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Article *in* Implant Dentistry · August 2016

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Maxillary Sinus Grafting With Biphasic Bone Ceramic or Autogenous Bone: Clinical, Histologic, and Histomorphometric Results From a Randomized Controlled Clinical Trial

Seyed A. Danesh-Sani, DDS,* Stephen S. Wallace, DDS,† Ali Movahed, DDS,‡ Edgard S. El Chaar, DDS, MS,§ Sang-Choon Cho, DDS,¶ Ismael Khouly, DDS, MS, PhD,|| and Tiziano Testori, DDS, MD#

Purpose: *The present, randomized, controlled clinical trial compared the histologic and histomorphometric results from maxillary sinus augmentation with either biphasic calcium phosphate (BCP) (60% hydroxyapatite and 40% β-tricalcium phosphate) or autogenous bone (AB) as bone-grafting materials.*

Material and Methods: *Ten patients received bilateral sinus elevation surgery with intraoral AB chips (control group) on one side and BCP (test group) on the contralateral side. After a healing period of 6 to 8 months, implant sites were created and trephine cores were harvested for histological and histomorphometric analysis of the grafted areas.*

Results: *The histological examination of biopsies showed BCP particles interconnected by bridges of a vital newly formed bone. Histomorphometry demonstrated that the amount of newly formed bone in the control group (36.8%) was significantly greater than that in the BCP (28.2%) group (P = 0.0032). BCP and AB cores revealed an average of residual graft particles of 32.9% and 4.8%, respectively. The average percentage of soft tissue components was 38.9% in the BCP cores and 58.4% in the AB cores.*

Conclusions: *Based on our findings, the amount of vital bone formation was significantly higher for AB than that for BCP. However, BCP seemed to be a biocompatible and osteoconductive material that can be used with success as a bone substitute in maxillary sinus procedures. (Implant Dent 2016;25:1–6)*

Key Words: biphasic calcium phosphate, bone substitute, autogenous bone sinus augmentation, sinus floor elevation

The sinus augmentation (SA) procedure has been shown to be a successful and predictable approach for the augmentation of the posterior maxilla with the deficient crestal bone for the purpose of placing dental implants.[1,2] Traditionally, autogenous bone (AB), harvested from intraoral or extraoral sources, was used as the grafting material of choice in SA procedures.[3–5] However, increased morbidity rates, limited availability, and a high resorption rate of the AB graft were significant limitations of the use of AB.[6,7] To overcome these disadvantages, different types of bone substitutes have been used and evaluated. Bone replacement graft materials including allografts, xenografts, and alloplasts have been used successfully for SA.[8–12] Several studies have shown high implant survival rates following the utilization of bone substitutes in sinus grafting procedures.[2,13]

Biphasic calcium phosphate (BCP) is an alloplast bone graft material that has been used in both medical and dental fields.[14–17] This material is a biocompatible synthetic material that

*Resident, Department of Periodontology and Implant Dentistry, New York University College of Dentistry, New York, NY.
†Associate Clinical Professor, Department of Periodontology and Implant Dentistry, Columbia University College of Dental Medicine, New York, NY.
‡Clinical Researcher, Avicenna Research Institute, Dental Research Center, Oral Surgery Division, Mashhad University of Medical Sciences, Mashhad, Iran.
§Director, Advanced Program in Periodontics, Department of Periodontology and Implant Dentistry, New York University College of Dentistry, New York, NY.
¶Director, Department of Periodontology and Implant Dentistry, Advanced Program in Implant Dentistry, New York University College of Dentistry, New York, NY.
||Associate Director of Periodontology and Implant Dentistry, Bluestone Center for Clinical Research; Clinical Assistant Professor, Department of Oral and Maxillofacial Surgery, New York University College of Dentistry, New York, NY.
#Head, Section of Implant Dentistry and Oral Rehabilitation, Department of Biomedical, Surgical and Dental Sciences (Chairman: Prof. R. L. Weinstein), IRCCS, Galeazzi Institute, Milan, Italy; Private Practice, Como, Italy.

Reprint requests and correspondence to: Seyed A. Danesh-Sani, DDS, Department of Periodontology and Implant Dentistry, New York University College of Dentistry, 345 E 24th Street, New York, NY 10010, Phone: 2032152487, Fax: 2129927040; E-mail: sds521@nyu.edu

ISSN 1056-6163/16/02505-001
Implant Dentistry
Volume 25 • Number 5

DOI: 10.1097/ID.0000000000000474

consists of 40% beta-tricalcium phosphate (β-TCP) and 60% hydroxyapatite. Microscopic structure of this material shows granules with 90% porosity and interconnected pores of 100 to 500 μm. In addition, BCP is an osteoconductive material that acts as a scaffold for new bone formation during the graft maturation period.[15,16,18]

The purpose of the current prospective blinded, randomized, clinical trial was to compare the amount of vital bone formation in biopsies harvested 6 to 8 months after SA procedure with BCP or AB grafts.

METHODS AND MATERIALS

Ten healthy patients (age range: 25–72 years) who were edentulous in the posterior maxilla and chose to receive dental implants were selected. Inclusion criteria were the presence of less than 5 mm vertical height of the ridge bilaterally in the edentulous posterior maxilla, as measured on the serial sections of a computerized axial tomography scan. Exclusion criteria included patients with diabetes, osteoporosis or other metabolic disorders, smokers, and patients with maxillary sinus pathologic conditions. Patients who smoked any cigarettes, cigars, or pipes were excluded from the study.

All patients signed a written informed consent. The principles of the Declaration of Helsinki were followed in this study. The study and the consent forms were approved by the Ethics Committee of the Dental School.

Surgical Procedure

Because of insufficient alveolar bone ridge height, all the patients were treated by a 2-stage SA procedure. Antibiotic prophylaxis (amoxicillin 2 g or 600-mg clindamycin) was administered 1 hour before the surgery. After the elevation of the full-thickness mucoperiosteal flap, a lateral wall window was prepared by either infracture or the wall removal technique, as necessary. The Schneiderian membrane was then elevated from the floor and up to the medial wall. Based on the anatomy of the sinus, 2 to 4 g of material was used to fill the created space under the sinus membrane with either BCP (Straumann Bone Ceramic; Institute Straumann AG, Basel, Switzerland) on one side or with a particulate AB graft, harvested intraorally from the zygomatic buttress, the lateral sinus wall and the tuberosity area, on the other side. Particulate AB chips were harvested with a disposable manual bone scraper (Curved Safescraper; Meta, Reggio Emilia, Italy) before opening of a bony window.

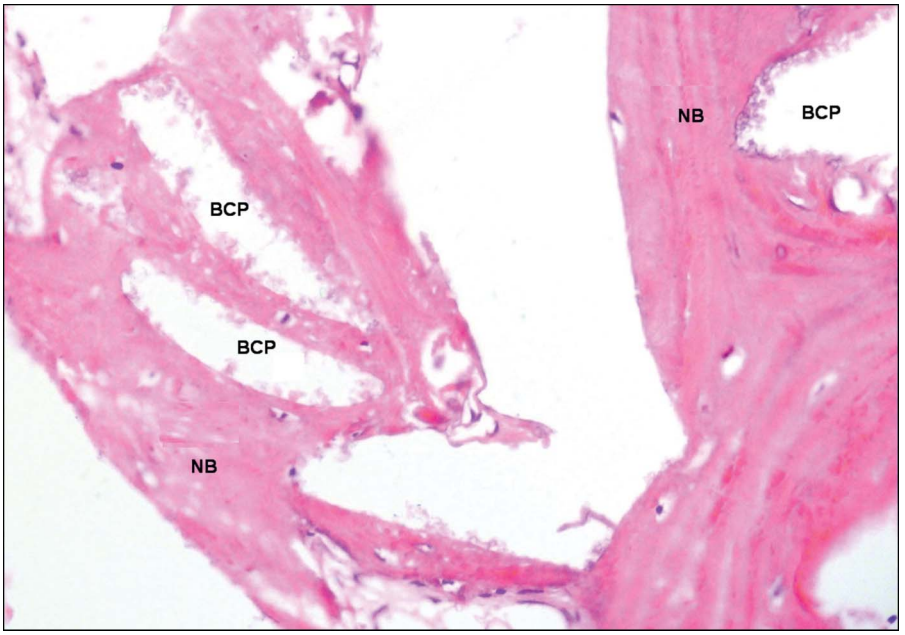

Fig. 1. High-power image of site augmented with BCP shows close contact between residual graft particles (BCP) and newly formed bone (NB) (hematoxylin and eosin; original magnification ×400).

Each sinus was independently randomized to either the control or test group by a computer-generated randomization code. At the time of surgery, a person who was not involved in the study opened the sealed envelope containing the randomization code.

The lateral wall window was covered with a bioabsorbable collagen barrier

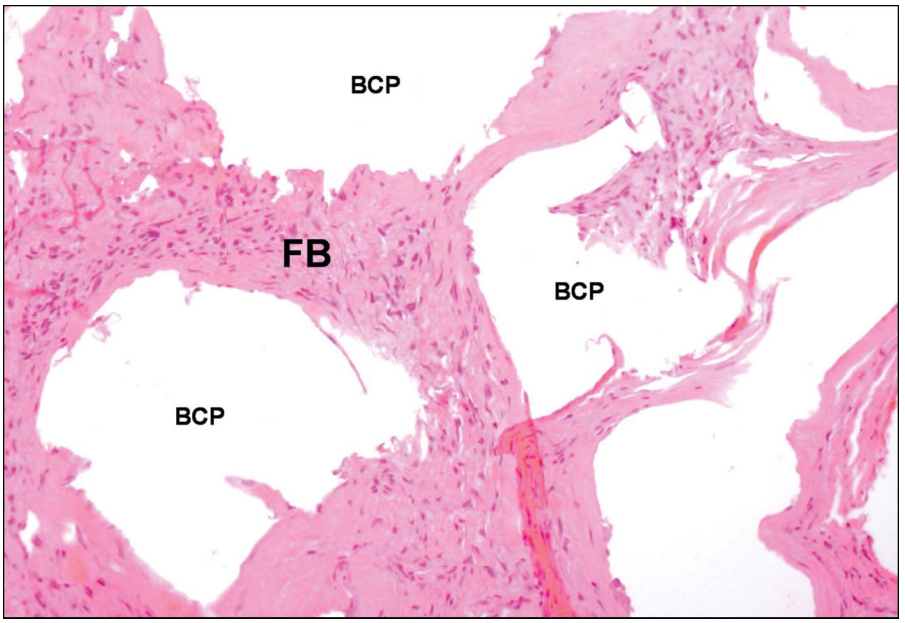

Fig. 2. Histological view of the grafted compartment for the BCP group shows dense fibrous tissue (FB) associated with the BCP particles (hematoxylin and eosin; original magnification ×200).

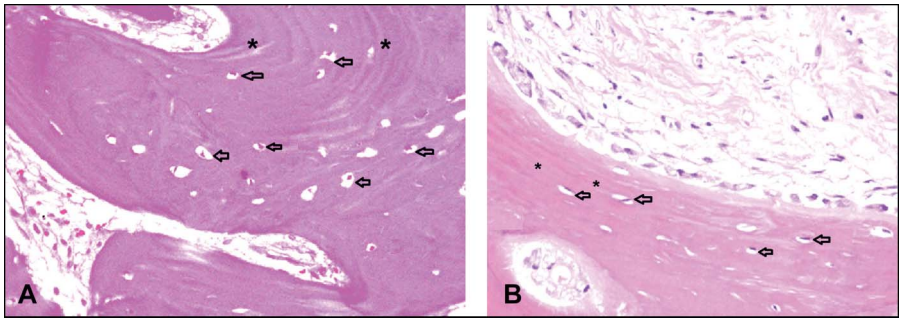

Fig. 3. Incremental appositional lines (*) and osteocytes (arrows) in mineralized matrix showing signs of remodeling in the augmented sites: (**A**) BCP group (hematoxylin and eosin; original magnification ×400) (**B**) AB group (hematoxylin and eosin; original magnification ×400).

membrane and tension free primary closure of the flap was achieved with expanded polytetrafluoroethylene sutures (Gore-Tex) or polyglactin 910 (Vicryl; Ethicon, Somerville, NJ), according to the operator's preference. Postoperatively patients were placed on 7 days of antibiotics coverage and rinsing with 0.12% chlorhexidine digluconate oral rinse twice daily for 2 weeks. Postoperative examination and suture removal were performed after 14 days.

After a 6 to 8 months healing period, implants were placed, during implant placement, biopsies were obtained using a trephine drill with copious irrigation from within the boundaries of the original lateral window without compromising implant placement. Bone core samples were 3.5 mm in diameter and 10 mm in length and taken from the site without compromising the implant placement. Fifty-two dental implants (Institute Straumann AG, Basel, Switzerland) were placed and after 4 months of healing were subsequently restored.

Clinical and radiological follow-up examinations were performed immediately after the surgery and furthermore after 6 and 12 months. Implant survival was based on quantitative and qualitative assessments of the individual implant as suggested by Albrektson et al.[19]

Histology

Bone core biopsies were fixed in 4% phosphate-buffered formaldehyde for 3 days and dehydrated in graded alcohol. The bone specimens were then cleared with xylene and embedded in methylmethacrylate supplemented with 20% plastoid-N and 0.13 g/mL perkadox. Sections 5 μm thick were cut longitudinally using a Jung K microtome (Leica microtome type sm2500 s; Leica, Wetzlar, Germany). The prepared slices were stained in hematoxylin and eosin (H&E) and observed in normal transmitted light under a microscope (Carl Zeiss, Oberkochen, Germany).

Tartrate-resistant acid phosphatase (TRAP) staining was used to verify the osteoclast origin of the giant cells present in the test group.

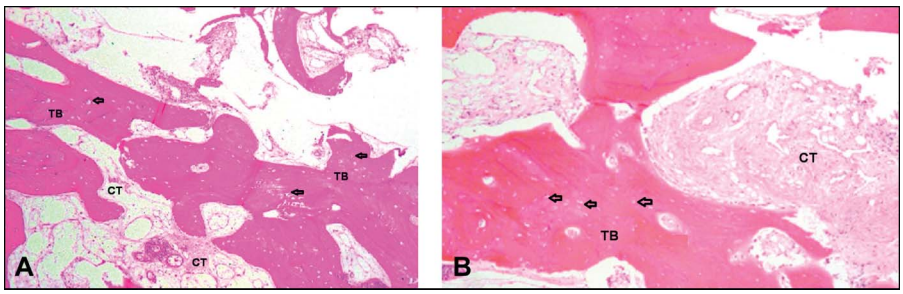

Fig. 4. Histologic view of augmented sites shows viable trabecular bone (TB) with osteocytes (arrows) and connective tissue (CT): (**A**) BCP group (hematoxylin and eosin; original magnification ×100) (**B**) AB group (hematoxylin and eosin; original magnification ×100).

Histomorphometry

The histomorphometric analysis was performed by digitizing the images from the microscope with a camera (Olympus BX50; Olympus Optical Co., Tokyo, Japan) and a frame grabber. The images from each area of the biopsy core were obtained and analyzed with the image analysis software (Imagelab 2000; Softium, Sao Paulo, Brazil) to determine the percentages of residual graft particles, newly formed bone, and soft tissue components (ie, bone marrow and/or connective tissue) in each specimen. To calculate histomorphometric measurements of these parameters, each component surface was demarcated and subsequently expressed as a percentage of the total field area.

Statistical Analysis

The averages and ranges for the percentage of newly formed bone, soft tissue components, and residual graft particles were calculated using statistical analysis. Paired *t* tests were used to determine possible differences between BCP and AB for variables of interest in the 20 bilateral cores, in which the grafted areas were allowed to heal for the same period before core retrieval.

RESULTS

Clinical Results

Cores were harvested 6 to 8 months postsurgery from 20 healed sinuses in 10 patients and evaluated histologically (Figs. 1–4). All patients provided bilateral cores.

During the study, 3 small Schneiderian membrane perforations occurred in the AB group and 2 small perforations occurred in the BCP group. All perforations were treated with collagen membranes (Bio-Gide; Geistlich AG, Wolhusen, Switzerland). No other surgical complications such as postoperative inflammation or infection were observed. One year after placement, neither implant failures nor surgical or prosthetic complications occurred resulting in implant survival rate of 100%.

Histologic Results

Test Group. The BCP particles were surrounded by a newly formed bone and

Table 1. Histomorphometric Results of Core Samples Taken From Sinuses Augmented With BCP and AB

		BCP, (%)			AB, (%)		
Patient	Healing Time (mo)	Newly Formed Bone	Soft Tissue Components	Residual Particles	Newly Formed Bone	Soft Tissue Components	Residual Particles
A	7.5	23	49	28	39	54	7
B	8	35	25	40	51	46	3
C	8	38	19	43	34	61	5
D	7	23	39	38	27	65	8
E	7	24	49	27	31	65	4
F	8	37	20	43	56	43	1
G	8	40	26	34	49	47	4
H	6	21	54	25	29	67	4
I	7.5	25	56	19	31	66	3
J	6	16	52	32	21	70	9
Mean	7.3	28.2	38.9	32.9	36.8	58.4	4.8

Amount of newly formed bone, residual graft particles, and soft tissue components for test (BCP) and control groups (AB) presented at different healing periods.

Table 2. Mean and SD of Histomorphometric Values, Amount of Newly Formed Bone, Residual Graft Particles, and Soft Tissue Components in Test (BCP) and Control Groups (AB)

	BCP (n = 10)		AB (n = 10)		
	Mean ± Standard Deviation	Range	Mean ± Standard Deviation	Range	*P**
Newly formed bone (%)	28.2 ± 8.4	16 to 40	36.8 ± 11.5	21 to 56	0.0032
Soft tissue components (%)	38.9 ± 14.9	19 to 56	58.4 ± 10	43 to 70	0.0001
Residual particles (%)	32.9 ± 8.1	19 to 43	4.8 ± 2.4	1 to 9	<0.0001

*Application of paired *t* test to determine possible differences between BCP and AB for variables of interest ($P = 0.05$).

soft tissue. The histological examination of biopsies showed BCP particles being interconnected by bridges of the newly formed bone (Fig. 1). Bone formation was preceded by the proliferation of osteogenic cells and angiogenesis in the pores of the particles. The pattern of the newly formed bone was not similar to the native lamellar bone and did not present an organized bone matrix. The medullary space was filled with a fibrous connective tissue and osteocytes were observed in the newly formed bone matrix (Figs. 2, 3A, 4A).

Control Group. In the group treated with AB, the boundary between the residual bone particles and the newly formed bone was not easily distinguishable in most cases (Fig. 3, B). Biopsy cores showed less organized trabeculae with bone marrow spaces with high vascularity. Fibroblasts and connective tissue were noticed in all specimens (Fig. 4, B). Remodeling signs within the bone matrix included the presence of osteocytes in the bone trabeculae, incremental appositional lines, and angiogenesis (Fig. 3, B).

Histomorphometric Results

Quantitative evaluation of the cores was performed and data related to the 2 groups are listed in Table 1. The average percentages of newly formed bone were 28.2% and 36.8% for the BCP and AB groups, respectively, and the average percentages of soft tissue components were 38.9% and 58.4%, respectively (Table 1). Histomorphometric results of the BCP cores showed 32.9% average residual graft particles. A similar variable analysis of the AB cores revealed an average of 4.8% residual graft particles.

Statistical analysis of histomorphometric results showed statistically significant differences between test and control cases regarding the volume of newly formed bone, residual graft particles, and soft tissue components (Table 2).

DISCUSSION

Several studies have shown the utilization of bone graft materials as substitutes for AB in the maxillary sinus floor elevation procedure.[20,21] Systematic reviews showed survival rates of more than 90% for implants placed in augmented sinuses with bone graft substitutes.[13,22] One of the main aspects that has been evaluated in histologic studies of bone graft materials is their osteoconductive capability.[23,24] Histologic analysis in this study confirmed the osteoconductive characteristics of BCP and showed direct contact of newly formed bone with the biomaterial which is in accordance with other studies in the literature.[15,16,25]

Previous studies have investigated the healing of AB in comparison with β-TCP in maxillary SA.[23,25,26] Although previous studies showed encouraging outcomes with β-TCP, furthermore randomized clinical trials are needed to evaluate the efficacy of this material. Bilateral SA is a good model for doing a split-mouth study because it provides us with an opportunity to compare different graft materials and eliminate the host as a variable. Although the shape of sinuses may be different in the same individual, using the same surgical methods and materials allows accurate comparison of bone graft materials. This randomized, controlled clinical trial evaluated implant survival rates and the amount of newly formed bone present 6 to 8 months after augmenting bilateral sinuses with BCP or AB.

AB was used as the control group since it has been considered the "gold standard" in hard tissue augmentation procedures.[27] Our findings support other studies in the literature that showed about 25% to 30% of vital bone formation in grafted areas.[12,16,28,29] In this study, the amount of new bone formation was significantly higher in the control group ($P = 0.0032$). Tosta et al[29] showed that obtaining more vital bones in grafted areas with AB does not seem to be clinically relevant regarding implant survival, as they did not notice implant loss in any of the analyzed groups. It is noteworthy to mention that there was a short follow-up period for evaluating implant survival in this study, and furthermore studies should be performed to assess long-term survival of implants placed in augmented sinuses with BCP. Combining AB with BCP has been suggested to improve the quality of the grafted area in more demanding clinical conditions.[15,30]

Previous studies described the lateral sinus wall, the zygomatic buttress, and the tuberosity area as appropriate harvesting regions when using a bone scraper, being adjacent to the recipient site when augmenting the sinus floor.[31,32] Our findings indicate that harvesting bone using bone scraper is associated with minimal morbidity and acceptable survival of the implants and prosthetic constructions.

Several investigations have revealed a direct relationship between graft maturation time and vital bone formation.[9,33,34] This trend of increased vital bone volume with increased healing time was observed in a previous study using BCP as a graft material.[16] In this study, the highest amount of bone formation was observed in both AB and BCP cores harvested 8 months after the procedure. Froum et al[16] achieved their best results regarding amount of new bone formation in BCP cores harvested 8 months postsurgery. Tosta et al[29] examined sinuses grafted with BCP at 9 months and showed higher amount of vital bone formation in comparison with this study. The histomorphometric results of our work showed that the total amount of vital bone volume would be increased by a longer healing time which compares favorably with the data reported in the literature.[16,25,29] However, core retrieval time in our study may be too short to notice these temporal changes in vital bone in the grafted area. Furthermore clinical investigations with greater sample size are required to evaluate the effect of healing time on the amount of bone formation and whether longer healing times are needed with BCP-grafted sinuses.

The average percentage of soft tissue components was 38.9% in the BCP cores. Soft tissue components of the cores include integral parts of bone such as connective tissue and marrow. It has been postulated that the soft tissue related to β-TCP particles consists of osteoblasts and a few osteoclasts which may have a possible beneficial effect for maturation and healing of the grafted area.[35] Therefore, the β-TCP constituent of BCP may increase the osteogenic potential of this material by maintaining bone-remodeling cells in place.[25]

BCP and AB cores revealed an average of 32.9% and 4.8% residual graft particles, respectively. There was significantly a lower percentage of soft tissue components in the test group and, consequently, a higher percentage of residual graft particles. Bone biopsies taken at 6 to 8 months after SA reveal the resorptive behavior of AB graft. Clinicians should consider the resorption rate of the AB graft which has been previously reported as one of the disadvantages of using this kind of graft.[7,36]

Conclusion

Based on the data presented in this randomized clinical trial, BCP seem to be osteoconductive and promotes new bone formation in maxillary sinus floor augmentation procedures. The amount of vital bone formation was significantly higher for AB than that for BCP. However, it is not well understood whether these differences have any clinical relevance. Additional studies with greater numbers of cases are required to evaluate the long-term survival of implants placed in sinuses augmented with BCP.

Disclosure

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

Approval

The principles of the Declaration of Helsinki were followed in this study. The study and the consent forms were approved by the Ethics Committee of the New York University College of Dentistry (approval # 88169).

Acknowledgments

This study was presented in the 2015 Italian Society of Periodontology (SIdP) meeting. No external funding, apart from the support of the authors' institutions, was available for this study.

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