Maxillary Sinus Grafting with Biphasic Calcium Phosphate Ceramics: Clinical and Histologic Evaluation in Man

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Purpose: *To evaluate the clinical and histologic aspects of bone formation in maxillary sinus augmentation using macroporous biphasic calcium phosphate (MBCP) comprising hydroxyapatite/tricalcium phosphate (HA/TCP) 60/40 as bone-grafting material.* ***Materials and Methods:*** *A total of 10 patients and 12 sinuses grafted with MBCP in two-stage sinus augmentation were included in the present study. After a healing period of 6 months, bone core biopsies were harvested during implant insertion and evaluated under light microscopy.* ***Results:*** *The histologic examination showed that the MBCP particles were in close contact with new bone in all biopsies. Histomorphometric evaluation demonstrated that newly formed bone constituted 28.3% ± 2.7%, residual grafted material 27.3% ± 1.2%, and marrow spaces 45.9% ± 1.9%.* ***Conclusions:*** *Histologic investigation showed that the MBCP grafted particles were embedded and integrated in the newly formed bone; this bone was in close and tight contact with the biomaterial particles. Data from the preliminary results demonstrated that MBCP is a biocompatible and osteoconductive material that can be successfully used as a grafting material for sinus floor augmentation.* Int J Oral Maxillofac Implants 2013;28:51–56. doi: 10.11607/jomi.2667

Key words: *bone regeneration, biphasic calcium phosphate, human histology, sinus augmentation*

The rehabilitation of the atrophic alveolar ridge in the edentulous posterior maxilla remains a major challenge in modern implant dentistry.[1–3] Among the techniques used to regain the height of residual bone, sinus floor augmentation has become a widely accepted method to augment the bone volume for implant placement.[4–10] Since the first use by Boyne and James,[11] several materials, including autogenous bone grafts, allograft, xenograft, and synthetic materials, were investigated in order to evaluate their suitability for sinus elevation procedures. Among different biomaterials, autogenous bone grafting remains the "gold standard" as it contains all the components necessary for regeneration, including viable bone cells and progenitors, as well as the appropriate growth differentiation factors.[12,13] However, bone regeneration after autologous bone grafting is quite variable, probably because of differences in the harvesting sites of the grafted bone. In addition, harvesting autologous bone (usually from iliac bone) results in donor site morbidity, which includes infection, pain and loss of function,[14,15] nd the percentage of patients experiencing complications with autogenous iliac grafts is significant (~8%).[16] A limited amount of intraoral bone makes harvesting and grafting difficult and autologous bone grafts from other sites may not be suitable for dental implantation due to poor quality.[15] Allograft and xenograft implants can partly compensate for these disadvantages.[3,17–22] Some studies recently demonstrated that calcium phosphate materials can be successfully used in sinus augmentation procedures.[23,24] Other studies showed that calcium phosphate–based biomaterials used as bone substitutes were biocompatible and osteoconductive, nontoxic, antigenically inactive, and bond directly to bone without any intervening connective tissue layer.[24–27] Several studies[28–31] reported on ectopic bone formation of calcium phosphate, showing that osteoinduction might be an intrinsic property of these biomaterials as demonstrated by the induction of bone when implanted intramuscularly in baboons.

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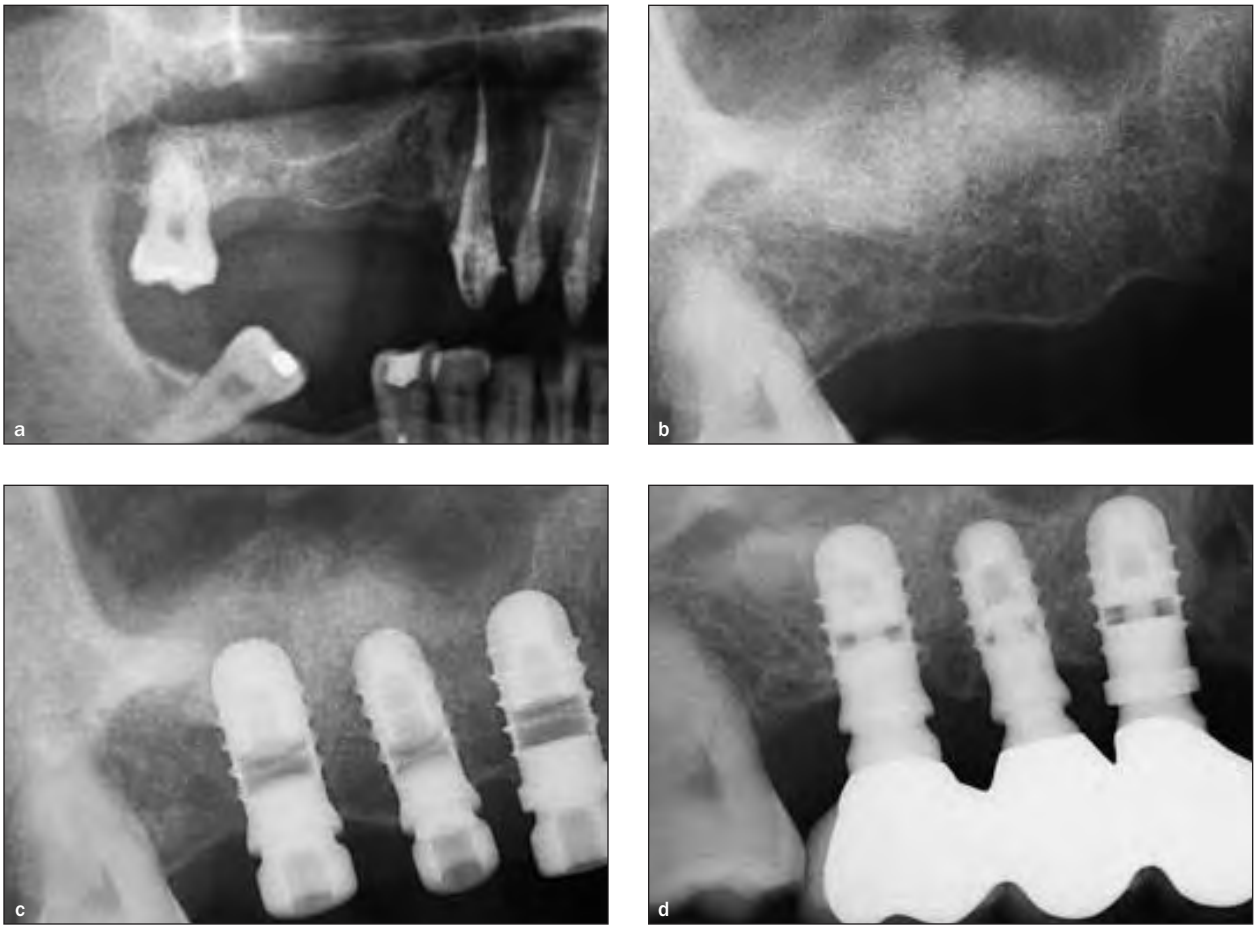

Figs 1a to 1d Overview of radiographic examination: *(a)* detail of preoperative panoramic radiograph, *(b)* periapical radiographic immediately after sinus augmentation by MBCP, *(c)* periapical radiograph 6 months after surgery, at the time of implant placement, and *(d)* radiographic examination after the delivery of a metal-ceramic prosthesis.

In general, it was reported that the materials consisting of hydroxyapatite (HA) are slowly resorbed, whereas tricalcium phosphate (TCP) bone graft substitutes are resorbed at a faster rate.[24]

A biphasic calcium phosphate (BCP) consisting of HA/TCP is a new bone graft substitute produced by a single process to prevent clustering and to establish a new homogenous molecule. Its 60:40 ratio of HA/TCP gives it two balanced phases of activity: a more stable phase of HA and a more soluble phase of TCP. The material is soluble and gradually dissolves in the body, seeding new bone formation as it releases calcium and phosphate ions into the biologic medium.[32] HA/TCP is recognized as an osteoconductive and bioactive material that harbors an intrinsic osteoinductive property.[33] Macroporous forms of BCP ceramics (MBCP) have been used in the last 20 years for bone substitution and dental applications.[34–37] Recently some studies have demonstrated the effectiveness of HA/TCP in sinus augmentation.[38–46]

The aim of this preliminary study is to evaluate the histologic pattern of healing and bone formation 6 months after sinus augmentation procedures using MBCP.

MATERIALS AND METHODS

A total of 10 patients (6 men and 4 women), ranging in age from 35 to 67 years (average 49 years), with insufficient residual bone height (< 5 mm) were selected for this study. The protocol of the study was approved by the Ethical Committee of the University of Guarulhos (UnG), São Paulo, Brazil. All the patients signed a written informed consent form. Inclusion criteria were: maxillary partial (unilateral or bilateral) edentulism involving the premolar/molar areas, and the presence of a residual bone height between the sinus floor and alveolar ridge ranging from 1 to 5 mm, as measured on the serial sections of a computerized axial tomography

(CAT) scan. Exclusion criteria were: smoking, patients with systemic diseases, and maxillary sinus pathology. At the initial visit, all patients underwent a clinical and occlusal examination; periapical and panoramic radiographs were taken; and CAT scans were performed (Fig 1a). A two-stage approach was performed in all patients for a total of 12 sinus elevation procedures (bilateral n = 2 and unilateral n = 8). MBCP, a mixture of 60% HA and 40% β-TCP, presented two types of porosity, 2/3 macropores and 1/3 micropores. The microporosity (pore diameter smaller than 10 μm) comprised all the spaces between the ceramic and was necessary to enable biologic fluid circulation and to promote ionic exchange. The macroporosity (a pore diameter from 300 to 600 μm) allowed the ceramic to be colonized by osteogenic cells able to form new bone tissue. MBCP granules were 1 to 2 mm in diameter, and were used 100% as bone substitute graft material to perform sinus augmentation procedures (Fig 1b). After a 6-month healing period, biopsy specimens were taken and a total of 30 implants (Leone) were inserted at the re-entry surgery (Fig 1c). The implants had been placed exactly in the sites where biopsy specimens were harvested, using a computed tomography (CT) template for guided bone surgery.

Surgical Procedure

Prior to surgery, the patients' mouths were rinsed with a chlorhexidine digluconate solution 0.2% for 2 minutes. Local anesthetic (Xylestesin, ESPE) with 2% adrenaline was administered. The maxillary sinus augmentation was performed as previously described.[11] After a horizontal crestal incision and two vertical incisions extending beyond the mucogingival junction, a full-thickness flap was reflected, in order to expose the maxillary sinus lateral bone wall. Under constant irrigation with copious saline solution, an osseous window of approximately 1 × 1 cm was demarcated and isolated using piezotome equipment. The isolated osseous window was subsequently removed and conserved in saline solution. The sinus membrane was exposed and carefully isolated, using specially designed elevators, to avoid undesired perforations. The cavity produced was filled with MBCP particles. After the sinus augmentation procedure was completed, the previously isolated bone window was repositioned to close the sinus lateral wall. Sutures were placed (Supramid, Novaxa) to ensure complete flap closure. Antibiotic prophylaxis (1 g Zimox, Pharmacia & Upjohn) was administered 1 hour before surgery and for 3 days afterward; the patients were given inflammatory and analgesic medication as well (Synflex 550 mg, Recordati).

Clinical and radiologic follow-up examinations were performed immediately after the surgery and 6 months later.

Histologic Processing

Six months after sinus floor elevation, at the time of dental implant placement, biopsy specimens were taken under local anesthesia with a 2.5-mm diameter trephine bur (Straumann) under copious irrigation with sterile saline. Ten biopsies were taken at the sites where dental implants would be placed. The specimens were immediately fixed in 10% buffered formalin and processed to obtain thin ground sections with the Precise 1 Automated System (Assing).[47] The specimens were dehydrated in an ascending series of alcohol rinses and embedded in a glycol methacrylate resin (Technovit 7200 VLC, Kulzer). After polymerization, the specimens were sectioned along their longitudinal axis with a high-precision diamond disk at about 150 μm and ground down to about 30 μm with a specially designed grinding machine. The slides were stained with acid fuchsin and toluidine blue. The slides were observed in normal transmitted light under a microscope (Laborlux S, Leitz). The histomorphometry was performed using the light microscope connected to a high-resolution video camera (3CCD JVC KYF55B), and interfaced to a monitor and personal computer (Intel Pentium III 1200 MMX, Intel). This optical system was associated with a digitizing pad (Matrix Vision) and a histometry software package with image capturing capabilities (Image-Pro Plus 4.5, Media Cybernetics).

RESULTS

Clinical Results

The healing process after sinus augmentation was uneventful. No postoperative complications were present. Six months after augmentation, the radiographic examination showed in all patients the presence of dense bone in the maxillary sinuses where MBCP was inserted. After 6 months, all patients received implants and underwent definitive prosthetic rehabilitation with ceramometal fixed prostheses (Fig 1d). Mean vertical height gain was 7.63 ± 2.40 mm (Table 1). One year after implantation, all 30 implants were clinically in function, and no surgical or prosthetic complications occurred. No clinical signs of sinus pathology were observed (Fig 2).

Histologic Results

At low-power magnification, it was possible to observe that almost all grafted particles were surrounded by trabecular bone (Fig 3). It was possible to observe the presence of osteoid material around only some particles. At higher magnifications, it was possible to observe the presence of rims of osteoblast in the process of depositing osteoid matrix (Fig 4). Many newly formed bone trabeculae, which appeared to be

Table 1 Mean Vertical Bone Gain, Obtained by CT Scans at Baseline and After 6 Months of Healing

Patient number	Virtual position of the future implant*	Residual bone crest height (mm)	Crestal height after augmentation (mm)	Vertical gain (mm)
1	14	7.3	13.4	6.1
	15	5.7	11.5	5.8
	16	4.5	9.7	5.2
2	24	6.5	12.0	5.5
	25	5.5	10.6	5.1
	26	2.0	9.6	7.6
3	25	5.0	12.4	7.4
	26	4.6	12.6	8.0
	27	2.2	10.6	8.4
4	14	8.2	15.9	7.7
	15	5.4	12.6	7.2
	16	3.5	9.7	6.2
5	14	6.5	13.6	7.1
	15	5.2	10.5	5.3
	16	2.2	10.3	8.1
6	24	7.2	13.6	6.4
	25	4.2	12.6	8.4
	26	2.5	13.2	10.7
7	25	4.2	15.2	11.0
	26	2.0	16.0	14.0
	27	1.8	13.4	11.6
8	15	4.5	10.2	5.7
	16	3.8	11.9	8.1
	17	3.4	12.0	8.6
9	15	7.5	11.0	3.5
	16	5.2	10.0	4.8
	17	3.2	12.8	9.6
10	25	6.4	12.3	5.9
	26	4.0	11.9	7.9
	27	2.4	14.5	12.1

*FDI tooth numbering system.

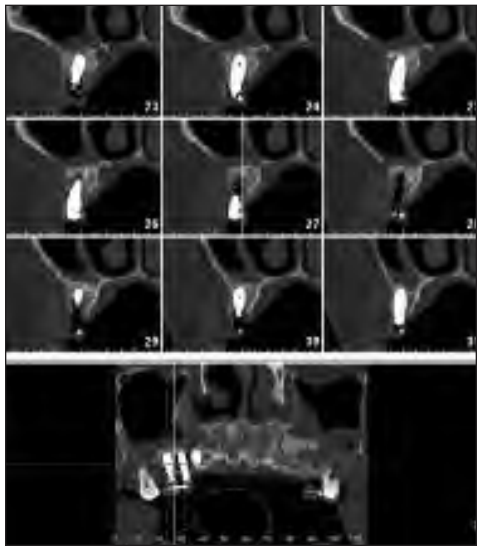

Fig 2 CT examination showing an adequate amount of radiopaque material and no signs of maxillary sinus disease.

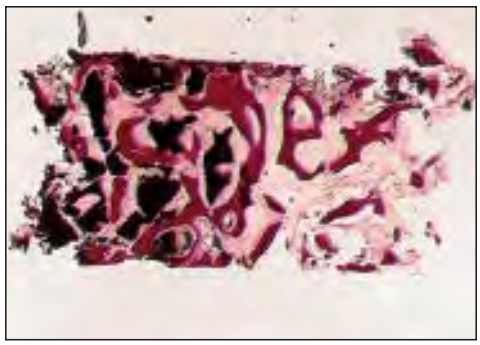

Fig 3 At magnification ×12, the bone core appeared to be comprised of trabecular bone with grafted particles embedded (toluidine blue–basic fuchsin).

strongly stained, were present in contact with newly formed bone (Fig 5). Preexisting bone was lined for the most part by newly formed bone in many regions of the specimens. In all specimens, no inflammatory cell infiltrate was present. No foreign body reactions were detected. The histochemical analysis for mineralized tissue (von Kossa) showed that the bone around the grafted particles was mature and highly mineralized. Some grafted particles appeared to be embedded and fused by newly formed bone. No gaps were present at the interface between particles and bone. Areas of resorption were present at the surface of some grafted particles (Figs 6 and 7). In some areas, small capillaries were present in the marrow spaces located between the particles. Histomorphometric evaluation demonstrated that newly formed bone constituted 28.3% ± 2.7%, residual grafted material constituted 27.3% ± 1.2%, and marrow spaces constituted 45.9% ± 1.9%.

DISCUSSION

The edentulous alveolar process typically undergoes extensive resorption should functional stimulation be absent. Once the bony thickness between the sinus floor and alveolar crest is reduced to less than 5 mm at the posterior maxillary area, it is usually necessary to augment the maxillary sinus floor for placement of dental implants.[11] The resorption of implanted grafts in the augmented maxillary sinus is a common phenomenon, which may substantially affect the long-term results of the process, and even autologous bone might undergo a dramatic decrease in height and volume over time.[4] Various biomaterials have been used in sinus augmentation procedures.[43] The amount of newly formed bone in the augmented sinus is believed to be an accurate indicator of the possibility of success.[42] Autogenous bone is considered to be the ideal grafting material, but its limited

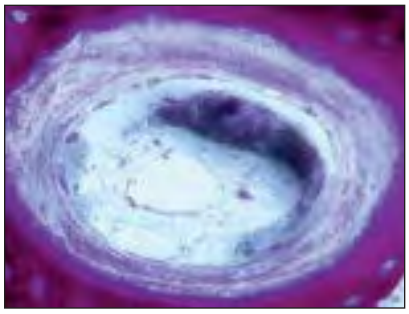

Fig 4 *(Left)* Osteoid material could be observed around some original particles (toluidine blue–basic fuchsin; magnification ×100).

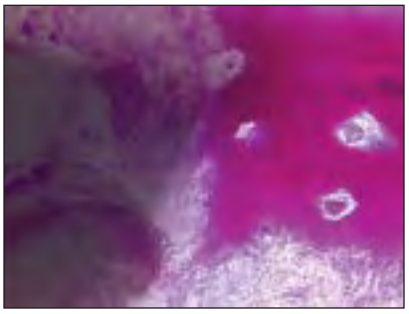

Fig 5 *(Right)* Newly formed bone trabeculae could be found in close vicinity to grafted original particles (toluidine blue–basic fuchsin, magnification ×200).

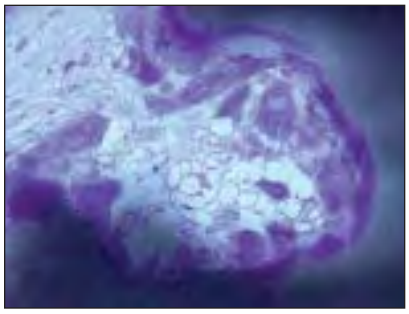

Fig 6 *(Left)* Areas of resorption were present at the surface of some grafted particles (toluidine blue–basic fuchsin, magnification ×200).

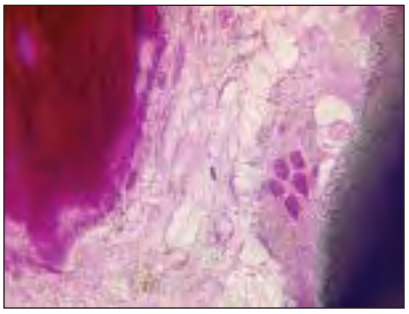

Fig 7 *(Right)* High-power magnification of a multinucleated cell, possibly an osteoclast, actively resorbing the grafted particle (toluidine blue–basic fuchsin, magnification ×200).

availability may limit its use.[48] On the other hand, allografts, xenografts, and alloplasts have an advantage in their availability.[48] A significant amount of newly formed bone has been reported with the use of porous HA.[3] HA has been reported to be biocompatible, and osteoconductive and does not induce a foreign body reaction or a toxic response.[46] In BCP, HA acts as a scaffold, and tricalcium phosphate (TCP) serves as the resorbable component.[46] The present histologic results showed that the BCP grafted particles were embedded and integrated in the newly formed bone; this bone was in close and tight contact with the biomaterial particles. The histomorphometric results (the percentage of newly formed bone and of residual grafted material) compare favorably with the data reported in the literature.[21,42,43,45,46] The very good results of the present study could be also explained by the porosity of the used grafted material. It has been shown that the macro- and microporosity of a given biomaterial plays a key role in osteoconduction, and an interconnecting porous structure is required for the ingrowth of bone into the material.[19] The porosity is also important in allowing the ingrowth of vessels, which support the proliferation and differentiation of the osteoblasts.[49–51] BCP has been shown to be biocompatible, osteoconductive and capable of supporting a good percentage of newly formed bone in the augmented sinuses.

ACKNOWLEDGMENTS

This work was partially supported by the Ministry of Education, University and Research (M.I.U.R.), Rome, Italy. The authors reported no conflicts of interest related to this study.

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