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박사학위논문

A clinical and histologic study of guided bone regeneration using the MBCP mixture in Mx

조선대학교 대학원

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A clinical and histologic study of guided bone regeneration using the MBCP mixture in Mx

상악에서 *MBCP*의 혼합물을 이용한 골재생술의
조직학적 연구

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A histologic study of guided bone regeneration using the MBCP mixture in human

지도교수 장 현 선

이 논문을 치의학 박사학위신청 논문으로 제출함.

2008년 4월 일

조선대학교 대학원

치 의 학 과

박 영 란

박영란의 박사학위 논문을 인준함.

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박 영 란
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골유도재생술이란 특이세포가 특이 조직을 형성한다는 원리에 근거하여, 6-8주간 차단막을 이용하여 치주창상으로부터 상피와 결합조직의 빠른 성장을 제한하면 주위 공간으로 상피, 결합조직이 서서히 자라게 되며, 그 동안에 골아세포에 의하여 신생골 형성을 유도한다는 것이다. 골유도재생술은 무치악부위 혹은 발치와에 임플란트를 식립해야할 경우 부족한 잔존치조제의 형성을 위해서, 혹은 발치와내의 골의 형성을 증진시키기 위해서 일반적으로 이용된다. 골유도재생술에 이용되는 이식재는 자가골, 동종골, 이종골, 합성골 등이 다양하게 이용된다. 자가골은 골형성효과는 우수하나 또다른 수술부위를 필요로 하고, 동종골과 이종골들은 감염의 가능성이 커서 사용에 제한이 있다. 최근 합성골의 사용에 관한 연구들이 보고되고 있으며 임상에서 MBCP(Micro-Macroporous Biphasic Calcium Phosphate, Biomatlante, France)의 사용이 증가하고 있는 추세이다. 그러나 골형성에 관한 조직학적 연구들은 미비하다. 이에 비번 연구에서는 임플란트 수술시 MBCP를 이용한 골유도재생술을 시행했던 28세부터 71세 까지 평균 52세의 12명의 환자(7명의 남자 환자와 5명의 여자 환자)를 대상으로 하였고 임플란트 수술전에 골유도재생술을 시행받았던 환자를 대상으로 하였다. 사용되는 재료는 MBCP를 사용하였던 환자를 선택기준으로 하였고, MBCP 단독사용, 다른 이식재들과 혼합사용, 비흡수성 혹은 흡수성 막과 함께 사용한 경우들을 모두 분석에 포함하였다.

골유도재생술후 임플란트 수술시행까지의 기간, 즉, 골재생을 평가하는 기간은 5개월에서 19개월까지 다양하였고, 평균적으로 9개월이었다. 이러한 치유 기간 후 임플란트 수술전에 내경 2 mm의 trephine bur를 이용하여 약 5 mm 길이의 bone core를 채취하였다. 채취된 bone core는 10% formalin을 이용하여 고정시키고 5% formic acid에 탈회시킨 후 파라핀에 매몰하고 5 ㎛두께로 절단한 후

hematoxylin-eosin 염색한 후 조직학적으로 분석하였다.

분석결과, 다음과 같은 결과를 얻었는데, 1. 분석된 연령은 28세부터 71세 까지 다양하였고, 평균 51세였다. 2. 분석된 12명중 남자는 7명, 여자는 5명이었다. 3. 골재생을 평가하는 기간은 5개월에서 19개월까지 다양하였고, 평균적으로 9개월이었다. 19개월정도로 장기간 소요된 경우는 환자 사정상 수술이 지연되어 평가기간이 긴 것으로 볼 수 있다. 4. 분석된 대부분의 조직에서 골형성이 잘 관찰되었고, 치밀결체조직도 관찰되었다. 5. 7, 9, 10개월 경우에도 이식재들이 잔존되어 있는 소견도 관찰되었다. 6. 19개월의 장기간 분석 예에서는 신생골 형성이 더욱 잘 관찰되었다.

본 연구결과 사람에서 골유도재생술시에 MBCP의 사용은 임상에서 임플란트 수술전 부족한 치조제의 증강, 발치와내 골유도재생술, 상악동거상술시에 예지성이 좋은 것으로 생각된다.

Introduction

The presence of sufficient bone volume is an important prerequisite for dental implant placement[1-4]. Guided bone regeneration (GBR) was generally done for future implant site improvement in severe alveolar bone resorption patients. The pattern of alveolar ridge resoption is divided into vertical, horizontal, and combined pattern. Materials used to increase the rate of bone formation and to augment the bone quantity including the autografts, allografts, xenografts, and alloplastic bone substitutes[6].

For ideal bone regeneration, the function of bone materials is needed osteogenesis, osteoinduction, and osteocondunction. Autogenous bone has above all function, but these techniques was needed patients to a second surgical site, which may increase morbidity, hospital stay, recovery, and cost[7]. There are also a greater risk for wound infection, more blood loss, and a slower return to normal function in large donor site. It is also reasonably challenging to contour and can undergo significant and unpredictable resorption[8].

Allogenic bone has commonly used alternative to the autogenous bone materials. The allografts is osteoinductive and osteoconductive potential, the most commonly used materials are demineralized freeze-deried allograft (DFDBA) and freeze-dried bone allograft (FDBA). The bioactivity of DFDBA seems to be dependent on the age of the donor, since the younger donor has a more osteoinductive properties[9]. And there is also a greater risk for infection.

Xenografts was also the most commonly used alternatives of autograft, allograft. Many researchers reported good biocompatibility and osteoconductive potential of xenografts (Bio-Oss). However, there is also a greater risk for infection.

Recently, synthetic bone is attempted to improve the results of GBR. Le Nihouannen D et al[10] reported that synthetic bone substitutes, such as calcium phosphate ceramics, give good results in clinical applications and

that the MBCP/fibrin material could be used in clinical bone filling applications. Combining these bioceramics with fibrin glue provides a mouldable and self-hardening composite biomaterial with the biochemical properties of each component[10]. Now, in dental clinic, clinician and patients all consider that bone material used GBR is essential infection-free, cost-effective, non-traumatic. Synthetic bone material is infection-free due to no animal resource, and non-traumatic due to no donor site.

The purpose of this study was histologically to evaluate effect of synthetic bone material, MBCP (Micro-Macroporous Biphasic Calcium Phosphate) in GBR patients.

Material and Methods

A. Materials

This study was performed on 12 patients from the age of 28 years to 71 years, their mean age was 52 years (7 male patients and 5 female patient). Informed consent was obtained from patients. The subjects were included GBR or sinus bone graft in maxilla.

After waiting for bone regeneration, implant surgery was proceeded several months later. Bone biopsy was obtained using the trephine bur during implant surgery. The inclusion criteria in this study was included GBR patients (or sinus bone graft) using the MBCP.

B. Methods

As the material used, MBCP (Biomatlante, France) were used alone. Sometimes, ICB (Rocky Mountain Tissue Bank, USA) or Bio-Oss was mixed with MBCP at GBR or sinus bone graft. And as a barrier membrane, Bio-Gide (Osteohealth Co.) or non-resorbable membrane was also used.

The period between GBR and implant surgery was varied from 5 months to 21 months, their mean period was 9 months. For bone biopsy, using a trephine bur 2 mm in diameter, the regenerated bone was collected in the medial side of the implant future site. The bone core 5 mm in length was collected.

The collected bone core was fixed using 10 % formalin, decalcified in 5 % formic acid, embedded in paraffin, sectioned longitudinally to 5 ㎛ thickness, and H & E staining was performed.

Results

In this study, the histologic study was performed on 12 patients from the age of 28 years to 71 years, their mean age was 52 years (7 male patients and 5 female patient). The healing period between GBR and implant surgery varied from 5 months to 19 months, the mean period was nine months. The longest period was 19 months. We thought the cause of the long period that the patient postponed the implant surgery (Table 1).

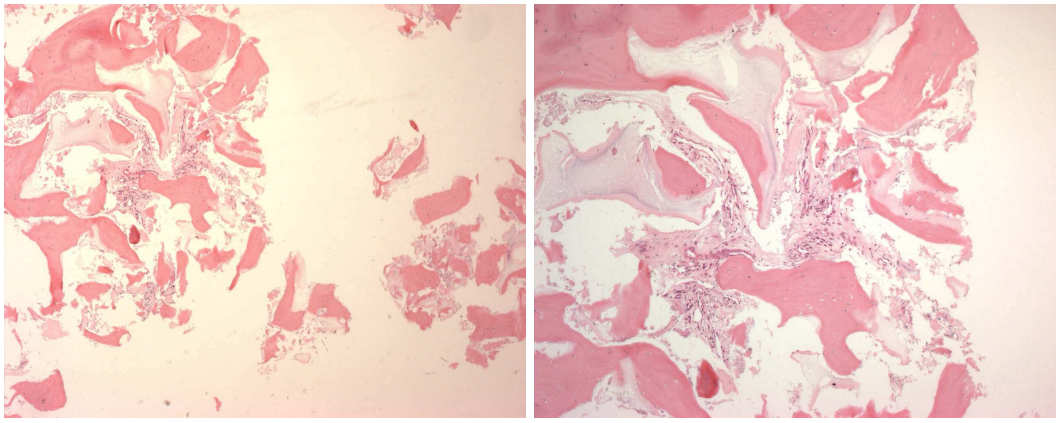
Table 1. Patient used in this study

No	Age	Sex	Site	Healing period (month)	GBR material	Tx	Implant survival period (momth)	
							After implant surgery	After Implant prothesis
1	50	F	Ant. Mx	10	MBCP, Grafton, Tefgen	GBR	30	18
2	71	F	Rt. Mx.	19	MBCP, Tefgen, GoreTex	GBR	18	2
3	58	F	Lt. Mx	5	MBCP, autogenous bone, Ti-reinforced mesh TR9W	GBR	36	?
4	66	M	Lt. Mx	8	MBCP, Grafton, Bio-oss	SBG	31	20
5	55	M	Rt. Mx.	10	MBCP, Grafton, Collatape	SBG	30	20
6	58	M	Rt. Mx.	9	MBCP, ICB, autogenous bone, Tefgen	SBG	33	21
7	39	F	Mx. Canine, Premolar	7	MBCP, Tefgen	GBR	27	16
8	33	M	Rt. Mx.	10	MBCP, Grafton, BioGide	SBG	21	?
9	50	M	Lt. Mx	7	MBCP, ICB, autogenous, Bio-Mesh	SBG	37	26
10	28	M	Rt. Mx.	7	MBCP, ICB, Collatape	SBG	38	26
11	60	M	Lt. Mx	7	MBCP, autogenous, Venous blood	GBR	23	13
12	56	F	Lt. Mx	8	MBCP, ICB, BioGide	SBG	37	27

Mx: Maxilla, Rt: Right, Lt: Left, MBCP:Micro-Macroporous Biphasic Calcium Phosphate, GBR: Guided bone regeneration, SBG: Sinus bone graft

Grafted particles that have not been absorbed yet were detected, and in their vicinity, new bone tissues were detected and the connective tissues were also observed (Fig. 1). The healing period was 10 months, and material used was MBCP, Grafton, and BioGide (Fig. 1,2).

A. B.



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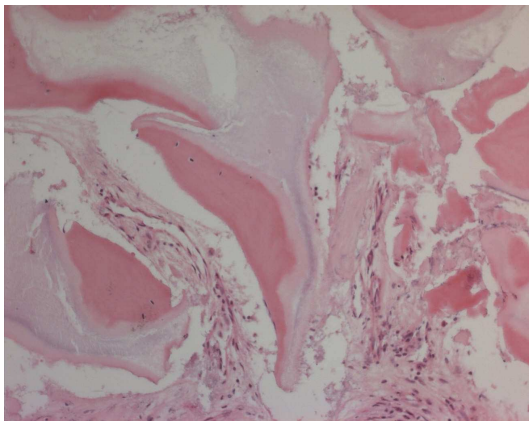
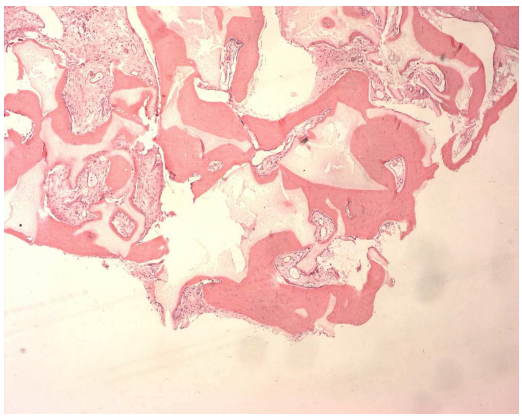


Fig. 1. Histologic features of GBR using the MBCP, Grafton, and BioGide. New bone formation was shown. After 10 months healing periods. hematoxylin-easin staining. magnification ×50(A), ×100(B), ×200(C)

MBCP particles that have not been absorbed yet were detected, and in their vicinity, new bone tissues were detected and the influx of connective tissues were observed. In the vicinity of the grafted bone, osteoblast-like cells were detected (Fig. 2).

A.



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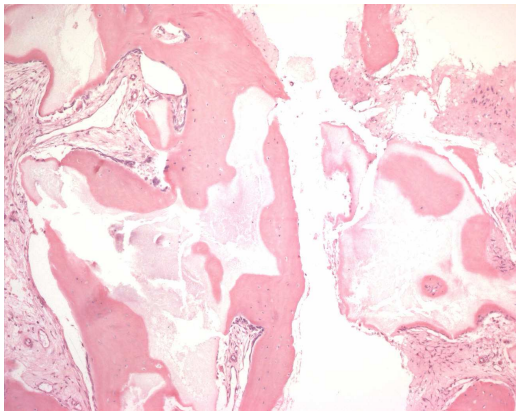

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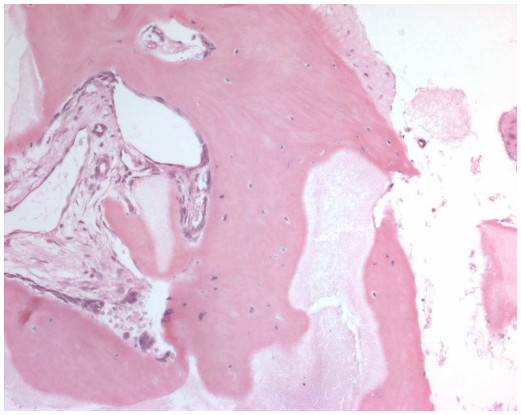
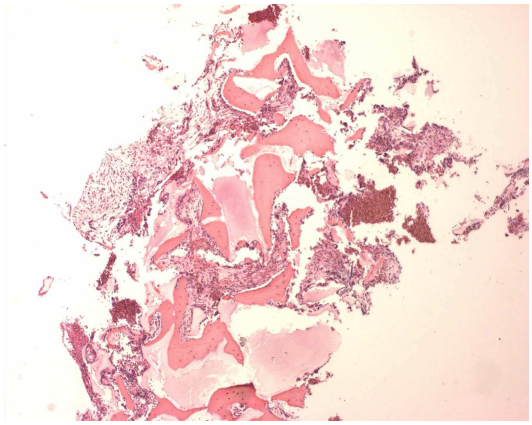


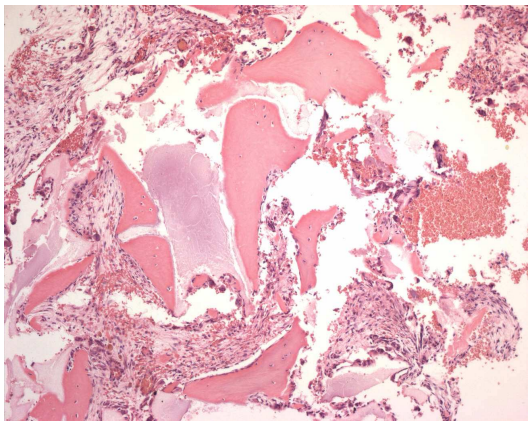
Fig. 2. Histologic features of GBR using the MBCP, Grafton, and BioGide. New bone formation was shown. Osteoblast-like cells were also detected. After 10 months healing period. hematoxylin-easin staining. magnification ×50(A), ×100(B), ×200(C)

MBCP particles that have not been absorbed yet were detected, and in their vicinity, new bone tissues were detected and the influx of connective tissues, blood, etc. was observed (Fig. 3,4). In the vicinity of the grafted bone, osteoblast-like cells were detected, and the osteoid released by them was shown, and multinucleated giant cells for the absorption of the graft materials were detected (Fig. 3,4). The healing period was 19 months, and used material was MBCP, Goretex, and Tefgen (Fig. 3,4).

A.



B.



C.

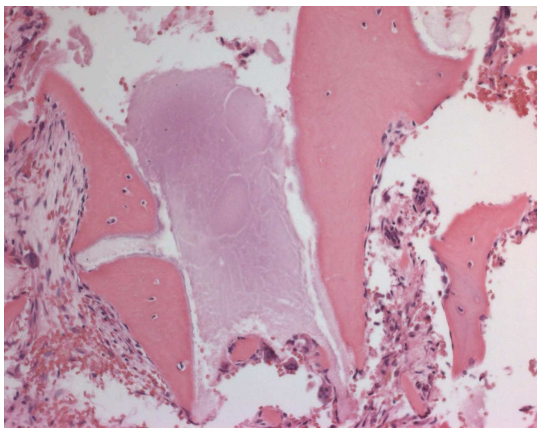
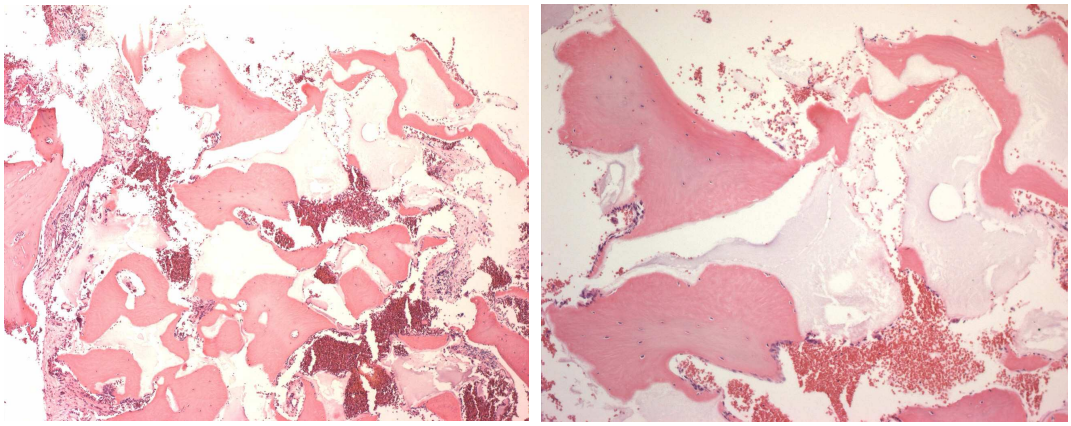


Fig. 3. Histologic features of GBR using the MBCP and Tefgen. New bone formation was shown. Osteoblast-like cells and osteoid tissue were also detected. After 19 months healing period. hematoxylin-easin staining. magnification ×50(A), ×100(B), ×200(C)

A. B.



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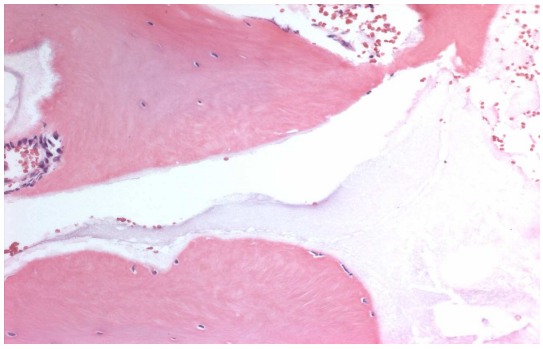
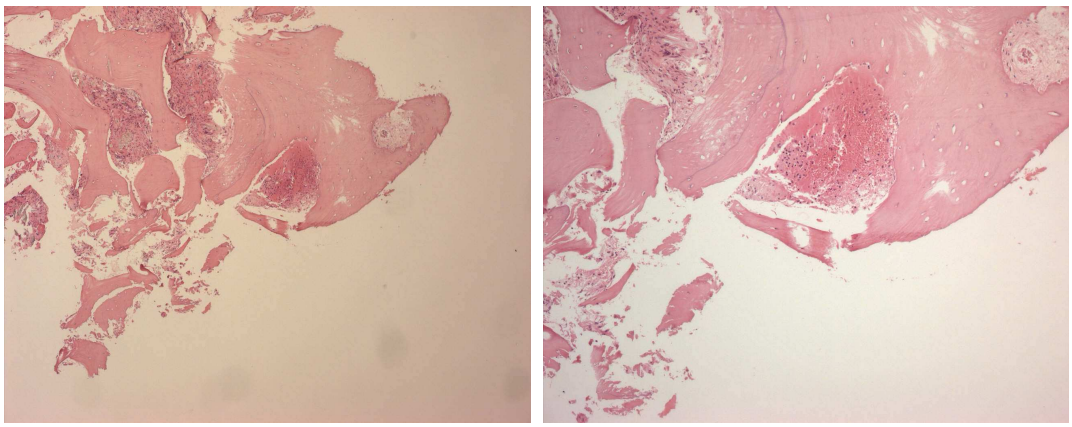


Fig. 4. Histologic features of GBR using the MBCP and Tefgen. Bone graft materials that have not been absorbed yet were detected. The influx of blood, etc. was observed. New bone formation was showed. Osteoid tissue were also detected. After 19 months healing period. hematoxylin-easin staining. magnification ×50(A), ×100(B), ×200(C)

It has been observed that the new bone area was showed and osteocytes were entraped in the lacuna, and in the vicinity of graft materials, simultaneous bone absorption and deposition were observed (Fig. 5). The healing period was 7 months, used material was MBCP, ICB, and Collatape.

A. B.



C.

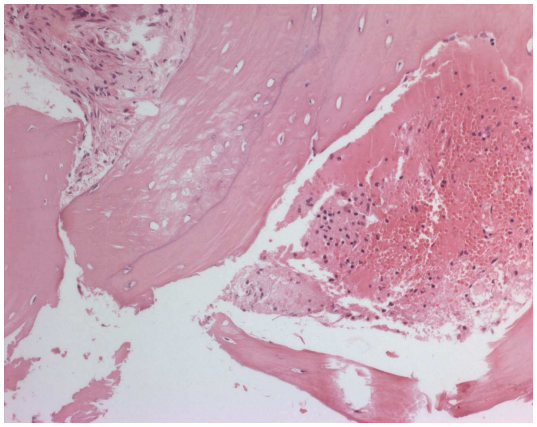
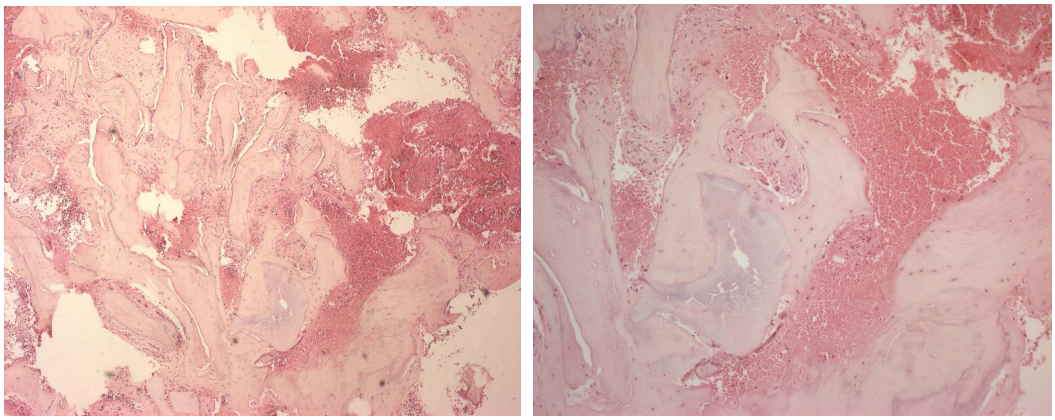


Fig. 5. Histologic features of GBR using the MBCP, ICB and Collatape. The connective tissue, blood, and mild imflammatory cells was observed. New bone formation was shown. Osteoid tissue were also detected. After 7 months healing period. hematoxylin-easin staining. magnification ×50(A), ×100(B), ×200(C)

In the vicinity of the grafted bone, osteoblast-like cells were detected, and osteoid tissues were showed along osteoblast-like cells. Bone graft materials was mostly absorbed. New bone tissues were detected and the connective tissues, blood, etc. was observed (Fig. 6). It has been observed that the new bone area was mature and osteocytes were entraped in the lacuna. The healing period was 7 months, and used material was MBCP, ICB, autogenous, and Bio-Mesh.

A. B.



C.

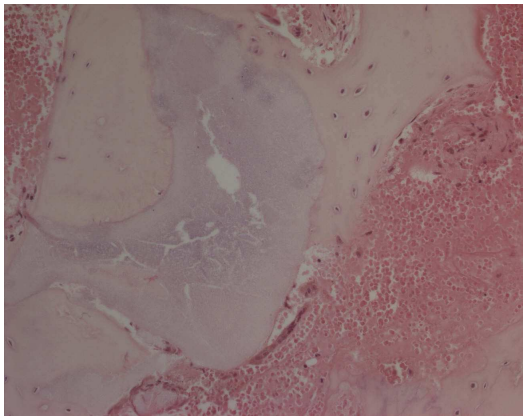
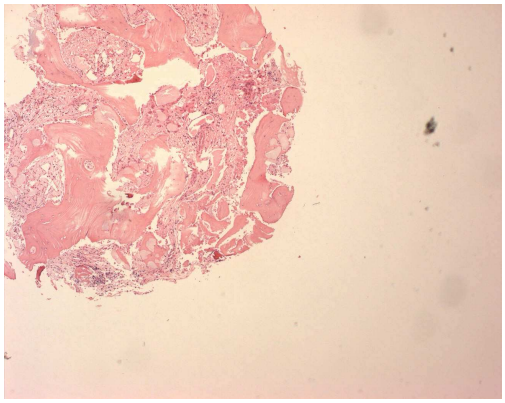


Fig. 6. Histologic features of GBR using the MBCP, ICB and Biomesh. New bone formation was shown. Osteoblast-like cells and osteoid tissue were also detected. After 7 months healing period. hematoxylin-easin staining. magnification ×50(A), ×100(B), ×200(C)

Bone graft materials that have not been absorbed yet were detected, and in their vicinity, new bone tissues were detected and the connective tissues and mild inflammatory cells were observed (Fig. 7). The healing period was 8 months, and used materials were MBCP, ICB, and Bioguide.

A.



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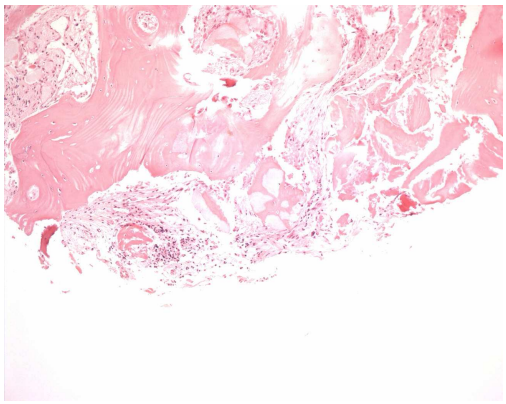

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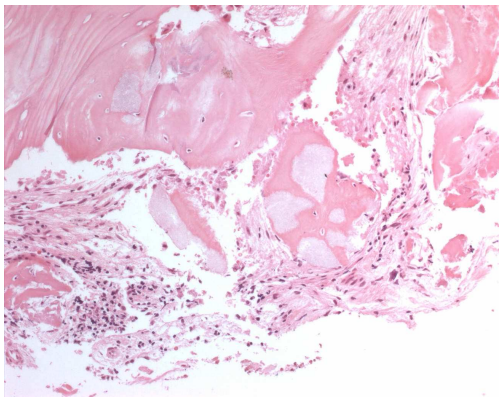
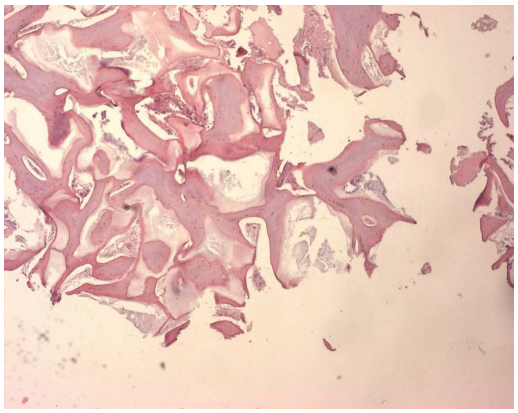


Fig. 7. Histologic features of GBR using the MBCP, ICB and BioGide. New bone formation was shown. Osteoblast-like cells and osteoid tissue were also detected. After 8 months healing period. hematoxylin-easin staining. magnification ×50(A), ×100(B), ×200(C)

Bone graft materials that have not been absorbed yet were detected, and in their vicinity, new bone tissues were detected and the connective tissues and mild inflammatory cells were observed (Fig. 8). The healing period was 9 months, and used materials were MBCP, ICB, autogenous bone, Tefgen.

A.



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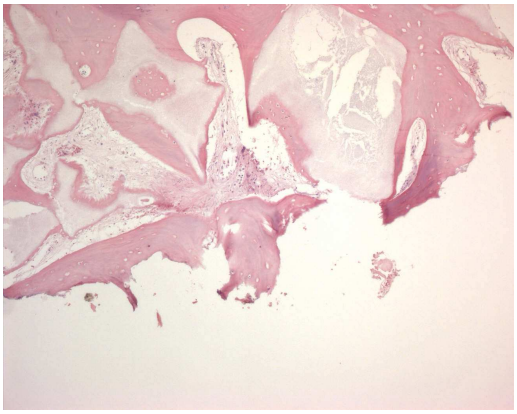

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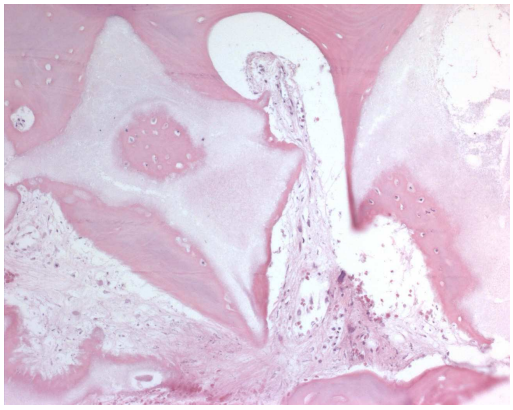
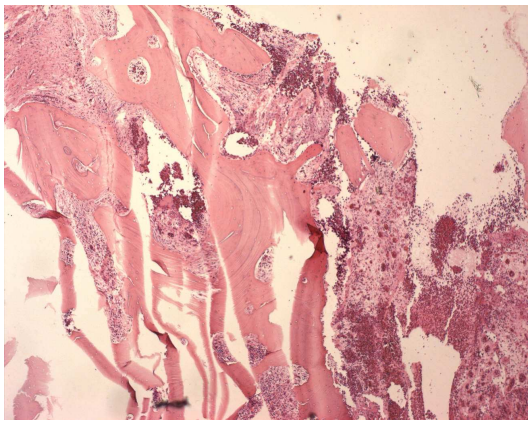


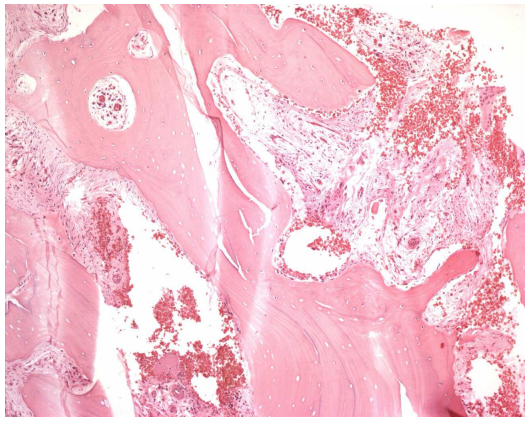
Fig. 8. Histologic features of GBR using the MBCP, ICB, Autogenous bone and Tefgen. New bone formation was shown. Osteoid tissue and connective tissue were also detected. After 9 months healing period. hematoxylin-easin staining. magnification ×50(A), ×100(B), ×200(C)

Bone graft materials was mostly absorbed. New bone tissues were detected and the influx of connective tissues, blood, etc. were observed (Fig. 9). It has been observed that the new bone area was mature and osteocytes were entraped in the lacuna. The healing period was 5 months, and used materials was MBCP, autogenous bone, and Ti-reinforced mesh TR9W.

A.



B.



C.

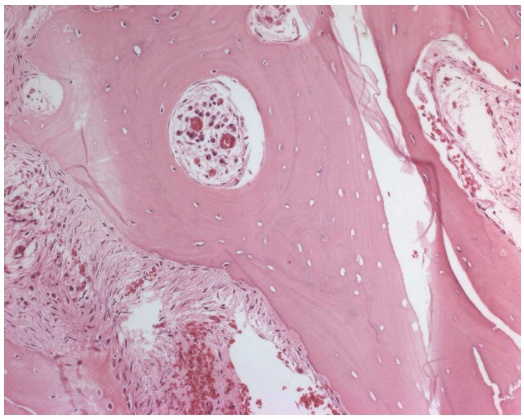
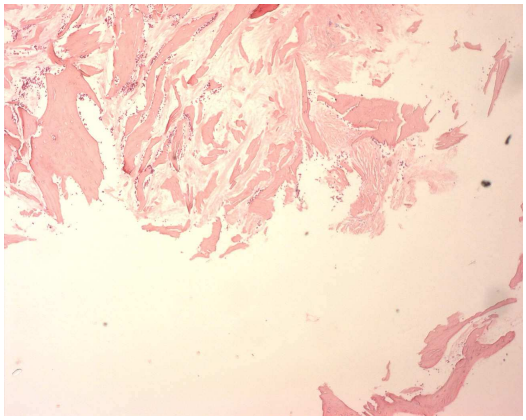


Fig. 9. Histologic features of GBR using the MBCP, Autogenous bone and Ti-reinforced mesh TR 9W. New bone formation was shown. The influx of connective tissue, blood, etc. was observed. Mature bone and osteoid tissue were also detected. After 5 months healing period. hematoxylin-easin staining. magnification ×50(A), ×100(B), ×200(C)

Bone graft materials did not resorbed mostly. Artificial bone materials were detected and the connective tissues were also observed (Fig. 10). The healing period was 10 months, and used materials were MBCP, Grafton, Collatape.

A.



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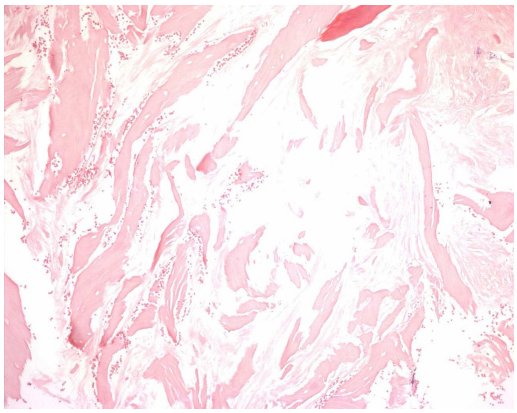


C.

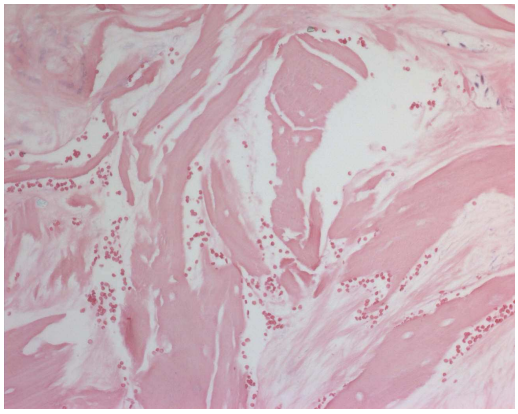
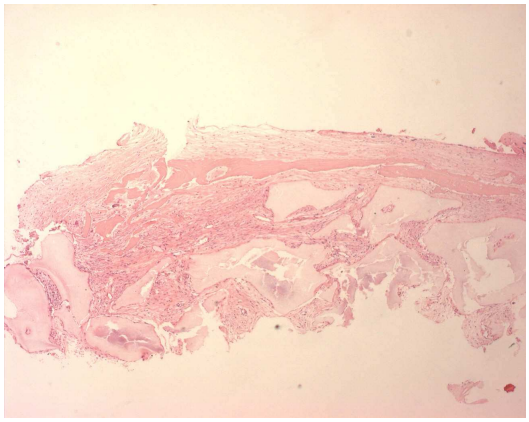


Fig. 10. Histologic features of GBR using the MBCP, Grafton and Collatape. New bone formation was shown. The influx of connective tissue, blood, etc. was observed. Mature bone and osteoid tissue were also detected. After 10 months healing period. hematoxylin-easin staining. magnification ×50(A), ×100(B), ×200(C)

Bone graft materials that have not been resorbed yet were detected, and in their vicinity, the osteoblast-like cells and connective tissue were detected (Fig. 11). The healing period was 10 months, and used material was MBCP, Grafton, and Tefgen.

A.



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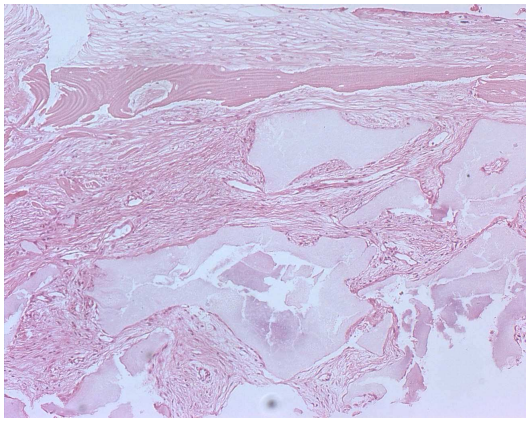


C.

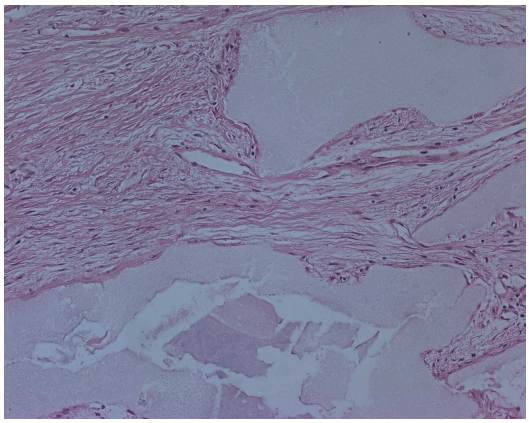
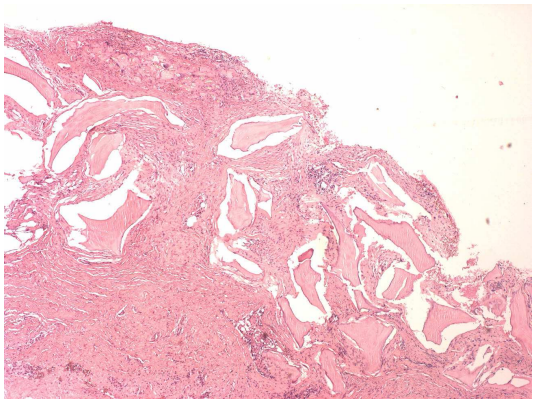


Fig. 11. Histologic features of GBR using the MBCP, Grafton, PRP and Tefgen. The influx of connective tissue and osteoblast-like cells were observed. After 10 months healing period. hematoxylin-easin staining. magnification ×50(A), ×100(B), ×200(C)

In the vicinity of the grafted bone, the connective tissue and mild inflammatory cells were detected, and multinucleated giant cells for the resorption of the graft materials were detected (Fig. 12). The healing period was 7 months, and used material was MBCP, Tefgen.

A.



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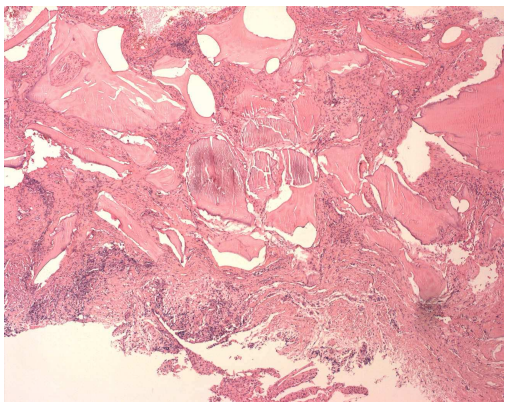

C.

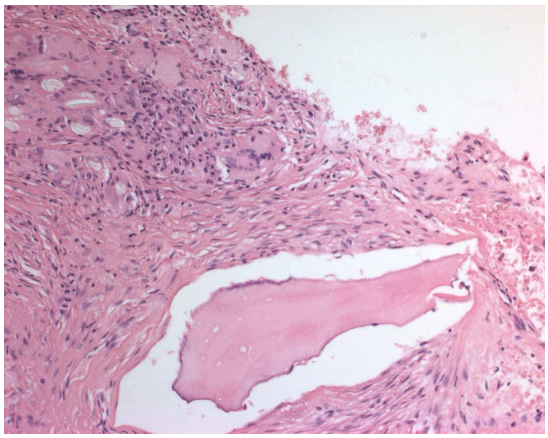

Fig. 12. Histologic features of GBR using the MBCP, Grafton, PRP and Tefgen. The influx of connective tissue and mild inflammatory cells were observed. After 7 months healing period. hematoxylin-easin staining. magnification ×50(A), ×100(B), ×200(C)

Discussion

Guided bone regeneration (GBR) generally need to enhance of bone formation in extraction socket or to rehabilitate deficient alveolar ridge when it is for implantation in edentulous area or extraction socket. The bone materials used GBR are varient as autogenous bone, allogenic bone, xenograft, and synthetic bone materials[11-14]. Autogenous bone is exellent for bone formation effect but donor site is needed. Allograft and xenograft is also good for bone formation but recently its use is restricted due to infection risk.

Recently, the use of synthetic bone material is increasing in GBR or sinus bone graft. Expecially, in dental clinic, Micro-Macroporous Biphasic Calcium Phosphate (MBCP) is increasing in GBR or sinus bone graft.

Sinus bone graft indicates the augmentation of the internal side of the maxillary sinus. It is named by sinus elevation, it could be defined as a surgical technique that allows the implant by increasing the vertical bone of the posterior maxilla through this. Tatum[15] has been reported for sinus elevation in 1976 for the first time in the Alabama implant meeting, and it has been applied widely until now.

Reviewing the survival rate of the implant placed in the area where sinus elevation was performed, in the cases used autogeneous bone alone or the mixture of hydroxyapatite (HA) plus autogenous bone, over 90 % high success rate has been reported[16].

In addition, in the cases using autogeneous bone alone, a bone substitute alone, or their combination, over 84 % success rate has been reported[17]. In addition, similarly, in the result of the success rate of implants placed in the area performed sinus elevation, in the 5 years follow up observation period of the cases used synthetic bone alone, the mixture of synthetic bone and heterogenic bone, allogenic bone alone, the combination of allogenic bone and synthetic bone, autogeneous bone alone, and the combination of autogeneous bones and heterologous bone, over 85 % success rate has been reported[18].

Albrektsson et al[19] suggested that considering the success rate of the implant

placed in the posterior molar area in the maxilla without sinus elevation, and comparing with the success standard for implants, it is determined to be satisfactory, and consequently, it could be considered as a basis that proves the predictictability, feasibility of the use of sinus elevation in the posterior molar area in the maxilla where the osteoid volume is not sufficient.

Based on the above results, in the cases performed GBR or sinus elevation using MBCP, we evaluated histologically for bone regeneration results in humans. The new bone formation in our MBCP cases with or without the use of a barrier membrane or other bone material was well shown. Non-absorbed bone material was also detected, but inflammation was rare.

In addition, Wallace and Froum [20] reported that the bone formation rate was superior in the cases using a barrier membrane in comparison with the cases without using it. In our study, we used barrier membrane a few cases. Author thought that the use of a barrier membrane contributed to the result obtained in our study.

In this study, author evaluated histologically for bone regeneration effect of MBCP in human who was done GBR or sinus bone graft as future site development for implantation. In all samples of our study, new bone formation was well found. The mean healing period was 9 months. Bone graft materials that have not been absorbed yet were detected after 7, 9, 10 months healing periods. But, in their vicinity, new bone tissues were detected and the influx of connective tissues, blood, etc. was also observed. Infammatory cell infiltration was rare. The longest period was 19 months, the subject showed active new bone formation. We suggest that MBCP can be predictable in GBR or sinus bone graft for future implant site development.

In order to adapt to surgical sites, bioceramics come in the form of blocks or granules, and are either dense or porous.[10]

Lee LT et al[21] reported the effectiveness of autologous fibrin glue and macroporous biphasic calcium phosphate (MBCP) as carriers in the osteogenesis process with/without mesenchymal stem cells. Using stem cells plus autologous fibrin glue as the carrier may accelerate new bone regeneration.[21] Le Nihouannen D et al[22] reported the osteoinductive potential of macro- micro-porous biphasic calcium phosphate (MBCP) ceramic granules with fibrin glue. They reported that these bone substitutes

exhibiting osteoinductive properties could be used for the reconstruction of large bone defects.

In this study, we evaluated bone formation effect of Micro-Macroporous Biphasic Calcium Phosphate (MBCP) used in GBR or sinus bone graft. Generally, good healing pattern was showed in all subjects. In the maxillary sinus elevation area and GBR area using the MBCP, the formation of new bone was detected histologically.

Conclusion

Based on the result of our study, we suggest that the MBCP can be predictable bone material at site development for implantation in dental clinic.

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저작물 이용 허락서

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연락처	011-9871-8275				
논문제목	한글 : 사람에서 MBCP의 혼합물을 이용한 골재생술의 조직학적 연구 영문 : A histologic study of guided bone regeneration using the MBCP mixture in human				

본인이 저작한 위의 저작물에 대하여 다음과 같은 조건아래 조선대학교가 저작물을 이용할 수 있도록 허락하고 동의합니다.

- 다 음 -

1. 저작물의 DB구축 및 인터넷을 포함한 정보통신망에의 공개를 위한 저작물의 복제, 기억장치에의 저장, 전송 등을 허락함.
2. 위의 목적을 위하여 필요한 범위 내에서의 편집·형식상의 변경을 허락함. 다만, 저작물의 내용변경은 금지함.
3. 배포·전송된 저작물의 영리적 목적을 위한 복제, 저장, 전송 등은 금지함.
4. 저작물에 대한 이용기간은 5년으로 하고, 기간종료 3개월 이내에 별도의 의사표시가 없을 경우에는 저작물의 이용기간을 계속 연장함.
5. 해당 저작물의 저작권을 타인에게 양도하거나 또는 출판을 허락을 하였을 경우에는 1개월 이내에 대학에 이를 통보함.
6. 조선대학교는 저작물의 이용허락 이후 해당 저작물로 인하여 발생하는 타인에 의한 권리 침해에 대하여 일체의 법적 책임을 지지 않음.
7. 소속대학의 협정기관에 저작물의 제공 및 인터넷 등 정보통신망을 이용한 저작물의 전송·출력을 허락함.

2008년 8 월 일

저작자 : 박 영 란 (서명 또는 인)

조선대학교 총장 귀하