Histological and Histomorphometrical Determination of the Biogradation of β-Tricalcium Phosphate Granules in Maxillary Sinus Floor Augmentation: A Prospective Observational Study

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Introduction: *We have recently used highly pure β-TCP (beta-tricalcium phosphate) as the bone grafting material to avoid highly invasive autogenous bone grafting. We evaluated the osseoconduction potential of highly pure β-TCP in sinus augmentation surgery treatment.*

Materials and Methods: *The study group comprised 13 patients who underwent maxillary sinus floor augmentation with β-TCP alone. Seven patients underwent sinus augmentation and implant placement simultaneously. Six patients were treated with a staged approach. Six months after surgery, specimens were obtained from 7 patients (for lateral biopsy) and 6 patients (for vertical biopsy).*

Results: *Histological and histomorphometrical analysis showed a mean bone proportion of 30.8% (vertical) and 12.0% (lateral) for new bone formation and good integration of the β-TCP. New bone formation was lower in the lateral biopsy specimens than in the vertical.*

Conclusion: *Highly pure β-TCP is a safe bone-grafting material with superior osteoconductive properties. Histologic and radiographic examinations indicate that β-TCP is slowly resorbed, which results in unresorbed graft material remaining even 6 months after the procedure, and that new bone replacement occurs slowly for approximately 1 year. (Implant Dent 2017;26:275–283)*

Key Words: calcium phosphate, biopsy, biomaterial resorption, CBCT

Tooth extraction results in vertical and horizontal resorption of the alveolar bone; thus, maxillary sinus pneumatization can simultaneously develop in the maxillary molar region after tooth extraction.[1,2] The use of autogenous bone, which is the gold standard, was first reported by Boyne and James[3] who used iliac bone grafts, and has been used as grafting material for maxillary sinus floor augmentation. The osteogenic, osteoinductive, and osteoconductive properties of autogenous bone are ideal; however, the use of autogenous bone places great physical stress on patients because of the need for surgery at the donor site. More than 30 years ago, a procedure for maxillary sinus floor augmentation was published and has become the established method. Reports indicate that this inlay graft method has a higher success rate than the onlay graft method and recovery may begin in the periphery of the graft and progress towards its center over time.[4,5] Therefore, it is possible that angiogenesis develops in the grafting material from many directions and issues concerning the strength of the grafted bone do not have to be considered because an external load is not exerted.[6,7] Thus, a surrounding environment suitable for host bone regeneration may be a reason to not use autogenous bone, which has a particularly high osteogenic property. Therefore, allogeneic bone, xenogeneic bone, and synthetic bone substitutes such as hydroxyapatite (HA) and β-TCP with or without

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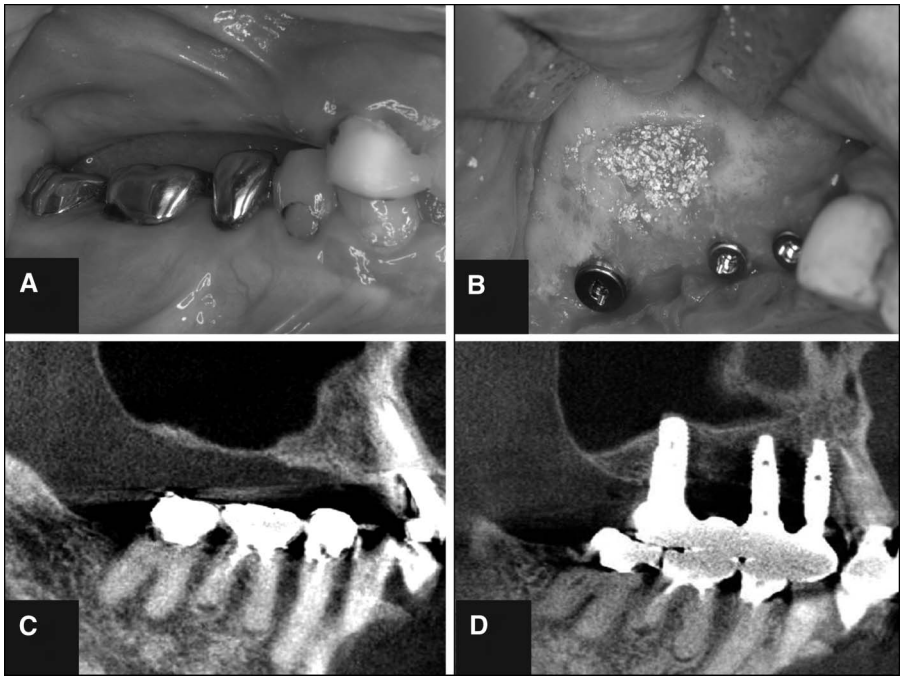

Fig. 1. The treatment protocol of the present study for the simultaneous approach. **A**, The preoperative intraoral photograph shows the right premolar and molar sites. **B**, Simultaneous maxillary sinus floor augmentation and implant insertion. **C**, The preoperative cone-beam computed tomography (CBCT) radiograph. **D**, The 1-year postoperative CBCT radiograph.

growth factors have all been applied as grafting materials in maxillary sinus augmentation. In the 1996 Sinus Consensus Conference, it was concluded that these materials had highly predictable outcomes and showed no difference in their success rates.[8] In Japan, synthetic bone-grafting materials such as HA and β-TCP have been used in dental and orthopedic surgery. Hydroxyapatite is the main component of bone. It has good affinity with bone proteins (eg, osteocalcin, osteopontin) and good osteoconductivity that activates osteoblasts and alkaline phosphatase (ALP). However, it also interferes with bone remodeling because it is not completely absorbed. In the field of orthopedics in Japan, HA has been used primarily for the internal fixation of fractures, arthroplasty, and bone reconstruction after tumor resection; however, because the material is incompletely absorbed, secondary fractures attributable to the insufficient strength and resilience of the agent have been reported.[9,10] By contrast, β-TCP, which Bhasker et al[11] developed and studied in the 1970s, is an ideal bone-grafting material because it replaces native bone through the process of absorption and elution. β-Tricalcium phosphate is effective for dental applications such as sinus augumentation.[12–14] β-Tricalcium phosphate was not initially approved for use in Japan. However, highly pure β-TCP was subsequently developed, and in 1999, this material was first approved for use in the field of orthopedic surgery.[15–17] Most clinical studies of highly pure β-TCP were performed in nondental fields. We previously evaluated clinically and radiographically the long-term prognosis of sinus augmentation treatment using highly pure β-TCP and reported that it was an effective bone-grafting material.[18] The purpose of the current study was to evaluate histologically and histomorphometrically the osseoconduction potential of highly pure β-TCP in sinus augmentation surgery.

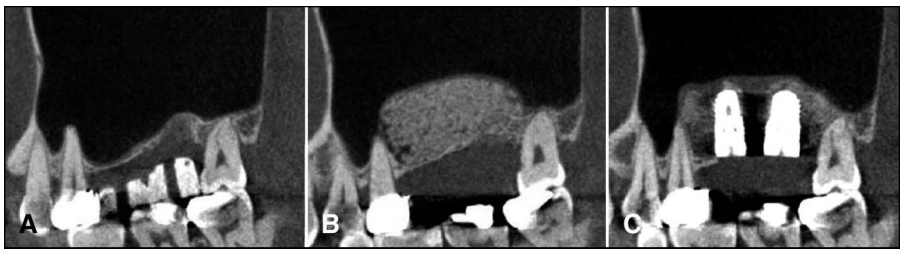

Fig. 2. The treatment protocol of the present study for the staged approach. **A**, The preoperative cone-beam computed tomography (CBCT) radiograph. (B) The postoperative CBCT radiograph after maxillary sinus floor augmentation. **C**, The insertion of the implant 6 months after maxillary sinus floor augmentation.

MATERIALS AND METHODS

All experiments were approved (approval number: 309) and followed the guidelines of Tokyo Medical and Dental University. This study was a prospective observational study. The study participants were patients who underwent maxillary sinus floor augmentation with β-TCP alone and implant placement for a unilateral maxillary defect at Clinic for Implant Dentistry at the Dental Hospital of the Tokyo Medical and Dental University (Tokyo, Japan) from January 2012 to January 2013. Patients with good primary stability of the implant due to existing bone underwent simultaneous implant placement. However, patients in whom simultaneous implant placement was deemed impossible because of the quality or amount of bone underwent implantation approximately 6 months after maxillary sinus floor augmentation. The biopsy specimens were collected from the lateral wall in in patients who had the simultaneous implant procedure and vertically from the scheduled implant site in patients for whom implantation was delayed (Figs. 1 and 2).

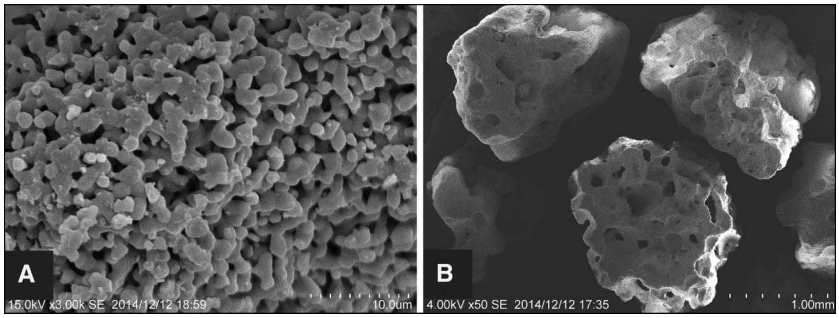

Fig. 3. Scanning electron microscope of OSferion (Olympus Terumo Biomaterials Corp., Tokyo, Japan). This product contains highly purified beta-tricalcium phosphate (β-TCP) produced through mechanochemical processing, and features 75% porosity with macropores with a diameter of 100 to 400 μm and micropores with a diameter of <1 μm. **A**, The low-power field image. **B**, The high-power field image.

Table 1. The Surgical Procedure, Patient Sex and Age, Implant System and Length, and Residual Bone Height at the Implant Site

Patient	M/F	Age (y)	System (No. of Implants)	Length of Implants (mm)	Residual Bone Height
Staged approach					
1	M	46	Straumann (3)	10, 10, 10	1.3, 3.8, 4.6
2	F	54	Xive (2)	9.5, 9.5	0.9, 4.0
3	M	50	Brånemark (2)	10, 10	1.2, 3.6
4	M	55	Straumann (2)	12, 12	1.0, 3.8
5	F	62	Brånemark (2)	10, 10	0.8, 4.6
6	F	56	Straumann (1)	10	1.4
			N = 12		2.6 ± 1.6*
Simultaneous approach					
7	F	54	Xive (3)	11, 11, 11	2.6, 3.9, 5.8
8	F	67	Xive (3)	9.5, 11, 11	3.0, 3.2, 6.7
9	F	55	Brånemark (2)	10, 10	2.8, 4.6
10	F	50	Brånemark (2)	10, 13	3.9, 5.6
11	F	56	Xive (2)	11, 11	3.0, 4.9
12	M	42	Xive (2)	11, 11	3.2, 4.6
			N = 14		4.1 ± 1.3*
Total (n = 12, 6 mo)			N = 26		3.4 ± 1.6*
13 (lateral: n = 1, 12 mo)	F	65	Xive (2)	9.5, 11	2.6, 5.6

The total number of patients is 13 patients, representing 13 maxillary sinuses and 28 implants.
Straumann (Straumann, Basel, Switzerland); Xive (Dentsply, Mannheim, Germany); Brånemark (Nobel Biocare, Zürich, Switzerland).
*The data are presented as the mean value ± the standard deviation.

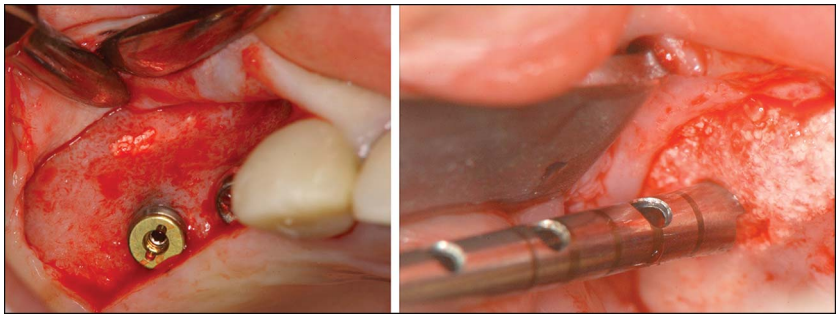

Fig. 4. The clinical findings of the open sinus on biopsy 6 months after surgery. The degree of residual grafting material varied depending on the patient (a φ2 mm trephine bur was used).

Patient Selection

Patients were eligible for the study if they met the following criteria: (1) the preoperative computed tomography examination showed a distance of <5 mm from the alveolar crest of the planned site of implant insertion to the maxillary sinus floor and (2) they had good oral hygiene without any severe periodontal disease or any major dental problems that may have affected postoperative surgery results. Patients were excluded from the study if they met the following criteria: (1) they were completely edentulous and postoperative denture wearing may have affected the results, (2) they required sinus floor augmentation and buccal onlay graft at the same time because of a narrow bone width or they required large-scale bone graft or floor augmentation such as that for guided bone regeneration and split crest, (3) they had insufficient occlusal clearance or an extremely poor tooth crown-to-root ratio, based on Cawood and Howell classification V, (4) they had a history of diabetes, osteoporosis, bisphosphonate administration, immunological diseases (eg, rheumatoid arthritis and chronic sinusitis), otolaryngological problems, or other untreated systemic disease, or were smokers. In this study, all patients provided informed consent with regard to bone-grafting material use, the surgical procedure, biopsy, and multiple cone-beam computed tomography (CBCT) scans. This study was performed with the approval of the Ethics Committee of Tokyo Medical and Dental University, Tokyo, Japan (approval number: 309).

Surgical Procedure

Patients underwent preoperative examinations, after which maxillary sinus floor augmentation and implant placement were performed by a simultaneous approach or by a staged approach. A skilled surgeon performed the maxillary sinus floor augmentation using the technique of Boyne et al.[3] Patients were maintained under intravenous sedation with local anesthesia (2% lidocaine hydrochloride solution containing epinephrine 1:80,000). An incision was formed in the alveolar crest at

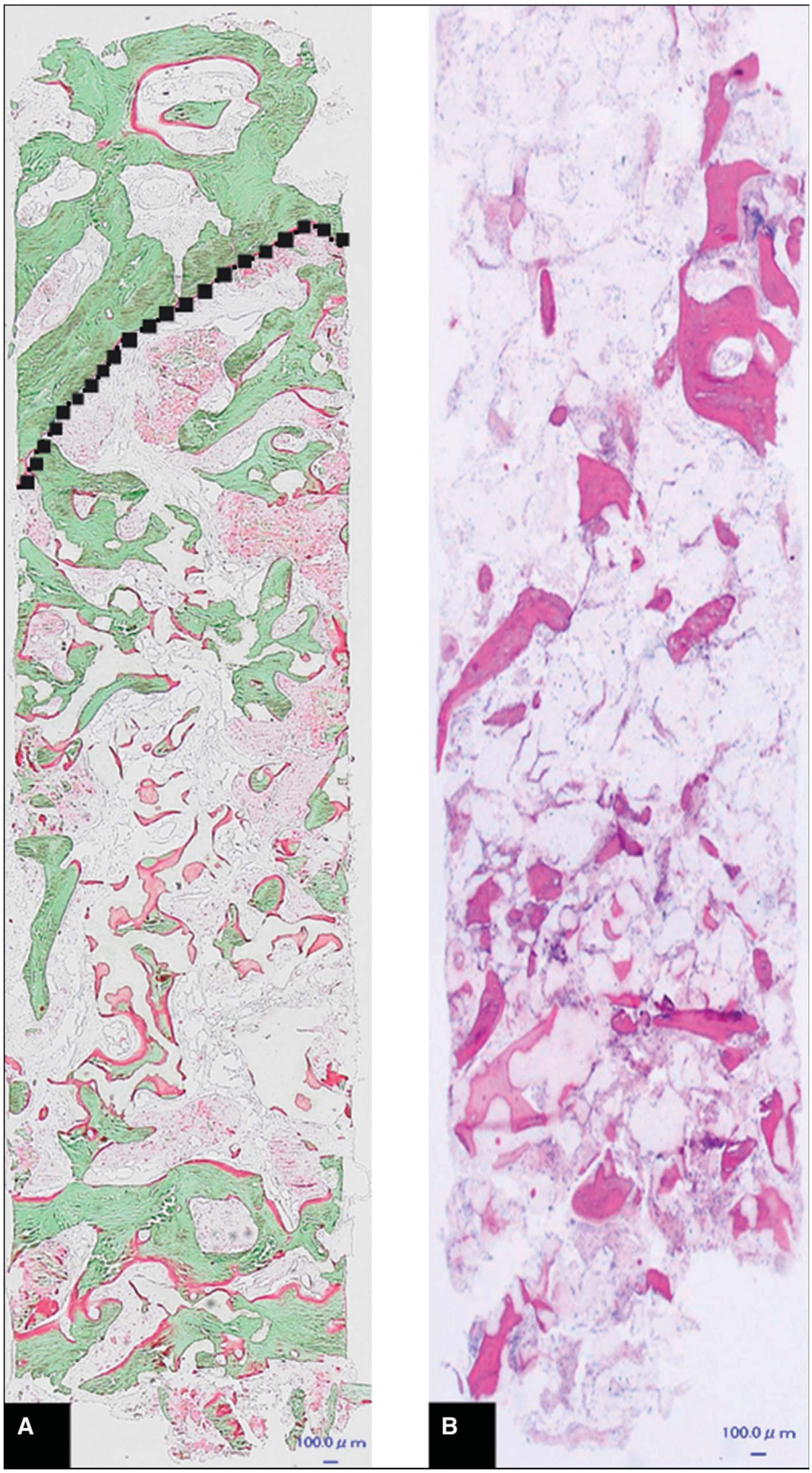

Fig. 5. **A**, A vertical specimen (the dotted line indicates that the transplantation site is below the margin of the existing bone). **B**, A lateral specimen (all regions are the transplantation sites).

the buccolingual midline of the defect region and a mucoperiosteal flap was separated. A vertical incision was formed at least one tooth away and in the defect region ≥10 mm away. To avoid perforating the mucous membrane of the maxillary sinus as much as possible, the lateral wall was molded using an elliptical bur, diamond bur, or piezoelectric device until just reaching the mucous membrane of the maxillary sinus, and the lateral wall of the maxillary sinus was fractured using a bone damper (ie, the trap door method). The mucous membrane of the maxillary sinus was carefully elevated from the inferior wall of the maxillary sinus using a sinus curette. The lower margin of the lateral wall was determined as 2 mm higher than the existing bone, and the upper margin was determined by the length of the inserted implant fixture. In patients undergoing the simultaneous approach, the implant cavity was then prepared in accordance with the protocol of the implant manufacturer. The bone-grafting material, which was soaked beforehand in physiological saline, and the fixture were installed simultaneously.

The wound was then sutured using horizontal mattress sutures and simple sutures using nylon thread. To prevent infection, the cephem antibiotic cefcapene pivoxil hydrochloride (100 mg 3 times daily for 1 week) was administered after surgery. If inflammation of the maxillary sinus persisted, the prescription was extended 1 week afterward. In addition, the patients were prescribed the anti-inflammatory agent loxoprofen sodium (60 mg 3 times daily for 1 week). They were instructed to disinfect the oral cavity by gargling with a mouthwash (0.12% chlorhexidine gluconate) 3 times daily for approximately 2 weeks. The sutures were removed approximately 2 weeks after the surgery, and the wound was then checked monthly to assess the progress of postoperative healing.

Bone-Grafting Material

The grafting material was OSferion (Olympus Terumo Biomaterials Corp., Tokyo, Japan), which consists

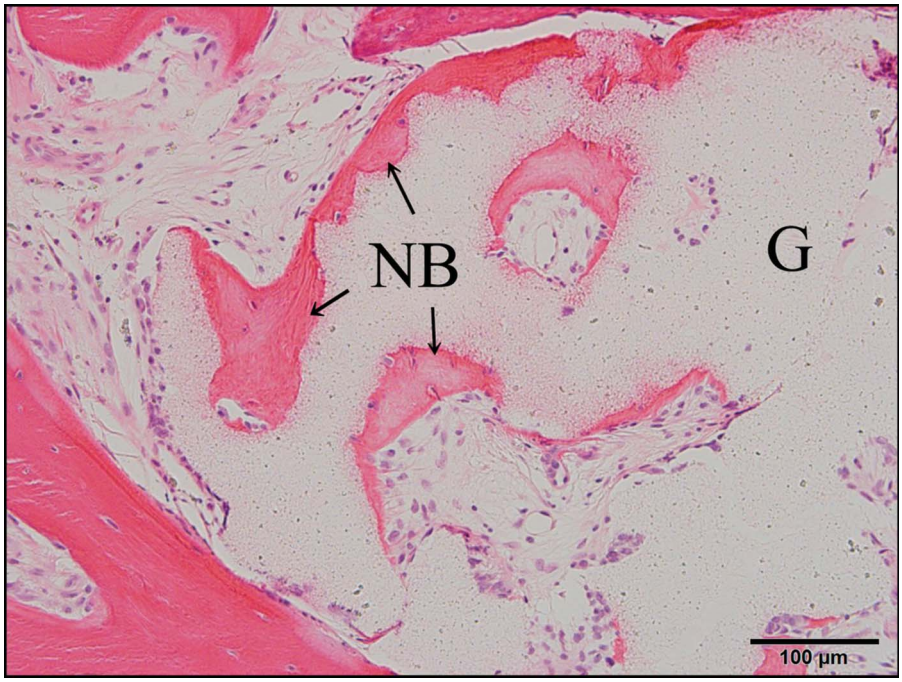

Fig. 6. Hematoxylin and eosin staining of the biopsy samples 6 months after surgery. Most of the beta-tricalcium phosphate (β-TCP) has remained, although the granules have been replaced by new bone associated with bone cells. No added substances exist between the new bone and β-TCP. G, residual β-TCP; NB, new bone.

of β-TCP calcium phosphate [$(Ca_3PO_4)_2$] and has a biphasic crystalline structure (G1-1 diameter of 0.1–1.5 mm). This grafting material possesses osteoconductive and absorptive properties; therefore, autogenous bone should replace it over time. OSferion was synthesized by a mixture of dicalcium phosphate dihydrate ($CaHPO_4 \cdot 2H_2O$) and calcium carbonate ($CaCO_3$) at a molar ratio 2:1 in a pot mill. After the slurry was dried at 80°C and sintered at 1050°C, calcium-deficient hydroxyapatite was converted to β-TCP (ie, a mechanochemical method). This method of preparation is distinctive in that it allows the Ca/P ratio to be easily regulated and produces a highly pure sinterable powder. OSferion is a highly pure product in which the x-ray diffraction pattern shows a monolayer of β-TCP. It has 75% porosity with macropores of diameter 100 to 400 μm and micropores of diameter <1 μm, which is the optimum configuration for the promotion of angiogenesis and surface absorption. Increasing the surface area creates the porosity and the compressive strength is approximately 3 MPa. OSferion has been reported as a safe bone-grafting material with high purity and biocompatibility, based on physical, chemical, biological, and implant tests[17,19] (Fig. 3).

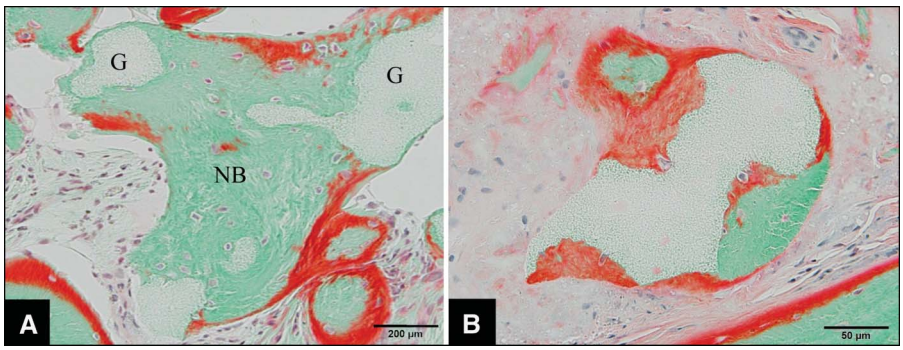

Fig. 7. Villanueva–Goldner bone staining of samples obtained 6 months after surgery. Osteoids are on the surface of the new bone, which suggests that the new bone is still replacing the grafting agent. Osteoblast-like cells are distributed around the transplanted bone. The red portions indicate the osteoids. G, residual beta-tricalcium phosphate; NB, new bone.

Histological Examination

From the patients who underwent simultaneous implant placement, tissue was sampled from the lateral wall using a trephine bur to avoid the implants or adjacent tooth at the time of the second-stage surgery. Biopsies included only the transplantation site, and were collected so that the biopsy site did not contain existing bone. From the patients who underwent the staged implant placement, vertical specimens were obtained from the future implant bed. One sample was collected from each patient, and samples were collected using a trephine bur with an inner diameter of 2 mm.

After the collection, the samples were fixated immediately in 10% buffered formalin solution. The specimens were then prepared by first dehydrating and degreasing them, and then embedded in a methylmethacrylate resin block for sectioning, using an ISOMET-1000 (Buehler, IL); 6-μm sections were obtained using a microtome to produce Villanueva–Goldner bone staining specimens and hematoxylin and eosin staining specimens.

Histomorphometrical Analysis

The slides were observed by transmission light microscope and fluorescence/phase contrast microscope (Biozero BZ-8000; Keyence, Japan) to examine the morphology of specimens; thereafter, images were captured by a built-in camera for histomorphometrical analysis. Images from each patient were compiled into a database to allow for whole measurements. The ratios of new bone, residual graft material, and

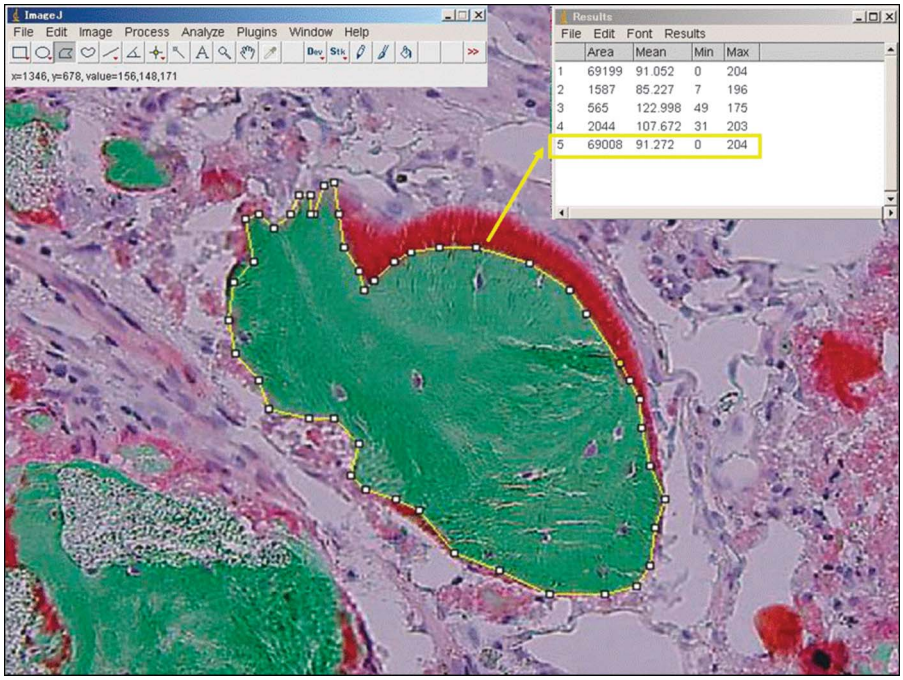

Fig. 8. The ratios of new bone, residual graft material, and soft tissue were measured using the image analysis software Image J (public domain).

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Radiographic Examination

Patients underwent CBCT evaluations 3 times: before surgery, immediately after surgery, and at 6 months after surgery. We used a dental CBCT device (FineCube; Yoshida Dental, Tokyo, Japan). The imaging mode was set to the standard mode with a voxel size at 0.146 mm^3 and field of view of φ82.00 mm × 75.1 mm.

Statistical Analysis

In this study, statistical analysis of the ratio of new bone and residual β-TCP of 12 patients at 6 months after surgery was conducted using the Mann–Whitney *U* test. Significance was set at $P < 0.05$.

RESULTS

Clinical Evaluation

The mean age of the 13 patients was 56.1 years (range, 45–69 years) and the mean residual bone height: existing bone height to the maxillary sinus at implant site was 3.4 ± 1.6 mm ([staged procedure] 2.6 ± 1.6 mm: [simultaneous procedure] 4.1 ± 1.3 mm). Twenty-eight implants were placed in the premolar and molar regions. Details of the cases are in Table 1. Seven patients were treated simultaneously by sinus augmentation and implant placement, and 6 patients were treated with the staged approach. Six months after the sinus augmentation surgery, biopsy specimens were obtained from each patient (7 patients, lateral biopsy; 6 patients, vertical biopsy).

Implant osseointegration was achieved in all patients without any complications. During the observation period between January 2012 and January 2016, the implant survival rate was 100%. The mean postoperative observation period was 3 years and 6 months (range, 37–46 months). At the time of biopsy, macroscopic observation of the lateral wall of the maxillary sinus revealed different degrees of β-TCP replacement by new bone. Twelve samples were collected for biopsy at approximately 6 months after maxillary sinus floor augmentation, and one sample was collected ≥1 year after surgery because this time was convenient for the patient to visit hospital (Fig. 4; Table 1).

Histological Examination

Tissue samples were collected from all patients and examined histologically at 6 months after sinus floor augmentation surgery. Most of the β-TCP remained, and the granules had been replaced by new bone. In sections stained with Villanueva–Goldner bone staining, osteoids were on the surface of the new bone, which suggests that the grafting material was still being replaced by the new bone. No added substances were observed on the new bone interface; β-TCP was completely fused to the new bone. Osteoblast-like cells were securely fused to the β-TCP surface; therefore, it was expected that active bone formation would progress. Tissue samples obtained 12 months later indicated that, over time, the residual β-TCP had decreased and had become buried in the trabecular bone (Figs. 5–7).

Table 2. Histological Examination Results

Patient	New Bone	β-TCP
Staged approach		
Vertical specimens (%)		
1	18.5	8.8
2	30.0	2.8
3	37.6	5.1
4	35.9	12.4
5	38.4	11.9
6	24.6	9.0
Mean	30.8	8.3
Median	33.0	8.9
Simultaneous approach		
Lateral specimens (%)		
7	13.2	31.6
8	9.9	30.3
9	10.2	44.0
10	9.5	22.7
11	17.5	34.7
12	11.5	35.9
Mean	12.0	33.2
Median	10.9	33.2
P (vs the vertical specimen)	0.004	0.004
13 (lateral, 12 mo) (%)	34.20	6.90

The ratios of new bone and residual β-TCP to the overall tissue are calculated. Vertical specimens (from 6 patients) were obtained 6 months after surgery, and lateral specimens (from 7 patients) were obtained 6 months after surgery, except for 1 lateral sample which was obtained ≥1 year after surgery. The ratio when the entire measurement site is considered is 100%; the *P* values are based on the Mann–Whitney *U* test.

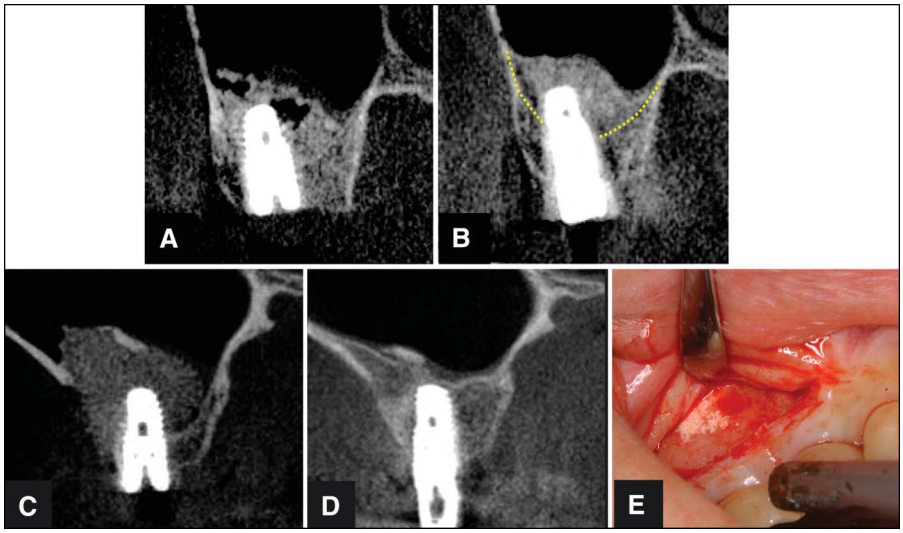

Fig. 9. **A**, Radiographic examination of a patient immediately after surgery and (**B**) 6 months after surgery. The beta-tricalcium phosphate (β-TCP) could be differentiated from existing bone on cone-beam computed tomography (CBCT) even 6 months after surgery. The dotted line indicates the margin between the existing bone and the transplanted bone. **C**, Radiographic examination of another patient immediately after surgery. **D**, Radiographic examination of the implant at 12 months after surgery. The margin between the β-TCP and the existing bone is unclear because of bone remodeling progression. **E**, A patient in whom healing was confirmed at the lateral site 2 years after maxillary sinus floor augmentation during apicoectomy on a neighboring tooth. Some areas have hardened, although complete absorption has not occurred.

Histomorphometrical Analysis

The ratio of new bone and the ratio of residual β-TCP after 6 months, given that the entire biopsy site was 100%, was 30.8% ± 8.0% and 8.3 ± 3.8% (6 vertical biopsy sites), respectively, and 11.7% ± 3.0% and 33.2% ± 7.0% (6 lateral biopsy sites), respectively. In one patient who was followed up for ≥1 year (and had undergone a lateral biopsy), the new bone ratio was 34.20% and the residual β-TCP ratio was 6.9%, which clearly demonstrated that the replacement of β-TCP by new bone had progressed (Fig. 8; Table 2).

Statistical Analysis

We compared the lateral biopsy group and the vertical biopsy group by statistical analysis using the Mann–Whitney *U* test with significance level set at 5%. The results indicated that the lateral biopsy group showed significantly little new bone and a large amount of residual β-TCP in comparison with the vertical biopsy group ($P = 0.004$).

DISCUSSION

In the present study, we used β-TCP, which is a bone substitute with an absorptive property with high biological affinity and osteoconductive properties. The material does not have osteoinductive properties; therefore, graft success depends on whether angiogenesis and the growth of surrounding cells occur on the grafting agent's surface and into the macrostructure of the grafting agent. β-Tricalcium phosphate is absorbed and degraded more rapidly than HA; therefore, it is a promising material that may be completely replaced by autogenous bone. In their experiment, Artzi et al[20] compared bovine bones and β-TCP in filling defect areas in dogs. They reported that β-TCP was absorbed within 24 hours and replaced by autogenous bone. By contrast, with bovine bone, approximately 30% of the granules remained. Thus, β-TCP was considered the ideal grafting material.[20] Absorption and degradation are affected by the production process, purity, and pore properties. β-Tricalcium phosphate is difficult to produce because the temperature and the pH have to be carefully controlled during the production process and many opportunities exist for contamination. X-ray diffraction analysis shows that contamination by HA, aluminum, and silicon occurs in some instances. Such impurities have a negative impact on histological affinity. OSferion contains highly purified β-TCP produced through mechanochemical processing and accelerates the optimum configuration for the promotion of surface absorption, angiogenesis, and bone formation.[15,17] Jarcho[21] reported that the mechanism of the resorption of β-TCP and replacement to new bone seems to be 2 different processes: (1) solution-mediated disintegration and (2) cell-mediated disintegration. The solution-mediated process causes diffusion from high concentration to low concentration, and it has a sufficient effect on the elution and resorption processes because it is in contact with the blood over a wide area during the early grafting phase. Based on histological research on animals, OSferion is absorbed primarily through biological absorption by cells, and osteoblasts differentiate to secrete the bone matrix, which subsequently leads to calcification and absorption by tartrate-resistant alkaline phosphatase-positive cells. Matunaga et al[22] analyzed how osteoclasts resorb OSferion by using scanning electron microscopy. They reported OSferion was resorbed by mature osteoclasts with the formation of multiple spine-like crystals at the exposed areas, independently of clear actin ring formation. We believe that OSferion disintegration progressed because of phagocytosis caused by a cell-mediated process.[21–23]

During the observation period, the survival rate of the implant and success rate of maxillary sinus floor augmentation were 100%. Histological examination by biopsy confirmed the presence of osteocytes in the new bone; β-TCP histologically caused no foreign-body reaction or inflammatory changes, and was replaced by autogenous bone. Furthermore, histomorphometrical analysis after 6 months revealed a mean new bone ratio of 30.8% and 11.7% in the vertical and lateral biopsy specimens, respectively. In previous reports on maxillary sinus augmentation using β-TCP (Cerasorb; Curasan AG, Kleinosteim, Germany), Szabo et al[12] compared bilateral maxillary sinus augmentation at 6 months postsurgery in

patients who had β-TCP or iliac bone grafts and reported a new bone ratio of 36.5% in the β-TCP group and 38.3% in the control group (ie, autogenous bone). In a similar experiment, Suba et al[13] reported a new bone ratio of 32.4% in the β-TCP group and 34.7% in the control group (ie, autogenous bone), which were similar outcomes to those for the autogenous bone. By contrast, Zijderveld et al[14] conducted a comparative clinical study of maxillary sinus augmentation using β-TCP (Cerasorb) and autogenous bone (ie, intraoral). They reported a new bone ratio of 17.0% in the β-TCP group (control group, 41.0% [autogenous bone]), which indicated that the autogenous bone graft was more effective.[14] In the present study, we obtained biopsy samples through the lateral window of the sinus in approximately one-half of the patients. Zijderveld et al[14] performed lateral biopsies, whereas Szabó et al[12] and Suba et al[13] performed vertical biopsies from the alveolar crest. It may be that bone regeneration within the maxillary sinus gradually progresses from the periphery of the bone graft towards its center. Based on this assumption, it seems that the area near the sinus window is quite unfavorable for bone regeneration, which therefore may explain previous reports and our new bone ratio results (ie, vertical, 30.8%; lateral, 11.7%).[24] Lateral biopsies may not accurately reflect osseointegration in the area surrounding the implant. In addition, there was only one patient who underwent biopsy ≥1 year after surgery. This patient had much stronger resistance to the trephine bur on biopsy sampling, compared with all other patients who had undergone the biopsy procedure 6 months after surgery. A lateral biopsy specimen was obtained; however, it exhibited a new bone ratio of 34.20%, which was similar to the value in autogenous graft alone. Therefore, at 6 months after surgery, the replacement of β-TCP by new bone was probably ongoing, and more time was required for remodeling. Furthermore, based on radiographic assessment, it was thus presumed that the rate of bone regeneration would be enhanced at ≥1 year (Fig. 9).[18,25] Previous studies and the histological analysis performed in the present study both confirmed that OSferion is an excellent bone graft material that allows slow bone modeling.[15,16,18]

Conclusion

OSferion is a safe bone-grafting material with superior osteoconductive properties. Maxillary sinus floor augmentation with this material is clinically effective. Histological and radiographic examination provided supporting evidence that β-TCP (beta-tricalcium phosphate) is characterized by slow resorption that results in the graft material remaining unrebsorbed even 6 months after the procedure, and that new bone replacement occurs slowly for approximately 1 year. Lateral biopsies tended to have a low percentage of new bone, and they may not accurately reflect new bone growth in the area surrounding an implant.

Disclosure

The authors have no financial interest, either directly or indirectly, in the products or information mentioned in the article.

Approval

This study was performed with the approval of the Ethics Committee of Tokyo Medical and Dental University, Tokyo, Japan (approval number: 309).

Acknowledgments

The bone-grafting material β-TCP (OSferion) was kindly supplied by Olympus Terumo Biomaterials Corp. (Tokyo, Japan).

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