The Effects of Synthetic Peptide on Bone Regeneration in Rat Calvarial Defects

Jung-Yoo Choi

The Graduate School

Yonsei University

Department of Dental Science

The Effects of Synthetic Peptide on Bone Regeneration in Rat Calvarial Defects

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of Jung-Yoo Choi is approved.

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Thesis Supervisor: Seong-Ho Choi

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Chong-Kwan Kim

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Kyoo-Sung Cho

The Graduate School

Yonsei University

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Table of Contents

LIST OF FIGURES

LIST OF TABLES

Abstract

The Effects of Synthetic Peptide on Bone Regeneration in Rat Calvarial Defects

Significant interest has emerged in the design of cell scaffolds that incorporate peptide sequences that correspond to known signaling domains in ECM and BMP proteins.

The purpose of this study was to evaluate the bone regenerative effects of the synthetic peptide in a critical-size rat calvarial defect model. An eight millimeter diameter standardized, circular, transosseus defects created on the cranium of forty rats were implanted with synthetic peptide, collagen, and both synthetic peptide and collagen. The control group did not use any material. The healing of each group was evaluated histologically and histomorphometrically after 2- and 8-week healing intervals.

Surgical implantation of the synthetic peptide and collagen resulted in enhanced local bone formation at both 2 and 8 weeks compared to the control group. When compared among the experimental groups, they showed a similar pattern of bone formation. Defect closure and new bone area were significantly different in synthetic peptide and collagen group at 8 weeks.

In conclusion, concerning the advantages of biomaterials, the synthetic peptide can be an effective biomaterial for damaged periodontal regeneration.

Key Words: synthetic peptide, collagen, bone regeneration

The Effects of Synthetic Peptide on Bone Regeneration in Rat Calvarial Defects

Jung-Yoo Choi, D.D.S.

Department of Dental Science
The Graduate School, Yonsei University
(Directed by Professor Seong-Ho Choi,D.D.S., M.S.D.,Ph.D.)

I. Introduction

There are various purposes for periodontal treatment and there are various approaches to such treatment. Among the various purposes, the ultimate purpose of periodontal treatment is to regenerate the periodontal tissue loss caused by periodontal disease. Periodontal regeneration means the healing pattern of new attachment, new bone formation, new cementum and new periodontal ligament. Many approaches are available to regenerate periodontal tissue such as root conditioning which enhances cell adhesive capacity, bone grafts used for bony defect regeneration, and guided bone regeneration using specific cell migration and Bone Morphorgenetic Protein (BMP) and other various growth factors are the methods used as well. Among the various methods used, the autogenous bone graft has shown successful results clinically in periodontal regeneration for decades. However, it requires

additional surgery site, ankylosis may be induced and there are limitations in extracting a large amount of bone. In consequent, there has been an interest in developing a new type of bone graft material due to these limitations.

In regard to this, there have been many studies on bone regenerative materials, such as rhBMP-2, 4, BMP-2, 4, 5, 6, 7 (Sampath, Maliakat et al. 1992; Gitelman, Kobrin et al. 1994) and RGD. These proteins are known to proliferate, adhere, and differentiate osteoblasts which are mainly involved in bone formation. BMPs (Bone Morphogenetic Proteins) are complex growth factor of transforming growth factor-B (TGF-ß) superfamily which induces bone and cartilage regeneration. Urist designated BMPs for the fact that there might be a specific protein which takes part in bone formation when implanting a decalcified bone specimen in the dermis of a mouse which caused heteromorphic bone around the bone specimen (Urist 2002). Among the BMPs, rh-BMP-2, 7, which have been synthesized from the DNA technique are known to have the best osteoconduction. In one of the studies, a composite of gelatin and rhBMP-2 released rhBMP-2 in the proper way as well as demonstrating the largest amount of bone formation (S.J. Hong et al., 2006).

Recently, there have been studies on protein transduction domain which can transmit protein that are difficult to penetrate intracellularly effectively. The phenomenon of the penetration of peptide have shown the possibility of therapeutic effect of fast half-life for its fast penetration intracelluarly. Peptides are consisted of

specific amino acid sequence that can penetrate the cell membrane spontaneously (Frankel and Pabo 1988; Schwarze and Dowdy 2000; Schwarze, hruska et al. 2000). Peptides are short polymers formed from linking, in a defined order, α-amino acids. The link between one amino acid residue and the next is known as amide bond or peptide bond. Proteins are polypeptide molecules (or consist of multiple polypeptide subunits). The distinction is that peptides are short and polypeptides or proteins are long.

In regard to this, the synthetic peptide has been developed with the interest of developing an osteoconductive biomaterial. Significant interest has emerged in the design of cell scaffolds that incorporate peptide sequences that correspond to known signaling domains in ECM proteins (Benoit et al., 2005). Peptides offer the advantages of increased stability, the ability to incorporate them at much higher concentrations than full proteins, and relatively straightforward and simple syntheses of short sequences (Benoit et al., 2005). The synthetic peptide was based on the Bone morphogenetic protein-2(BMP-2) which promotes the formation and regeneration of bone and cartilage, and also participates in organogenesis, cell differentiation, cell proliferation, and apoptosis.

The synthetic peptide was developed for its various advantages when compared with BMP-2. It is more economical in that the raw material is cheaper than BMP-2. It is very stable in terms of temperature storage. Peptides are known to denaturize in

room temperature. However, the sequence is short in the synthetic peptide. It can be stored in a freeze-dried condition for over 2 years. It can also be stored in room temperature in a dry environment, whereas BMP-2 is a cold chain that can only be stored for a short time, for example, 6 months in 4 °C.

On this basis, the purpose of this study was to evaluate the effects of bone regeneration of the synthetic peptide in surgically created rat calvarial defects.

II. Materials and Method

A. Materials

1. Animals

Forty male Sprague-Dawley rats (body weight 200-300g) were used in this study. Animal selection and management, surgical protocol, and preparation followed the routines approved by the Institutional Animal Care and Use Committee, Yonsei Medical Center, Seoul, Korea.

Table 1. A figure of animals

	2 weeks	8 weeks
Control	5	5
Collagen	5	5
Synthetic peptide(no carrier)	5	5
Synthetic peptide and Collagen	5	5
Total (n=40)	20	20

B. Experimental Procedures

1. Experimental group design

The animals were divided into four groups of 10 animals each and allowed to heal

for 2 weeks (5 rats) or 8 weeks (5 rats). Each animal received one of the four experimental treatments: a sham-surgery control in which no material was applied to the defect, collagen carrier control, synthetic peptide only, synthetic peptide and collagen.

2. Designing of the synthetic peptide

The significant sequence was analyzed among the whole amino acid sequence among the protein such as growth factors and extracellular matrix (ECM) which is involved in bone formation, the early attachment, proliferation, and differentiation of the osteocyte. In case of the Bone Morphogenetic Protein-2 (BMP-2), bone forming cell, osteoblast, has a specific binding site and in terms of ECM, considering that the sequence is involved in cell attachment, the synthetic peptide was recombined based on the sequence, which the osteoblasts recognize the sequence of synthetic peptide as protein and was recombined to induce attachment, proliferation, and differentiation. N- and C- terminals were stabilized through amidation, and acetylation. Among the whole amino acid sequence of Bone Morphogenetic Protein-2 (BMP-2), fibronectine and vitronectine, the amino acid sequence which plays the core role involved in proliferation and differentiation of osteoblasts was selected and analyzed. A part of these sequences was modified by peptide synthesizer and the synthetic peptide was formed. The final product after synthesis was purified to a level over 95% using HPLC and the mass was analyzed through NMR. The synthesis and purification of

synthetic peptide was consulted to Peptron. Co. Ltd. SHIMAZU instrument was to determine the flow rate which was 1.0ml/min and the detection was performed at 220nm and it was purified at 98.6%. The concentration of the synthetic peptide was loaded with 10μl (mass: 2288).

3. Surgical protocol

The animals were anaesthetized by an intramuscular injection (5 mg/kg body wt.) with Zoletil®[§] and Rompun®[*]. An incision was made in the sagittal plane across the cranium and a full thickness flap was reflected, exposing the calvarial bone. A standardized, circular, transosseous defect, 8 mm in diameter was created on the cranium with the use of a saline cooled trephine drill[#]. After removal of the trephined calvarial disk, Collatape®[‡] (1mm x 1mm) and synthetic peptide were applied to the defects. The animals were divided into four groups of 10 animals each and allowed to heal for 2 (5 rats) and 8 (5 rats) weeks. Each animal received one of three experimental conditions: synthetic peptide only, collagen only, synthetic peptide and collagen. The periosteum and skin were then closed and sutured with 4-0 Monosyn[**].

[§] Zoletil®, Virbac, Carros, France

[*] Rompun®, Bayer HealthCare, USA

[#] 3i, FL, USA

[‡] Collatape®, Integra LifeSciences Corporation, NJ, USA

[**] Monosyn 4/0, Braun Aesculap AG&CO.KG, Tuttlingen

4. Evaluation methods

1) Clinical findings

Wound healing was generally observed uneventful.

2) Histologic procedures

The animals were sacrificed by CO_2 asphyxiation at 2 and 8 weeks postsurgery. Block sections including the experimental sites were removed. Samples were fixed in 10% neutral buffered formalin solution for 10 days. Samples were decalcified 5% formic acid for 14 days, and embedded in paraffin. Serial sections, 5μm thick, were prepared at intervals of 80μm, stained with Hematoxylin/Eosin(H-E) and examined using a light microscope. The most central sections from each block were selected to compare histologic findings among the groups.

3) Histomorphometric analysis

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. A digitizer was used to trace the defect outline versus new bone formation, and a percentage of bone fill was determined. The following histomorphometric parameters were measured from each sample(Fig. 1).;

[††] Image-Pro Plus®, Media Cybernetics, Silver Spring, M.D.

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

- **Defect closure (%)** : the distance (at each side of the defect) between the defect margin and the in-growing bone margin in millimeters x 100
- **New bone area (mm^2)** : all tissues within the boundaries of newly formed bone, i.e., mineralized bone and fatty marrow and fibrovascular tissue / marrow and residual biomaterial.
- **Bone density (%)** : the newly formed bone within the new bone area in millimeters x 100

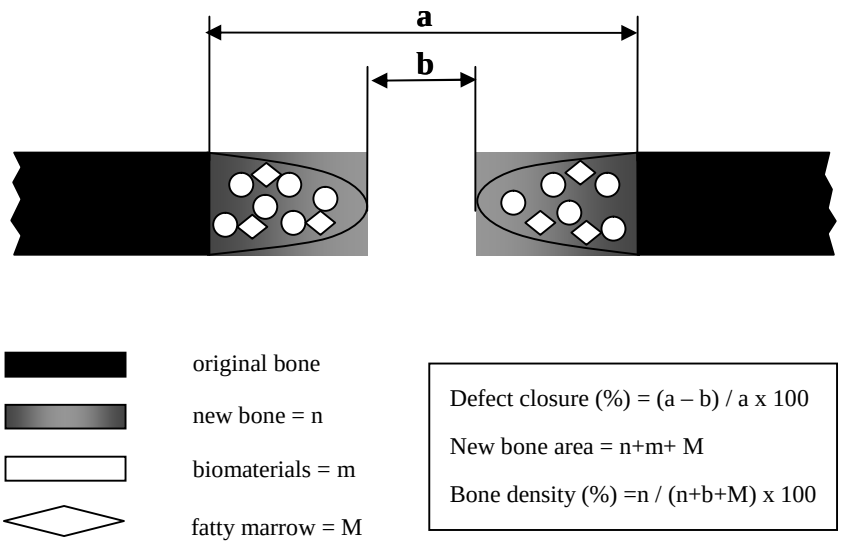

Figure 1. Schematic drawings of calvarial osteotomy defect showing histomorphometric analysis

5. Statistical Analysis

Histomorphometric recordings from the samples were used to calculate means and standard deviations (m±SD). To analyze the effect of both time and condition and to detect the interaction effect between time and condition, the two-way analysis of variance was used ($P<0.05$). ANOVA and Post-hock test were used to analyze the difference among the groups at each time point ($P<0.05$). For the comparison between 2 and 8 weeks in a same group, statistical significance was determined by paired t-test ($P<0.05$).

III. Results

1. Clinical Observations

Wound healing was generally uneventful and appeared similar for the experimental groups. Material exposure or other complications of the surgical sites were not observed.

2. Histologic observations

1) Sham-surgery control group (Figures 2, 3)

i) 2 weeks (Figure 2)

At two weeks post-surgery, the defects were filled with thin, loose connective tissue. The control group showed minimal new bone formation origination from the defect margins. Osteoblasts were observed surrounding the new bone formation. Soft tissue healing and new bone formation can be said to be carried out by looking at the inflammatory cells.

ii) 8 weeks (Figure 3)

At eight weeks post-surgery, there was a relatively consistent density of connective tissue around minimal new bone formation. However, loose connective

tissue could still be observed. The bone forming cells, osteoblasts were observed at the bottom of new bone formation.

2) Collagen Group (Figures 4, 5)

i) 2 weeks (Figure 4)

The defects were filled with loose or dense, fibrous connective tissue and limited new bone formation was observed at the defect margin at 2 weeks. Collatape remained in the subepithelium and there was no resorption and it maintained the external form and was surrounded by connective tissue.

ii) 8 weeks (Figure 5)

The resorption of the Collatape progressed much. There was almost no infiltration of inflammatory cells. There was an increase in bone volume and there was no invagination of the peripheral tissue.

3) Synthetic Peptide-no carrier (Figures 6, 7)

i) 2 weeks (Figure 6)

There was almost no resorption and there was slightly new bone formation, a slight increase in volume as well. There was not much defect closure yet at 2 weeks. The margin was differentiated with the peripheral tissue.

ii) 8 weeks (Figure 7)

There was a great amount of resorption. The new bone formation increased compared to the 2 weeks' group. There was resorption, however the exterior was roughly maintained. There was a greater closure compared to the 2 weeks. Osteoblast-like cells and very few giant multinucleated cells were able to be detected in the periphery of the margin whereas the center showed almost no new bone formation.

4) Synthetic peptide and collagen (Figures 8~11)

i) 2 weeks (Figure 8, 9)

There was not much bone regeneration or defect closure. The resorption has not yet progressed and the volume was maintained. No osteoblast-like cells were detected. The defect closure was less when compared to the synthetic peptide or collagen.

ii) 8 weeks (Figure 10, 11)

At eight weeks post-surgery, new bone formation was moderate. There was loose connective tissue formation around the defect area and there was no infiltration of inflammatory cells. Collagen was almost resorbed. The defect area was replaced by the parallel pattern of connective tissue.

3. Histomorphometric analysis

The results of the histomorphometric analysis are shown in Tables 2-4. There was a minimal new bone formation in the control group. Defect closure and new bone in collagen and the synthetic peptide group was significantly different from that in the control group ($P<0.05$).

In defect closure and new bone area at 8 weeks, the collagen group had a significantly greater value than the synthetic peptide group ($P<0.01$). There were statistically significant differences between the results obtained at 2 and 8 weeks in the collagen group ($P<0.05$). There was not a significant bone growth in the synthetic peptide(no carrier), whereas there was an increase in the 2 and 8 weeks of the synthetic peptide and collagen group.

Table 2. Defect closure (%) (group means ± SD; n=5)

	2 weeks	8 weeks
Control	13.9 ± 3.4	15.6 ± 7.2
Collagen	22.6 ± 9.3*‡‡	26.9 ± 10.4*‡
Synthetic peptide(no carrier)	40.7 ± 1.5**††	41.3 ± 9.6*†
Synthetic peptide and Collagen	45.5 ± 0.9 **††‡	52.4 ± 1.4*††‡‡

*: Statistically significant difference compared to control group (P<0.05) **(P<0.01)

†: Statistically significant difference compared to collagen group (P<0.05) ††(P<0.01)

‡: Statistically significant difference compared to newly formed synthetic peptide group (P<0.05) ‡‡(P<0.01)

Table 3. New bone area(mm^2) (group means ± SD; n=5)

	2 weeks	8 weeks
Control	0.2 ± 0.2*	0.3 ± 0.2
Collagen	2.9 ± 1.6*‡	1.9 ± 3.3*‡
Synthetic peptide(no carrier)	3.1 ± 0.5*	3.0 ± 0.4*
Synthetic peptide and Collagen	3.8 ± 0.7*‡	4.3 ± 0.9*††‡‡

*: Statistically significant difference compared to control group (P<0.05) **(P<0.01)

†: Statistically significant difference compared to collagen group (P<0.05) ††(P<0.01)

‡: Statistically significant difference compared to newly formed synthetic peptide group (P<0.05) ‡‡(P<0.01)

Table 4. Bone density (%) (group means ± SD; n=5)

	2 weeks	8 weeks
Control	89.6± 12.3	92.6 ± 4.9
Collagen	12.8 ± 3.0*††	86.3 ± 11.9*‡‡
Synthetic peptide(no carrier)	43.5 ± 13.5*	43.9 ± 11.8*††
Synthetic peptide and Collagen	46.6 ± 0.7*††	84.4 ± 0.9*‡‡

*: Statistically significant difference compared to control group ($P<0.05$) **($P<0.01$)

†: Statistically significant difference compared to collagen group ($P<0.05$) ††($P<0.01$)

‡:Statistically significant difference compared to newly formed synthetic peptide group ($P<0.05$) ‡‡($P<0.01$)

IV. Discussion

The main object of the periodontal treatment besides symptom relief is to functionally regenerate the damaged periodontal tissue. There are many methods introduced for regenerating damaged periodontal tissue such as autogenous bone grafts and Guided Bone Regeneration (GBR). Due to the limitations of autogenous bone, many clinicians are now in search for new osteoconductive biomaterials.

The purpose of this study was to evaluate the bone regenerative effects of the synthetic peptide in a critical-size rat calvarial defect model. An eight millimeter diameter standardized, circular, transosseus defects created on the cranium of rats were implanted with synthetic peptide, collagen, and both synthetic peptide and collagen. The healing of each group was evaluated histologically and histomorphometrically after 2- and 8-week healing intervals.

The critical-size rat calvarial defect used in this study was a very convenient model for evaluating bone regenerative effects of biomaterials. This model is relatively accessible, simple, and reproducible because spontaneous healing do not occur in the control specimen (Frame, 1980). It has been shown effective to evaluate the potential for bone formation (Schmitz et al., 1986; Caton et al., 1994; Kleinschmidt et al.,; Selvig et al., 1994; Freeman et al., 1973). In addition, after bone augmentation, this model has some compressive force, which is similar to intraoral conditions. It has

many similarities to the maxillofacial region, as anatomically the calvaria consists of two cortical plates with a region of intervening cancellous bone similar to the mandible, and physiologically, the cortical bone in the calvaria resembles an atrophic mandible. Other advantages are that the observation can be focused on the healing process of the bone, since there are no major nerves or blood vessels around the rat calvaria and that the parameters can be simply and accurately measured in each specimen.

The materials that were used were the synthetic peptide and collagen. The synthetic peptide has been developed with the interest of developing an osteoconductive biomaterial. Based on many studies of effective results of BMP-2, the synthetic peptide consists of 21 amino acid sequence, alteration of just one amino acid sequence from the entire BMP-2 sequence. There are 2 epitopes in BMP receptor. However the precise receptor-binding region in BMP-2 has not yet been clarified (Saito et al., 2003).

The amount of the synthetic peptide was used 10μl loading (mass: 2288). This was ten times that of the BMP-2 concentration. The amount was considered from the cell test and 100 times that of the actual concentration is thought to be the best concentration. The gel type was used to reduce the volume and the ease of use.

In tissue engineering technique, the key concept is that an isolated cultured cell on a scaffold is transplanted into the target tissue for its regeneration (Masuko. et al.,

2005). The collagen was used as a scaffold in this study. Collagen is known to have some osteogenic effects. Collagen is well associated within the tissue and has an enhanced chemotactic effect on fibroblast to migrate upwards toward the membrane during the initial healing stage. It reduces membrane exposure and allows blot clot formation by platelet aggregation, thereby acting as a supporting body for initial angiogenesis and tissue formation. However, collagen is less likely used for barrier since its absorption rate is faster than its regeneration time.

In the present study, collagen stabilized the gel type of the synthetic peptide which has a disperse effect. When the synthetic peptide was used with collagen, the effect was enhanced and the results were significant when compared with the control groups or when used with a single biomaterial.

In histometric analysis, the defect closure, new bone area, and bone density were compared. The measurement was done by using a computer program named Image Pro Plus program. The specimen was obtained from the middle coronal section. The measurement of length of the new bone formation is to compare the amount of cell migration. The further the cells migrate, there is a high possibility for bone union. As the length growth of the cells increase, in considering the thickness, more bone formation could be predicted. Therefore, this could be said to be a good marker for membrane's bone regenerative capacity.

Irrespective of the types of bone graft material used, all defect sites exhibited bone

formation in a similar pattern and there was more new bone at 8 weeks. At 2 weeks, parallel pattern within was observed and newly formed bone without any significant adverse reaction was seen. Newly formed bone with osteocytes was evident mainly at the periphery of the defects, and osteoblast-like cells exhibiting a dense arrangement adjacent to the newly formed bone suggest continued bone apposition at the initial healing stage. However, less bone formative activity was found at the central aspects of the defects. Multinucleated giant cells were observed in the periphery of the synthetic peptide material. There was no evidence of fatty marrow or cartilage formation.

At 8 weeks, the quantity of the new bone was greater than that observed at 2 weeks and the specimens showed a more advanced stage of remodeling and consolidation. The newly formed bone consisted of woven bone and lamellar bone, and showed cement lines separated earlier from more recently deposited bone and concentric rings of the Haversian system. However, collagen remnants and dense arrangement of osteoblast-like cells were detected at 8 weeks. There was no evidence of fatty marrow or cartilage formation.

Many studies presented that BMP-2 is effective in bone formation (S.J Hong et al., 2006) and the best carrier used for BMP-2 is collagen. In one of the studies (Song et al., 2005), the new bone area showed 1.3 ± 0.8 mm^2 at 2 weeks and 2.4 ± 0.5 mm^2 at 8 weeks. This was almost similar to the present study. In the present study, collagen was

mostly absorbed forming new bone. This was more prominent in 8 weeks. Compared to the effective results of BMP-2, the synthetic peptide did not show a significant new bone formation. No significant differences were seen between the time intervals. The initial healing is important in implant healing. There was no significant difference between the time intervals. 2 and 4 weeks could have been a better comparison. In addition, the liquid type of synthetic peptide could have been lost around the rim for its disparity. This could be changed to granules or powder type or could be reinforced with a carrier. When used with the synthetic peptide and collagen, the new bone formation was enhanced. The concentration could be altered through further studies. The experimental group design and different time interval may have yielded better results. The synthetic peptide was developed to be effective in minimal gap in osseous defects during implantation. However, in the present study, it was a whole defect model. When embedding this material in implants, it could be possible to enhance bone formation with a scaffold such as collatape, which will also increase the stability of the material.

More research is necessary on the synthetic peptide in bone regeneration. It can be improved in various ways. The synthetic peptide may need more research in its sequence and concentration. However, the synthetic peptide can be said to be effective in damaged periodontal tissue regeneration in small gap defects concerning its results and various advantages.

V. Conclusion

The purpose of this study was designed to evaluate the periodontal tissue regenerative effects of the synthetic peptide.

The results of the present study indicate that the synthetic peptide has a bone regenerative effect and carries the possibility of being used as a bone regenerative material on the implant surface, reducing the need for second surgery. Peptide has the possibility of being successful in marginal bone gain.

More research is necessary on the synthetic peptide in bone regeneration. It can be improved in various ways. The synthetic peptide may need more research in its sequence and concentration. However it can be concluded that the synthetic peptide can be effective in damaged periodontal tissue regeneration for its various advantages when compared to other protein based biomaterials, especially in small gap defects.

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VII. Legends

Figure 1. Schematic drawing of calvarial osteotomy defect showing the histometric analysis.

Figure 2. Representative photomicrographs of defect sites receiving control at 2 weeks postsurgery. At 2 weeks, the augmented area was covered with dense connective tissue. Minimal new bone formation was observed (×20).

Figure 3. Representative photomicrographs of defect sites receiving control at 8 weeks postsurgery. At 8 weeks, more bone formation was observed in the base when compared to 2 weeks (×20).

Figure 4. Representative photomicrographs of defect sites receiving collagen only at 2 weeks postsurgery. The defects were filled with loose or dense, fibrous connective tissue and limited new bone formation was observed at the defect margin at 2 weeks (×20).

Figure 5. Representative photomicrographs of defect sites receiving collagen only at 8 weeks postsurgery. The resorption of collagen progressed much. There was an

increase in bone volume and there was no invagination of the peripheral tissue (×20).

Figure 6. Representative photomicrographs of defect sites receiving synthetic peptide only at 2 weeks postsurgery. There was almost no resorption and there was slight new bone formation, a slight increase in volume as well (×20).

Figure 7. Representative photomicrographs of defect sites receiving synthetic peptide only at 8 weeks postsurgery. There was a great amount of resorption. The new bone formation increased compared to the 2 weeks' group. Osteoblast-like cells and very few giant multinucleated cells were able to be detected in the periphery of the margin whereas the center showed almost no new bone formation (×20).

Figure 8. Representative photomicrographs of defect sites receiving synthetic peptide and collagen only at 2 weeks postsurgery. There was not much bone regeneration or defect closure (×20).

Figure 9. Representative photomicrographs of defect sites receiving synthetic peptide and collagen only at 2 weeks postsurgery. There were no osteoblast-like cells detected (×50).

Figure 10. Representative photomicrographs of defect sites receiving synthetic peptide and collagen only at 8 weeks postsurgery. At 8 weeks post-surgery, new bone formation was moderate. There was loose connective tissue formation around the defect area and there was no infiltration of inflammatory cells. Collagen was almost resorbed (×20).

Figure 11. Representative photomicrographs of defect sites receiving newly formed synthetic peptide and collagen only at 8 weeks postsurgery. There was loose connective tissue formation around the defect area and there was no infiltration of inflammatory cells. The defect area has been replaced by parallel pattern of connective tissue (×50).

VIII. Figures

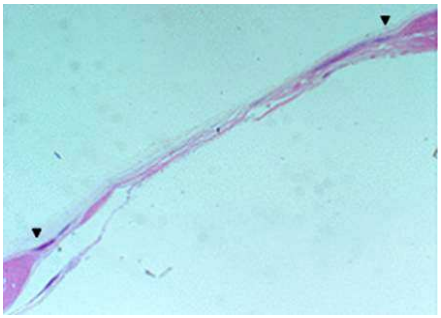

Figure 2. Control 2 weeks (×20)

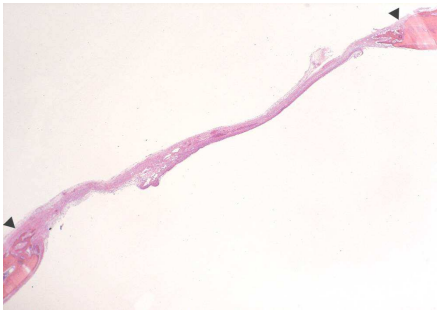

Figure 3. Control 8 weeks (×20)

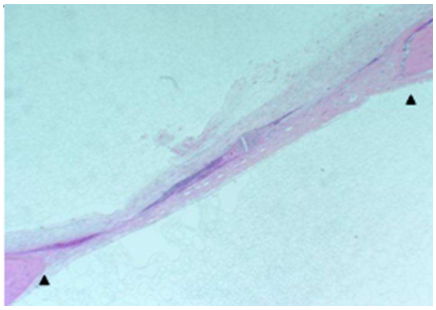

Figure 4. Collagen 2 weeks (×20)

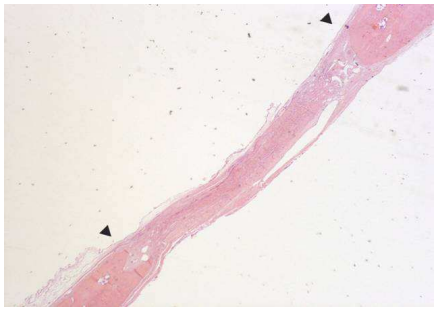

Figure 5. Collagen 8 weeks (×20)

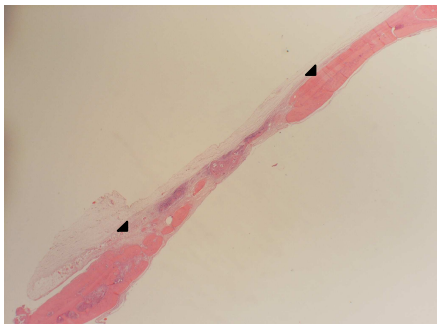

Figure 6. Synthetic peptide 2 weeks (×20)

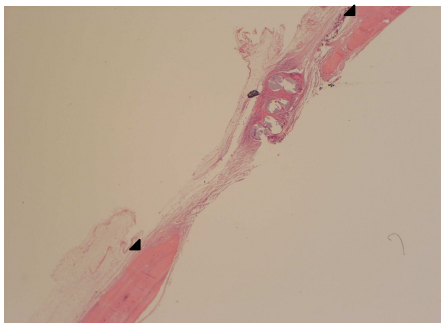

Figure 7. Synthetic peptide 8 weeks (×20)

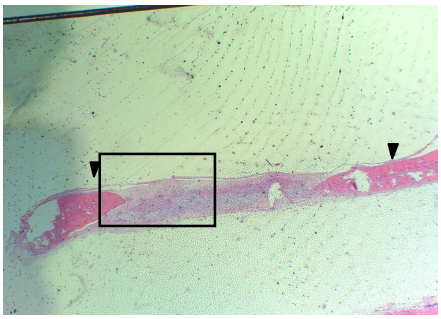

Figure 8. Synthetic peptide and Collagen 2 weeks (×20)

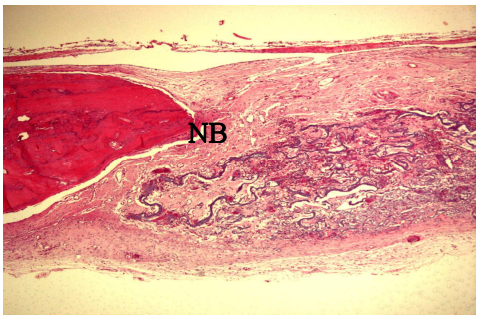

Figure 9. Synthetic peptide and Collagen 2 weeks (×50)

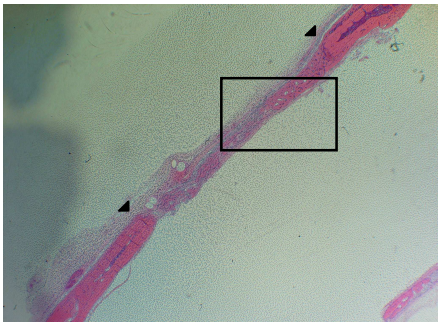

Figure 10. Synthetic peptide and Collagen 8 weeks (×20)

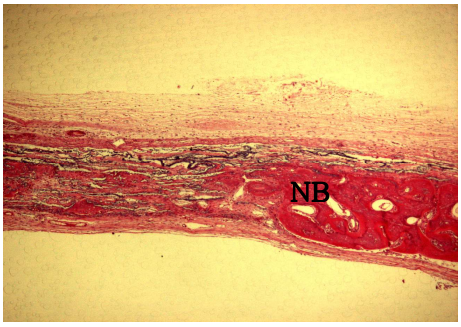

Figure 11. Synthetic peptide and Collagen 8 weeks (×50)

국문요약

합성 펩타이드를
이용한 백서 두개골의 골재생 효과

세포 scaffold 내에 특정 아미노산 배열로 이루어진 펩타이드를 개입시켜 ECM 이나 BMP 등의 단백질 전달 영역에 대한 연구가 활발히 이루어지고 있다.

본 연구는 합성 펩타이드를 이용하여 외과적으로 형성된 백서 두개골에서 골재생 효과를 확인하고자 하였다. 40 마리의 웅성백서를 4 개군으로 나누 어 두개골에 8mm 직경의 표준화된 원형의 두개골 결손부를 형성한 후 아무것 도 처리하지 않은 군을 대조군으로 하고 나머지 3 군에 각각 합성 펩타이드, 콜라겐 그리고 합성 펩타이드와 콜라겐을 함께 처리하였다. 각 군의 웅성백서는 2 주와 8 주에 희생되었으며 골재생 양상을 조직학적, 조직계측학적으로 분석 평가하였다.

합성 펩타이드와 콜라겐을 처리한 군은 골재생이 2 주, 8 주에서 유의성 있게 증가하였다 ($P<0.01$). 다른 실험군들과 비교하였을 경우, 합성 펩타이드로 처리한 군은 비슷한 양상의 골재생을 보였다. Defect closure 와 new bone area 는 합성 펩타이드와 콜라겐을 처리한 군의 8 주에서 유의한 차이를 나타냈다.

결론적으로 본연구에서 합성 펩타이드는 다른 댄백질 계통의 생체재료에 비해 장점을 지니고 있으며, 손상된 치조골의 결손부의 재생에 효과적인 골이식재로 생각된다.

핵심되는 말: 합성 펩타이드, 콜라겐, 골재생