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박사학위논문

Histologic study of sinus grafting with Bio-Oss for implant placement

조 선 대 학 교 대 학 원

치 의 학 과

정 태 영

Histologic study of sinus grafting with Bio-Oss for implant placement

임프란트 식립을 위한 Bio-Oss를 이용한 상악동거상술후 조직학적 평가

2005년 2 월 일

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치 의 학 과

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Histologic study of sinus grafting with Bio-Oss for implant placement

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이 논문을 치의학 박사학위신청 논문으로 제출함.

2005년 2 월 일

조 선 대 학 교 대 학 원

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2004년 12월 일

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국문초록

임프란트 식립을 위한 Bio-Oss를 이용한 상악동거상술후 조직학적 평가

정 태영
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구강악안면외과학 전공

본 연구의 목적은 20명의 임프란트 환자에서 골이식재(Bio-Oss)를 이용하여 상악동거상술을 시행한 후 조직학적으로 평가하여 그 유용성을 알아보는 데 있다.

평가 방법은 생검된 조직을 대상으로 이식재가 분포된 전체 면적중 신생골이 형성된 면적이 차지하는 비율을 백분율로 계산하였으며, 이를 bone-forming index (BI)라 명명하였다. 이와 같이 계산된 BI를 토대로 Bio-Oss 이식후 시간 경과에 따른 신생골 형성정도를 비교 평가하고, 이식재의 흡수, 신생골편의 융합, 신생골간의 섬유화, 층판골(lamellar bone)의 형성 등을 관찰하였다.

Bio-Oss를 이용한 상악동거상술은 높은 임프란트 성공율을 보였다. 그러나 시간이 경과함에 따라 신생골 형성이 시간에 비례해서 증가하지는 않았다. 임프란트 실패가 초기에만 발생하는 것이 아니라 이식후 8개월과 9개월후에도 발생하였다. 즉 Bio-Oss를 이용한 상악동거상술은 완전 골 재생이 필요하지 않은 부위에서 사용이 가능하며, 상악동 골이식술후 흡수를 방지하기 위해 사용될 수 있다. 향후 보다 장기적이고 체계적인 연구가 필요하리라 생각된다.

Introduction

The lack of sufficient alveolar bone height has long been a deterrent to the placement of root form dental implants in the posterior maxilla. Inadequate bone volume and poor bone quality are frequent findings in the posterior maxilla and often represent a challenging clinical situation for the placement of endosseous implants. This lack of height may be the result of alveolar bone loss following tooth loss, periodontal disease, pneumatization of the maxillary sinus, or a combination of these[1,2]. A bone augmentation procedure is usually required to complete treatment[3].

Sinus grafting is a well-accepted surgical procedure for augmenting the atrophic posterior maxilla[1,4,5]. The primary factors considered in sinus grafting are the effects of the selected graft material, the time allowed for graft maturation, and the effect of the barrier membrane placement on the creation of vital bone in the sinus cavity. In addition, variables related to implant design, implant surface morphology, and the long-term stability (repneumatization) of the grafted bone volume are of secondary importance, as are the correlations of these variables with the implant success rate[2].

Methods for increasing bone volume to facilitate implant placement have been reported[5,6]. Bone graft materials have been developed, including autogenous bone, allografts, xenografts, or a combination of these materials[3]. As an augmentation material, autogenous bone is considered the so-called gold standard because remodeling takes place without an immunological response.

Some patients find the second surgical procedure required in the donor area to be too uncomfortable and prefer the use of bone substitutes. As there are a large number of bone substitutes available, surgeons must consider the biocompatibility and function of these materials with respect to the gold standard when making recommendations and assisting in the treatment-planning process[7].

Bio-Oss (Geistlich Shne AG, Wolhusen, Switzerland), a frequently used alternative bone substitute, has been evaluated in several animal[8,9] and clinical studies[10-12]. Bio-Oss is derived from bovine porous bone material that has been processed to yield natural anorganic bone material which lacks the organic component. Bio-Oss is reported to have good tissue acceptance and to provide a scaffold for new bone deposition with natural osteotrophic properties[6].

Histologic data regarding the outcomes of treatments involving sinus grafting procedures in humans are scarce[11]. Therefore, this study examined the usefulness of a

bone transplant material (Bio-Oss) in 20 patients who required maxillary sinus grafting for implant placement.

Materials and Methods

This study was approved by IRB Committee of Chosun University. Thirty-six sinus grafting was performed in 20 patients with an alveolar crest bone height in the posterior maxilla of 3-5 mm before grafting. The sinuses were grafted with Bio-Oss only. Informed consent was obtained from all patients.

Patient selection

Patients were included in the study if no systemic or local contraindications were encountered; namely, there was no history of uncontrolled diabetes, no radiation therapy to the head or neck in doses over 5,000 rads, no chemotherapy within the 12 months preceding surgery, no active sinus infections, no uncontrolled periodontal disease, and no psychological problems that would prevent long-term treatment. Smokers were advised to reduce or refrain from smoking. Smoking was not an exclusion criterion in this investigation because only 3 of the 20 patients smoked more than ten cigarettes per day.

Surgical technique

Immediately before surgery, the patients rinsed with a 0.2% chlorhexidine digluconate solution for 2 minutes. Local anesthesia was obtained with lidocaine containing epinephrine, 1:100,000.

A crestal incision, slightly displaced toward the palate, was made, and a vertical releasing incision was placed in the canine area to facilitate flap elevation. A mucoperiosteal flap was elevated, exposing the lateral wall of the sinus. A bony window, averaging 15 X 10 mm, was outlined using a no. 6 round carbide bur and without perforating the sinus membrane. After the mobility of the window was obtained, the sinus membrane was elevated starting from the inferior border of the osteotomy site. The lateral window was pushed inward and elevated superiorly, creating a new horizontal ceiling, as the membrane was carefully dissected from the medial and inferior walls of the sinus.

The grafting material (Bio-Oss) was hydrated with saline solution and gently packed into the sinus until it filled the entire cavity. Immediate implant placement was indicated when sufficient native bone quality and quantity were available to achieve primary stability after placement. The procedure was delayed 6 to 9 months after grafting for

cases in which it was considered impossible to anchor and stabilize an implant in the subsinus ridge. Screw-type, machined-surface implants were used in the patients.

All the implants were submerged. The abutments were connected during two distinct postoperative periods, at 6 and 13 months post-implant placement. Bone cores from the grafted sites were taken for histologic examination. Three to 4 weeks after soft tissue healing, the final abutments were connected, implant stability was tested manually, and prosthetic treatment was carried out. The average follow-up period was 24.4 months (range 12 to 36 months).

Histologic examination

Bone cores were harvested from the lateral wall using a 2 mm diameter trephine bur under sterile saline irrigation. The biopsies were retrieved from areas located between the implants at about 10 mm from the alveolar ridge, at a mean depth of 7 mm. The bone cores were fixed in 10% neutral buffered formaldehyde immediately, decalcified in a hydrochloric acid mixture, and doubly embedded in celloidin and paraffin wax. Serial sections of 5 ㎛ thickness were obtained and stained with hematoxylin and eosin. Bone-forming index (BI) means percentage of new bone after sinus grafting.

Results

Twenty patients studied included 9 women and 19 men ranging in age between 21 and 81 years, with a mean age of 53.1 years. For cases in which initial implant stability was obtained, the sinus floor elevation and implant placement were performed simultaneously. A total of 67 implants were placed with sinus augmentation.

The follow-up occurred 1-3 years after prosthetic treatment. In two cases, infection occurred. One implant needed an extended integration time. Three implants were lost.

There were no postoperative sinus complications. All the biopsies were obtained at 2 to 13 months after surgical therapy. There were no complications, and all the patients tolerated the procedures well. A survival rate was 95.5% (64/67 implants) for the individual implants and failure rate was 4.5% (3/67 implants) (Table 1, Figures 1 - 6).

Table 1. Histomorphometric results after sinus floor elevation

Patient No	Elapsed time (Months)	BI (%)	Failure	Remarks
1	2	5		
2	3	10		
3	4	20	Failure	49/M
4	5	20		
5	5	20		
6	5	60		
7	6	30		
8	6	60		
9	7	65		
10	7	80		
11	8	20		
12	8	20	Failure	25/M
13	8	40		
14	9	10	Failure	55/F
15	9	95		
16	10	80		
17	11	40		
18	12	40		
19	12	70		
20	13	90		

M, male; F, female

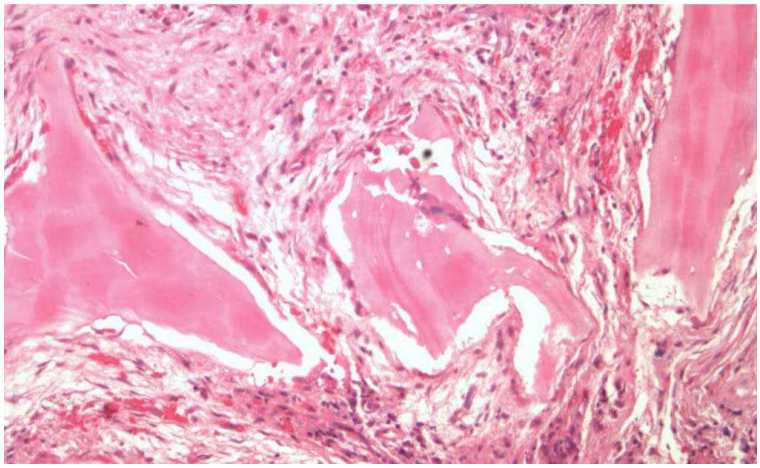

Figure 1. Histopathologic finding representing BI = 0.
Implanted Bio-Oss chips not showing new-bone forming activity are noted. The intervening stroma showed mild inflammation with fibrosis.

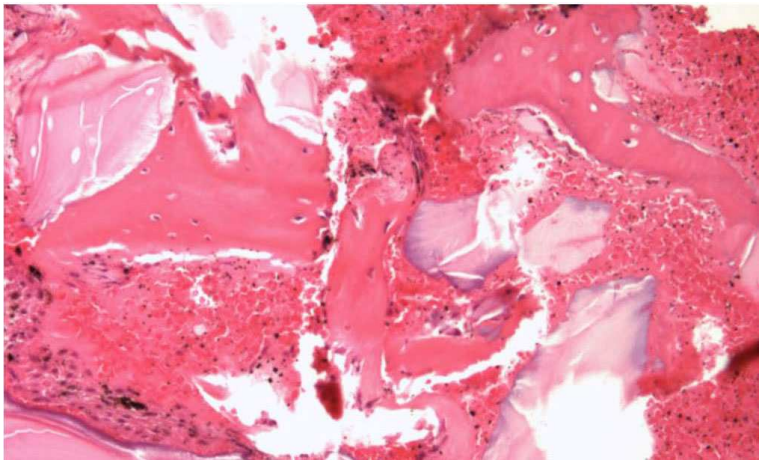

Figure 2. Histopathologic finding representing BI = 20.
Newly formed bony trabeculae with entrapped implanted chips are seen. The edges of most of the implanted chips have been resorbed.

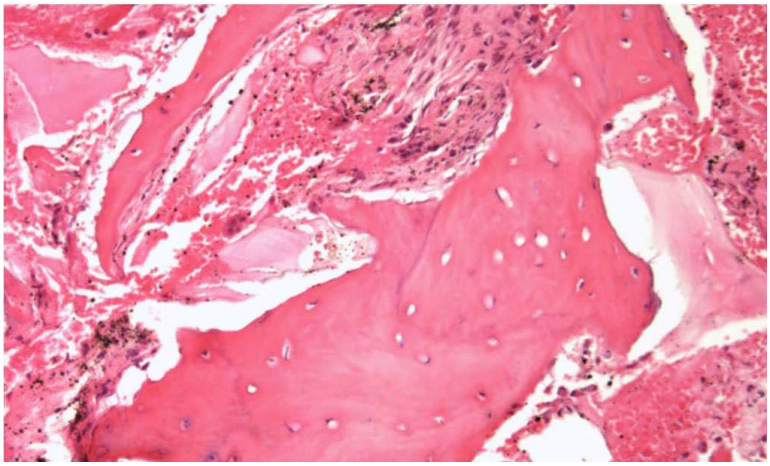

Figure 3. Histopathologic finding representing BI = 40.
Newly formed bone surrounding the implanted chips is fused. The intervening fibrotic stroma is still discernible.

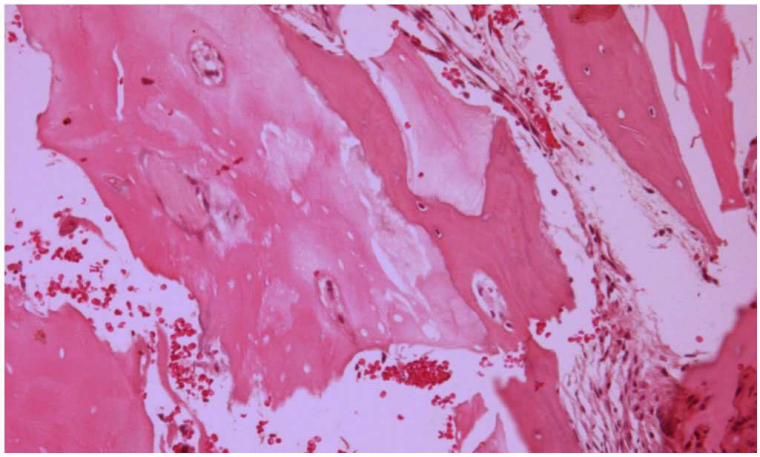

Figure 4. Histopathologic finding representing BI = 60.
New bone surrounding the implanted chip is fused more widely. Trabecular lamellae are seen.

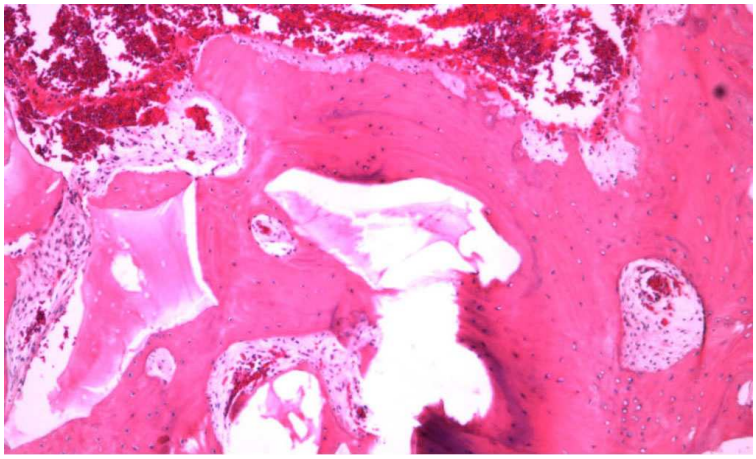

Figure 5. Histopathologic finding representing BI = 80.
Bony fusion forming more organized trabeculae is noted. The implanted chips are still entrapped in the new bone.

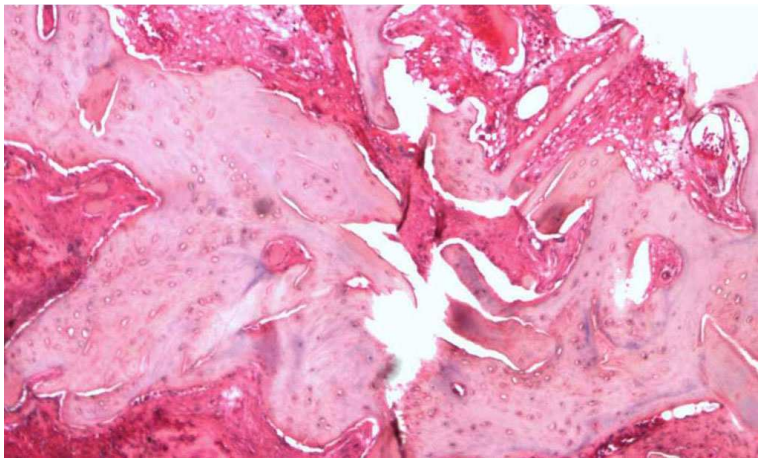

Figure 6. Histopathologic finding representing BI > 80.
More widely and tightly fused organizing trabeculae are seen. Trabecular lamellae are seen, while no obvious implanted chips are visible.

Discussion

Given the frequent lack of bone in the posterior maxilla, sinus augmentation has become a common treatment modality[13]. Sinus grafting has become a routine procedure to accommodate the maxillary bone to the needs of endosseous implants before prosthetic rehabilitation[14]. The ability to augment the sinus floor has expanded the scope of implant dentistry dramatically. Clinical and scientific studies of the efficacy of this procedure abound, but the best material to use for augmentation remains controversial, with autogenous bone, freeze-dried bone, xenografts, and alloplasts all being advocated[15,16].

Dental implant placement associated with sinus grafting in a severely atrophic maxilla can be performed in a one- or two-stage surgical procedure, depending on the height of the residual alveolar bone[17]. Peleg *et al.*[18] advocate a single-step procedure for patients with as little as 3 mm of alveolar bone height before augmentation grafting. Cordioli *et al.*[16] recommend 3 to 5 mm of bone height before grafting for predictable simultaneous implant placement. Mazor *et al.*[17] recommend a minimum of 4 to 5 mm for a one-stage procedure, while Kim suggests a minimum of 4 mm for a simultaneous sinus grafting and one-stage procedure[19].

Nishibori *et al.*[20] compared two sinus augmentation procedures, one grafted with demineralized freeze-dried bone (DFDB) and the other with autogenous iliac bone. The sample from the sinus grafted with autogenous bone was obtained 8 months postoperatively. The autogenous specimens demonstrated new bone formation with increased quantity and improved quality compared with the specimens obtained from the sites grafted with allogeneic bone. All eight of the implants placed in autogenous grafts were clinically osseointegrated at stage 2. These findings suggest that autogenous sinus grafts produce bone of adequate quantity and quality for implant placement.

Jensen and Sennerby[21] reported the placement and subsequent retrieval of titanium microimplants in a histologic investigation of the implant-tissue interface in conjunction with maxillary sinus grafting. Six implants were retrieved at 6 to 12 months after maxillary sinus augmentation with particulate autogenous bone grafts. Significantly more bone was found at autografted versus allografted implants. The use of autogenous bone for augmentation of the maxillary sinus floor resulted in a greater amount of viable bone surrounding the implant.

The use of bovine hydroxyapatite (Bio-Oss, Geistlich Pharmaceutical, Wolhusen, Switzerland) has been suggested for maxillary sinus grafting procedures before or in conjunction with implant placement[19,22]. Bio-Oss is deproteinized, sterilized bovine bone with 75 to 80% porosity and with a crystal size of approximately 10 nm in the form of cortical and cancellous granules and cortical and cancellous blocks. Bio-Oss has inner macropores of similar size to natural cancellous bone. Bio-Oss appears to be replaced by host bone more readily than is hydroxyapatite when used in alveolar ridge restoration, and it appears to undergo physiological remodeling with incorporation into the host bone. Moreover, Bio-Oss is highly biocompatible with oral hard tissues in animals and humans and meets the criteria of an osteoconductive material[22].

Wallace *et al.*[2] reported that the addition of 20% autogenous bone to a xenograft mix significantly increased the amount of vital bone in the core samples. The minimum amount of autogenous bone that is necessary for this increase could not be determined.

Young *et al.*[23] histologically compared Bio-Oss and autogenous bone grafts in adult rabbits. After 12 weeks, the implanted autogenous bone was actively resorbed by multinucleated cells, and new bone was formed in close apposition to the particles. By contrast, implanted anorganic xenogenic bone was degraded to a much lesser extent, and new bone was seen adjacent to the anorganic bone particles without signs of resorption.

Schlegel *et al.*[7] compared the usefulness of Bio-Oss and autogenous bone as materials for sinus augmentation. They reported that the restoration of the defects was achievable owing to the non-resorptive properties of Bio-Oss. The bone substitute appeared to behave like a permanent implant, whereas the volume of the area augmented by autogenous bone decreased over the observation period.

Different opinions have been expressed regarding the degradation of Bio-Oss. In some cases, the Bio-Oss was replaced by host bone rapidly[24], while, in other cases, few resorption lacunae were observed, indicating slow resorptive activity[9,25] or no resorption at all[11].

Resorption is an additional factor affecting the successful osseous penetration of bone substitute material. This so-called biodegradation should take place at a time appropriate to new active bone formation, so that the integrity of the conducting structure is not put at risk. Should the bone substitute material survive as a conducting structure, the newly formed bone tissue is merely a filler[26].

The resorption of bovine bone substitute material is controversial. Some publications

based on animal studies have detected histological evidence of the resorption of Bio-Oss[25,27-29]. Schlickewei and Paul[30] described the resorption of the xenogenic material as a physiological remodeling process that takes 1 to 5 years in humans. Other authors also suggest the slow, but predictable, resorption of Bio-Oss. Using a rabbit model, Klinge *et al.*[27] found that Bio-Oss was resorbed progressively over a 14-week period in adult rabbits. Osteoblasts were close to the particle surface. Clergeau *et al.*[31] reported that some anorganic bovine bone particles remained at 36 weeks, while Wallace *et al.*[2] observed the complete absence of anorganic bovine matrix after 20 months. Berglundh and Lindhe[25] also noted a significant decrease in the volume of Bio-Oss particles between 3 and 7 months after implantation in beagle dogs. They concluded that Bio-Oss becomes integrated and subsequently replaced by newly formed bone. Zitzmann and Schrer[32] obtained 100% success with Bio-Oss-grafted sinuses using Branemark System implants in a one- or two-stage procedure. Valentini *et al.*[33] reported that the Bio-Oss density showed a slight decrease in 12-month biopsy samples as compared with 6-month samples, suggesting slow yet active resorption of the Bio-Oss material. However, the sample size was too small to allow a statistical evaluation.

These data contrast with the observations of Pinholt *et al.*[34], who reported the very slow substitution of anorganic bone in rats. Dis *et al.*[35] found only limited resorption of Bio-Oss particles at 9 months. Avera *et al.*[36] found Bio-Oss particles present in the graft area in humans at 44 months. Piattelli *et al.*[22] reported that graft particles were present after 4 years in augmented human sinus specimens. In experimental alveolar ridge augmentation in rats using Bio-Oss, Pinholt *et al.*[34] found giant cells and an inflammatory reaction around the material.

Bio-Oss appears to undergo slow resorption. Similar results were seen in a study on dogs in which most of the grafting material was still in place after 5 months of observation[37]. Wetzel *et al.*[37] asserted that the bone graft appeared to have acted as a scaffold along which new bone formed.

Radiographic examination has documented the presence of Bio-Oss granules after up to 7 years[38], and Bio-Oss has been demonstrated histologically at 44 months after the augmentation of the alveolar ridge of the maxilla[39]. These results led us to doubt the resorbability of the material.

Schlegel *et al.*[7] found that the xenogenous Bio-Oss was nearly undisturbed by resorption and measured a loss of approximately 15% after 90 and 180 days. The

histologic analysis did not demonstrate any signs of resorption of the Bio-Oss scaffold; only the ingrown native bone seemed to participate in the remodeling process. The initial volume reduction was explained by shrinkage of the connective tissue and its conversion in native bone. Bio-Oss was not resorbed, and native bone integrated into the material by penetrating the scaffold and forming vital bone layers on the avital trabeculae of the Bio-Oss structure. The interconnecting pores of the material allowed complete camouflage of this foreign body, and the ingrown vital bone layers participated in the turnover involved in the remodeling process.

The time allowed for bone healing before implant placement may be important, as new bone formation with the Bio-Oss particles is essential for the osseointegration of implants[11].

Our results are semi-qualitative and semi-quantitative, and evaluate the change in the bone-forming index (BI) with time after surgery and the quality of newly formed bone. In our experiment, it was impossible to group the patients consistently in order to determine representative results owing to the time differences. Therefore, the BI value was divided by a constant interval, and appropriate representative pictures are presented. It is impossible for us to state an interpretation along the lines that 'Fig. 1 was the result in Patient A with a certain number of months after surgery'. Future longer-term, systemic studies are required.

In this study, the bone-forming index obtained did not follow a progredient time curve. The healing responses of individual patients appeared to have a much greater effect on new bone formation than did the resting time of the xenograft.

CONCLUSION

Our findings support the use of Bio-Oss as a bone substitute in maxillary sinus grafting procedures. When used in sinus grafting, Bio-Oss may lead to appropriate osseointegration of a dental implant and can be used to create adequate bone volume before implant placement. Bio-Oss undergoes very slow resorption; in our specimens, Bio-Oss particles were present 14 months after their placement.

The outcome of this limited study indicates that Bio-Oss can be used as a material for sinus grafting in cases in which full bony regeneration of the augmented area is not required. The use of Bio-Oss can prevent unwanted early resorption of the augmented area in the sinus.

Long-term studies are needed to determine whether anorganic xenogenic bone may be regarded as a resorbable material and whether any side effects occur as a result of this material's tendency to linger in the recipient bed. Long-term follow-up studies after prosthetic loading of the inserted implants are also needed to prove whether an appropriate implant site can be obtained upon grafting using Bio-Oss.

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