive periodontal diseases. For many years, the gold standard for bone augmentation has been autogenous bone. However, autogenous bone grafting has limitation as inadequate supply, surgical modality, donor site pain and risk of infection. To overcome limitations of autogenous bone, many kinds of alternative biomaterials have been developed and used. Especially alloplastic graft materials have been concerned for easy obtain, economic and no disease transmission. In this study, to overcome the demerits of calcium sulfate, putty type calcium sulfate newly developed was used and mixed with alloplast.

Calcium sulfate used in this study is newly fabricated to overcome its disadvantages; brittleness, difficult handling properties, rapid resorption and reaction heating. Especially when calcium sulfate is used in the graft procedure, it is difficult

to control the setting time, solubility into blood and body fluid. To improve the handling properties, Calcium sulfate is mixed with Carboxylmethylcellulose (CMS).

4x4 mm intrabony periodontal defects were surgically created bilaterally at the distal sides of the mandibular second premolars and mesial sides of the fourth premolars in the beagle dogs and then bone augmentation procedure was treated. The surgical control group received a flap operation only. The Exp I group was treated with only Calcium sulfate bone graft binder. The Exp II group was treated with alloplastic material. The Exp III group was treated with both Calcium sulfate bone graft binder and alloplastic material. Calcium sulfate bone graft binder 0.17g and alloplastic material 0.25g is mixed and the mixed material is grafted. After 8 weeks, the periodontal regeneration was evaluated with histologic and histometric analysis.

The putty type calcium sulfate grafted group in the present study presented lower values in cementum formation and new bone formation than the control group. Though there was no statistically significant difference, the putty type calcium sulfate + alloplast grafted group showed the tendency of improved values in cementum formation and new bone formation than the other groups according to histologic examination.

The putty type calcium sulfate used in the present study was developed for easier formability and manipulation avoiding scattering or dissolving of the material with

blood or body fluid to improve regeneration of new bone but the usage of combination with the other materials is recommended.

Further studies on effect of calcium sulfate with various other bone graft materials and ideal ratios in mixing the two should be determined in the future.

Keywords: bone augmentation, bone graft material, putty type, calcium sulfate, alloplast

The Effect of Calcium Sulfate with Alloplast on the Periodontal Regeneration in One-wall Intrabony Defect of Beagle Dogs

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I. INTRODUCTION

In periodontal treatment, the goal of bone augmentation procedures is to stimulate the new bone growth into the defect site damaged by destructive periodontal diseases. Since Naber and O`Leary (1965) introduced the bone augmentation procedures, many procedures for bone regeneration have been developed, but all have their limitations.

For many years, the gold standard for bone augmentation has been autogenous bone because of its retaining cell viability, a high potential of revascularization as well as low transmission of disease (Bhan, 1966). However, autogenous bone grafting has limitation as inadequate supply, surgical modality, donor site pain and risk of infection. To

overcome limitations of autogenous bone, much kind of alternative biomaterials, which is allograft, xenograft, and alloplast, have been developed.

Allograft is divided into the two kind of type: freeze-dried bone allograft (FDBA) and demineralized freeze-dried bone allograft (DFDBA). In late 1980s, Mellonig et al (1989) reported that in human alveolar defect study, DFDBA & FDBA have enhanced bone regenerative effect as compared HA (Barnett, et al., 1989).

Xenograft is made from an animal and another term used is an anorganic bone. In general, xenograft made of coral and bovine bone is stable and similar to bone structure of human (Pinholt, et al., 1991). After Xenograft is grafted, it plays a role as the scaffold for migration of osteoblast, revascularization, formation of woven bone (Spector, 1994). In 1999, Young et al reported that anorganic bovine bone materials appear new bone formation in rabbit.

Although the clinical use of autogenous bone, allograft and xenograft have positive results, it is interesting to develop alloplastic graft materials, which are more easily obtained, economic, and no disease transmission.

For at least 40 years, calcium sulfate has been used to stimulate the new bone growth in orthopedic and dentoalveolar field (Peltier and Orn 1958). Radentz and Collings (1965) have noted that in case of calcium sulfate plantation more compactive and quantative bone regeneration is regenerated.

Peltier and Orn (1958) and Bell (1964) reported that calcium sulfate has high biocompatibility and its average resoption period is 4~7 weeks. Yamazaki et al. (1988) have reported that Calcium sulfate is a carrier of BMP and Sottosanti et al have suggested that in DFDB grafting with Calcium sulfate, it accelerate the osteoinductive functions of DFDB (Sottosanti, et al.,1992; Sottosanti, et al.,1993; Kim, et al.,1988). Kim et al. (1998) reported that Calcium sulfate does not seem to have the osteoinductive effect by itself but could play a role as a space maintainer in the series of animal and human experiments and used calcium sulfate as a barrier. Calcium sulfate shows rapid resorption tendency after implantation into the defect and generates the heat when mixed with solution and setting period (Bell, et al., 1964). The heat of reaction should affect the tissue damage. Additionally calcium sulfate is too brittle to maintain the space of bone regeneration. But, Kim et al (2006) reported that paste type Calcium sulfate maintains the blood clot and stabilizes the wound and also maintains the space. Vance GS et al (2004) showed that allograft mixed with an experimental putty binder composed of carboxymethylcellulose and calcium sulfate produced significantly more bone fill than did the use of a xenograft with no carrier material. Aichelmann-Reidy (2004) reported that calcium sulfate, when used as a binder and barrier in combination with DFDBA, supported significant clinical improvement in intrabony defects.

In this study, to overcome the demerits of calcium sulfate, putty type calcium sulfate newly developed was used and mixed with alloplast. The aim of this study was

to evaluate the regenerative effects of the putty type calcium sulfate applied to preclinical one wall defects surgically created in beagle dogs and possibilities as scaffold for tissue engineering.

II. MATERIAL AND METHODS

A. Materials and animals

1. Calcium sulfate bone graft binder[$]

Calcium sulfate bone graft binder is a pre-measured proprietary calcium sulfate formulation containing surgical grade calcium sulfate α-hemihydrate, pharmaceutical grade carboxymeth ylcellulose (CMC) powder and a mixing solution. CMC is non-toxic, semisynthetic water-soluble polymer with widespread use in a diverse group of medical products such as tooth-paste, antibiotics, wound dressings, etc. CMC allows a calcium sulfate composite graft to maintain its shape and functionality in the clinician's hand, and when exposed to blood and saliva.

2. Alloplast[‡]

Alloplast is made of 70% HA and 30% β-TCP. It is composed of HA crystal β-TCP. The size of alloplastic material is 0.5~1mm. It is interconnected pore structure. The pore size is from 300 to 500 μm. The interconnected porous scaffold is comprised from biocompatible HA and the surface is coated with bioresorbable β-TCP.

[$] CALMATRIX®, Lifecore Biomedical, Minnesota, USA
[‡] Osteon®, GENOSS Biomaterial Company, Gyeonggi-do, Korea

3. Animals

A total of five male beagle dogs, each weighing about 15 kg, were used in this study. The animals had intact dentition and 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 were fed a soft diet throughout study, in order to reduce chance of mechanical interference with the healing process during food intake.

B. Methods

1. Surgical and postsurgery protocol

The mandibular first and third premolars had been extracted previously and the extraction sites had been allowed to heal for 8weeks. At reconstructive surgery, buccal and lingual mucoperiosteal flaps were elevated and 4x4 mm intrabony periodontal defects were surgically created bilaterally at the distal sides of the mandibular second premolars and mesial sides of the fourth premolars. The surgical control group received a flap operation only. The Exp I group was treated with only Calcium sulfate bone graft binder. The Exp II group was treated with alloplastic material. The Exp III group was treated with both Calcium sulfate bone graft binder and alloplastic material. Calcium sulfate bone graft binder 0.17g and alloplastic

material 0.25g is mixed and the mixed material is grafted. The dogs were sacrificed at 8 weeks after the experimental surgery.

2. Histologic and histometric analysis

Tissue blocks, which included teeth, bone and tissue, were removed, rinsed in saline, then fixed in 10% buffered formalin for 10 days. After being rinsed in water, the block section were decalcified in 5 % formic acid for 14 days, and embedded in paraffin. Serial sections, 5 um thick, were prepared at intervals of 80 μm. The four most central sections from each block were stained with hematoxylin /eosin (H-E) and examined using a light microscope. The most central section from each block was selected to compare histologic findings between groups. Computer-assisted histometric measurements were obtained using an automated image analysis system[††] coupled with a video camera on a light microscope[‡‡]. Sections were examined at 20x magnification.

[††] Image-Pro Plus®, Media Cybernetics, Silver Spring, MD, U.S.A

[‡‡] Olympus BX50, Olympus Optical Co., Tokyo, Japan

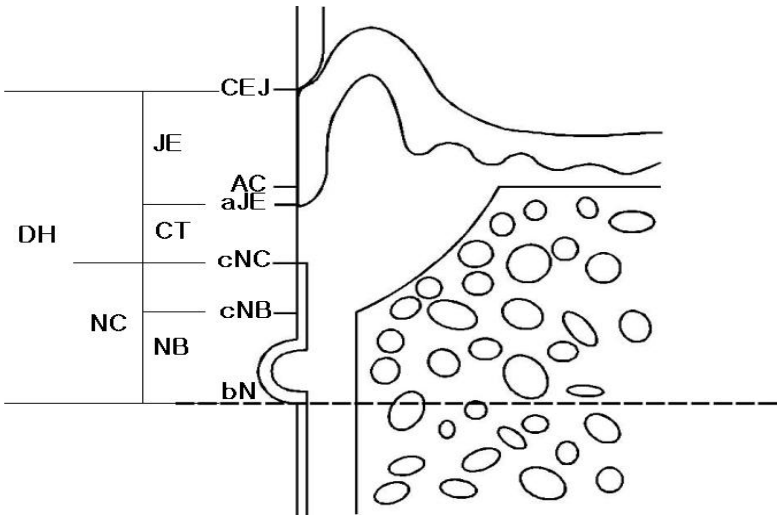

Figure1. A schematic diagram depicting the experimental design, the landmarks and the parameters used in histometric analysis.

CEJ: cementoenamel junction DH: defect height
JE: junctional epithelium migration CT: connective tissue adhesion
NC: new cementum regeneration NB: new bone regeneration
bN: base of notch a: apical c: coronal

3. Statistical analysis

Histometric recordings from the four sections from each defect were used to calculate the mean scores for each animal. The data in each group was statistically analyzed using ANOVA *cost hoc* test.

Ⅲ. RESULT

A. Clinical observations

Surgical procedures were uneventful and without complication in all dogs. Wound closure was successfully maintained throughout the experiment for all defects. Healing process was generally uneventful.

B. Histologic findings

In the control group, the apical migration of junctional epithelium was observed (Figure 2). The periodontal ligament fibers were generally oriented in a direction parallel to the root surface in suprabony area. Dense connective tissue was shown (Figure 3). No site showed signs of ankylosis. There was little or no sign of inflammatory cell infiltration. Above the apical notch, a very small amount of new cementum and bone had formed along the root surface (Figure 3).

In the group of Exp I, the apical migration of junctional epithelium was observed (Figure 4). But the coronal extension of new bone and new cementum was little than the other experimental group (Figure 4and 5). There was a little remnant of calcium sulfate examined (Figure 5).

In the group of Exp II, remnant of allopalst was examined and the coronal extension of new bone and new cementum was examined (Figure 6 and 7).

In the group of Exp III, the coronal extension of new bone and new cementum was more than the other experimental group and there was no remnant of calcium sulfate examined (Figure 8). In some parts, osteoblast and osteoids were observed around the bone marrow and cementoblast was also examined (Figure 9). The lamella bone could be distinguished and periodontal ligament fibers were observed between new bone and new cementum (Figure 9). Regeneration of new bone was observed around the alloplast grafted (Figure 11 &12).

C. Histometric analysis

Table 1 and 2 show the results of the histometric analysis. The amount of new alveolar bone formation in Exp III was greater than those of the other groups, but there was no statistically significant difference ($P>0.05$). The amount of new cementum formation of Exp III was greater than those of the other groups, but there was no significant difference from other groups ($P>0.05$). In apical migration of the connective tissue adhesion, statistically significant difference was observed between Exp III and the Exp I ($P<0.05$).

In general, the amount of new alveolar bone and new cementum formation were

showed low tendency in Exp II but there was no statistically significant difference (P>0.05).

IV. DISCUSSION

The ultimate goal of periodontal therapy is to regenerate the supporting tissue that was destroyed. Although, various bone graft materials such as allograft, xenograft and alloplast have been already developed and used to help regeneration, they have some shortcomings.

The aim of this study was to evaluate the periodontal repair and the biomaterial reaction following implantation of a newly fabricated putty type calcium sulfate mixed with alloplast on the regeneration of 1- wall intrabony defects in the beagle dogs. Calcium sulfate used in this study is newly fabricated to overcome its disadvantages; brittleness, difficult handling properties, rapid resorption and reaction heating. Especially when calcium sulfate is used in the graft procedure, it is difficult to control the setting time, solubility into blood and body fluid.

To improve the handling properties, Calcium sulfate is mixed with Carboxymethylcellulose (CMS). CMC is non-toxic, semisynthetic water-soluble polymer with widespread use in a diverse group of medical products such as toothpaste, antibiotics, wound dressings, etc. CMC allows a Calcium sulfate composite graft to maintain its shape and functionality in the clinician's hand, and when exposed to blood and saliva and delays the resorption of calcium sulfate.

Calcium sulfate has been used in orthopedics for 100 years or more and in dentistry for 40 years. Calcium sulfate has rapid resorption rate. Bell et al. (1964) reported that the resorption rate of the plaster of Paris was fast any other materials tested. Though a rapid resorption rate is one of the requisite of ideal bone graft materials, Bell cautioned against the assumption that the plaster of Paris should be preferable to other types of bone or bone substitutes based on the resorption rate. Peltier et al. (1958, 1961) used calcium sulfate graft into bony defect of human and reported that calcium sulfate plays a role as space filler and it disappear in less than 2 months. Bahnl et al. (1966) state that space occupying material could decrease the chance of clot breakdown and increasing the chance of bone regeneration. Radenz & Collimg et al. (1965) reported that resorption of calcium sulfate started after 5days bone graft and continued until 2weeks. In radiographic findings, calcium sulfate grafted site appeared the more dens trabecular pattern than control site. Bier (1970) concluded that calcium sulfate disappear during 3~5weeks after implantation without foreign body reaction. In this study, there is no calcium sulfate remnant in the grafted site after 8weels and wound healed without severe inflammation and foreign body reaction. The calcium sulfate used in the present study was a putty type. This putty type was developed to overcome problems such as rapid resorption and difficulty in shape formation due to brittleness after setting. Easy formability of the material provides easier application into the defect and addition of polymer has been attempted

to avoid this.

Therefore, in the present study, CMC (Carboxymethylcellulose) was mixed to overcome the demerits of calcium sulfate. Despite the objective that there might be better results than pure calcium sulfate, the putty type calcium sulfate used in the present study presented lower values in cementum formation and new bone formation than the control group. This may be due to use of poor osteoinductive calcium sulfate alone in the defect, limiting new bone formation (Shaffer, et al., 1971). In addition, complete resorption of calcium sulfate after 8 weeks presents that addition of polymer failed to delay the resorption rate of calcium sulfate. Rather, it seemed to disturb the natural healing of the defect when compared with the findings in the control group. However, histological findings of sites applied with alloplast material and calcium sulfate showed greater new bone formation than the calcium sulfate only group and the controls.

Studies concerning the effect of calcium sulfate with other bone graft materials have been presented from the past. Frame et al. (1975) report that calcium sulfate may show osteoconductive effect when it is grafted with HA in rabbit mandible defect. Sottosanti (1993) reported that calcium sulfate delays epithelial and connective tissue ingrowth to produce regeneration of new bone when used as a GTR barrier, mixed with a DFDBA.

Kim et al. (2006) observed that surgical implantation of DBM and calcium sulfate, alone or in combination, may result in significantly improved level of attachment, regeneration of alveolar bone and cementum in dog study model. Vance et al. (2004) show that DFDBA mixed with Calcium sulfate and covered by a calcium sulfate regenerate higher percentage of vital bone fill at 4months than xenograft with collagen membrane in human periodontal defects. Also Aichelmann-Reidy et al. (2004) reported that significant gains in attachment level, reduction in probing depth, and increase in defect bone fill were achieved using calcium sulfate as mixed with DFDBA .The alloplast material used in the present study was composed of 70% HA and 30% β-TCP. The histological findings show remnants of HA after 8 weeks. The remaining HA particles may have provided some space maintaining scaffold effect in the defect and this may explain the results shown in calcium sulfate + alloplast material applied sites. The favorable result of calcium sulfate when used with another bone graft material is consistent with other studies of calcium sulfate. The material used in the present study was developed for easier formability and manipulation avoiding scattering or dissolving of the material with blood or body fluid. However, the results reveal that further studies on effect of calcium sulfate with various other bone graft materials and ideal ratios in mixing the two should be determined in the future.

V. CONCLUSION

The purpose of this study was to evaluate the regenerative effects of the putty type calcium sulfate applied to preclinical one wall defects surgically created in beagle dogs and possibilities as scaffold for tissue engineering. The putty type calcium sulfate grafted group in the present study presented lower values in cementum formation and new bone formation than the control group. Though there was no statistically significant difference, the putty type calcium sulfate + alloplast grafted group showed the tendency of improved values in cementum formation and new bone formation than the other groups according to histologic examination. The putty type calcium sulfate used in the present study was developed for easier formability and manipulation avoiding scattering or dissolving of the material with blood or body fluid to improve regeneration of new bone but the usage of combination with the other materials is recommended.

Further studies on effect of calcium sulfate with various other bone graft materials and ideal ratios in mixing the two should be determined in the future.

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국문요약

성견 1 면 골 결손부에서

calcium sulfate 와 합성골이식재의 치주조직 재생효과

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홍 성 배

골이식의 궁극적 목표는 치주질환에 의해 손상 된 결손부위에 신생골 형성을 촉진하는 것이다. 오랫동안 자가골 이식이 골이식술에 있어서의 황금률로 인정되어 왔으나 그 한계성 때문에 다른 종류의 골이식재 개발이 있어 왔다.

Calcium sulfate 는 오랫동안 정형외과나 치과 영역에서 골재생을 위한 물질로 이용 되어 왔다. 그러나 calcium sulfate 가 가지는 조작성의 한계, 경화 시 발생되는 열, 이식 후 빠른 흡수 등을 극복하기 위한 다양한 중합체를 첨가한 형태의 재료 개발과 다른 골이식재와 혼합 사용법 등이 시도되어왔다.

본 연구는 calcium sulfate 가 이식재로서의 한계성을 극복하기 위하여 외과적 등급의 calcium sulfate α-hemihydrate 에 약제 등급의 Carboxymethylcellulose

(CMS) 를 혼합하여 새롭게 개발된 putty type 의 calcium sulfate 를 이용하여 성견 1 면 골내낭에서의 치주조직 재생에 미치는 영향을 조사하였다. 4X4mm 크기의 성견 1 면 골 결손부에 putty type 의 calcium sulfate 를 이식한 후 골재생술을 시행한 군, 합성골 이식재를 이식한 군, putty type 의 calcium sulfate 와 합성골 이식재를 혼합 이식한 군, 그리고 동일한 결손부에 치은박리 소파술만을 시행한 군으로 구분하여 8 주간의 치유기간을 경과한 후의 치주조직 재생 효과를 관찰하였다.

Calcium sulfate 와 합성골 이식재를 혼합하여 이식한 군에서 다른 실험군과 비교하여 많은 양의 신생골의 재생과 신생백악질의 재생을 보였고 calcium sulfate 만을 이식한 실험군에서 가장 적은 양의 치주조직 재생 경향을 보였지만 통계적으로 유의한 차이는 보이지 않았다. 본 실험에서 사용된 putty type 의 calcium sulfate 는 8 주간의 치유기간 동안 거의 모두 흡수되어 신생골 형성에 필요한 공간유지 기능을 하지 못한 것으로 판단되며 오히려 이식 초기에 결손부에 혈병이 찬 후 조직치유가 일어나는 것을 저해하여 치주조직 재생에 효과적인 역할을 하지 못한 것이라 여겨지고 단독 사용에 조직 재생에 한계가 있는 것으로 보여진다. 반면 putty type 의 calcium sulfate 와 다른 골이식재를 적절히 조합해서 사용하면 결손부에서의 이식재의 형태 유지가 용이하고 재료가 혈액이나 체액에 녹아서 소실되는 문제점을 극복할 수 있고 조직 재생에 도움을 줄 수 있다고 기대 되지만 보다 더 다양한 골이식재의 병용과 혼합비율에

따른 골결손부에 대한 치유 효과에 대한 추가적인 연구가 필요하리라 생각된다.

핵심되는 말: 골재생술, 골이식재, putty type, calcium sulfate, 합성골이식재

LEGENDS

Table1. Histometric analysis: Height (mm)

Table2. Histometric analysis: Ratio (%)

Fig.2 A surgical control site showing apical migration of junctional epithelium
(H-E satin, an original magnification X 20)

Fig.3 A surgical control site showing apical migration of junctional epithelium and moderate regeneration of new bone and new cementum
(H-E satin, an original magnification X 100)

Fig.4 Calcium sulfate grafted site showing apical migration of junctional epithelium and minimal regeneration of new bone and new cementum
(H-E satin, an original magnification X 20)

Fig.5 Calcium sulfate grafted site showing that the level of new bone regeneration almost is almost the same level of the base of notch
(H-E satin, an original magnification X 100)

Fig.6 Alloplast grafted site showing the remnant of alloplast
(H-E satin, an original magnification X 20)

Fig.7 Alloplast grafted site showing that the level of new bone regeneration
(H-E satin, an original magnification X 100)

Fig.8 Calcium sulfate +Alloplast grafted site showing that the level of new bone regeneration and the remnant of alloplast

(H-E satin, an original magnification X 20)

Fig.9 Calcium sulfate + Alloplast grafted site showing osteoblast, cementoblast, and new cementum

(H-E satin, an original magnification X 100)

Fig.10 Calcium sulfate + Alloplast grafted site showing new bone regeneration around graft material.

(H-E satin, an original magnification X 200)

Fig.11 Calcium sulfate + Alloplast grafted site showing new bone regeneration around graft material.

(H-E satin, an original magnification X 200)

TABLES

Table1. Histometric analysis: Height (mm)

	DH	NB	NC	JE	CT
Control	3.88±1.14	1.19±1.08	1.20±0.79	1.61±0.94	1.08±0.47
Exp I	4.70±0.49	0.77±0.74	0.90±1.00	2.27± 0.33	1.53±0.17*
Exp II	3.53±0.11	1.35±0.98	1.32±0.86	1.28±0.70	0.92±0.16
Exp III	3.53±1.03	1.72±1.00	1.62±0.95	1.00±0.24	0.90±0.19

Control group: surgical control group received a flap operation only

Exp I: Calcium sulfate grafted group. Exp II: Alloplast grafted group.

Exp III: Combination group of calcium sulfate and alloplast

* A statistically significant difference from other group (P<0.05)

DH: defect height JE: junctional epithelium migration CT: connective tissue adhesion;

NC: new cementum regeneration NB: new bone regeneration

Table 2. Histometric Analysis: Ratio (%)

	NB/DH	NC/DH	JE/DH	CT/DH
Control	31	31	42	28
Exp I	16	19	48	33
Exp II	38	37	36	26
Exp III	49	46	28	25

Control group: surgical control group received a flap operation only

Exp I: Calcium sulfate grafted group. Exp II: alloplast-grafted group.

Exp III: Combination group of calcium sulfate and alloplast

DH: defect height JE: junctional epithelium migration CT: connective tissue adhesion;

NC: new cementum regeneration NB: new bone regeneration

FIGURES

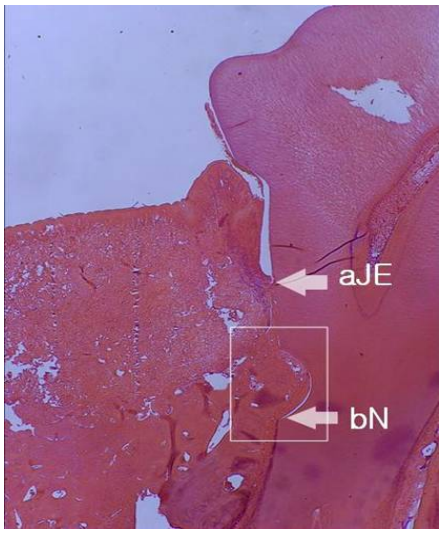


Fig.2 Control (X20)

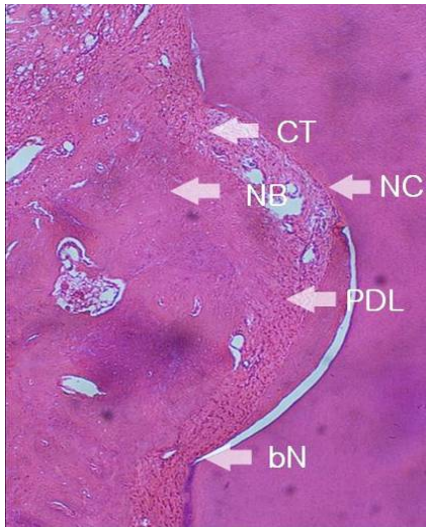
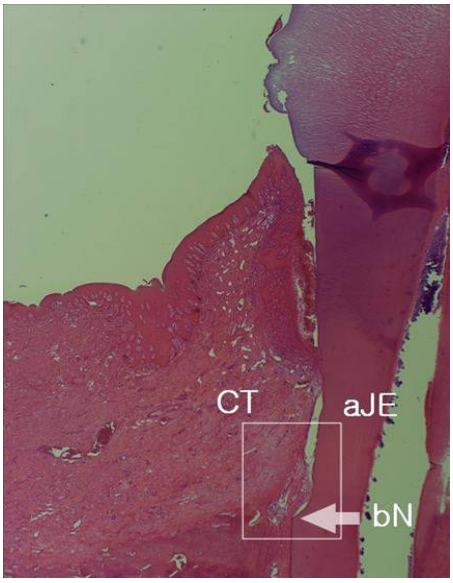


Fig.3 Control (X100)

aJE: The apical extent of junctional epithelium

bN: The base of the reference notch NC: new cementum

NB: new bone CT: connective tissue PDL: periodontal ligament



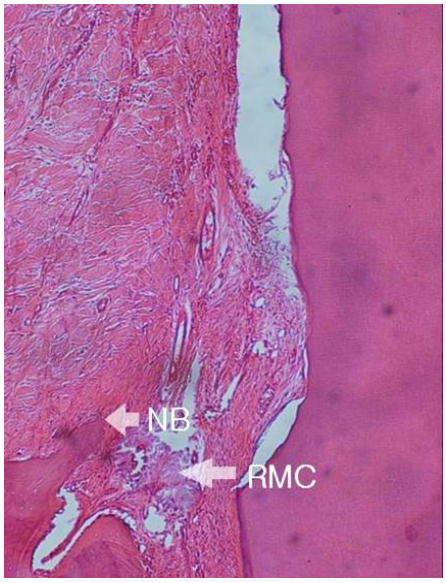
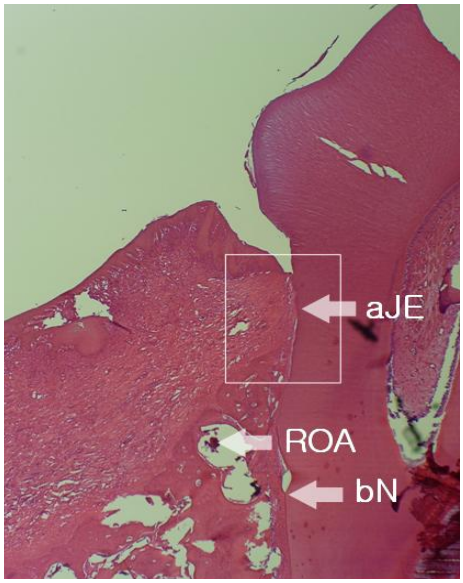


Fig.4 Exp I group (X20) **Fig.5 Exp I group group (X100)**

aJE : The apical extent of junctional epithelium

bN: The base of the reference notch NB: new bone

CT: connective tissue RMC: remnant of Calcium sulfate



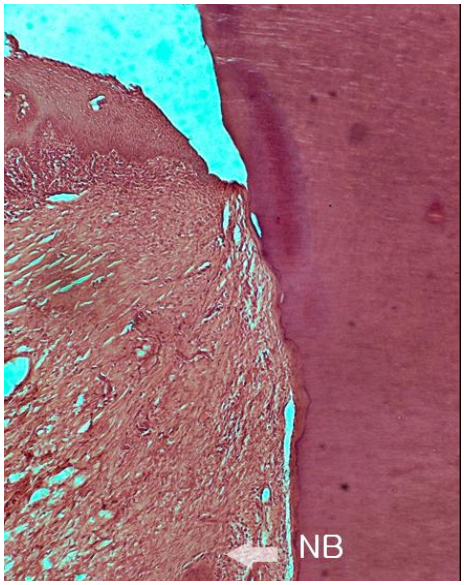
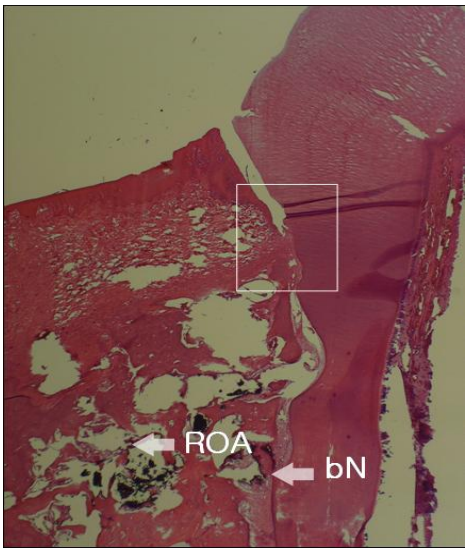


Fig.6 Exp II group (X20) **Fig.7 Exp II group (X100)**

aJE: The apical extent of junctional epithelium

bN: The base of the reference notch NC: new cementum

NB: new bone CT: connective tissue ROA: remnant of alloplast



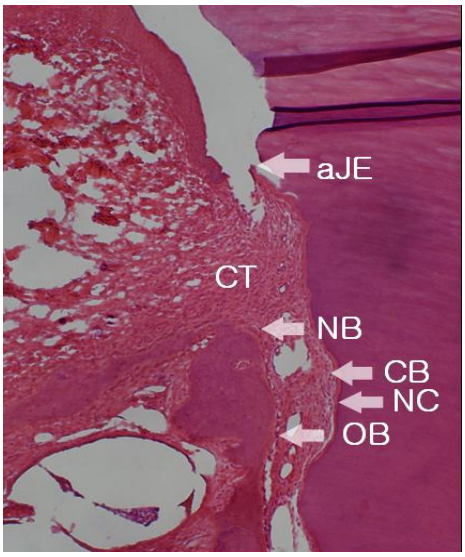


Fig.8 Exp III group (X20) **Fig.9 Exp III group (X100)**

aJE: The apical extent of junctional epithelium

bN: The base of the reference notch NC: new cementum

NB: new bone CT: connective tissue ROA: remnant of Alloplast

CB: cementoblast OB: osteoblast

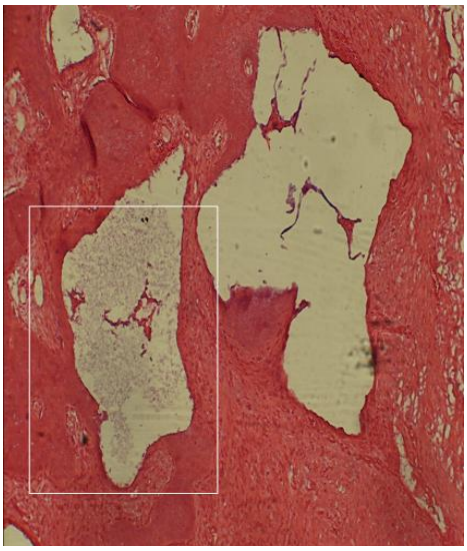


Fig. 10 Exp III group (X100)

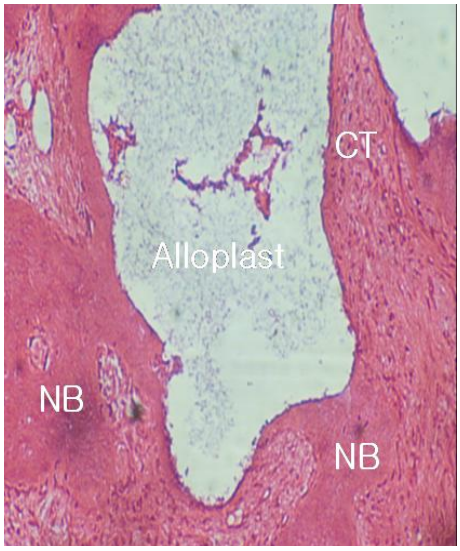


Fig. 11 Exp III group (X200)

NB: new bone CT: connective tissue