Simultaneous Sinus Augmentation with Implant Placement: Histomorphometric Comparison of Two Different Grafting Materials. A Multicenter Double-Blind Prospective Randomized Controlled Clinical Trial

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Purpose: *Sinus elevation via the lateral approach for implant rehabilitation of atrophic posterior maxillae is considered a safe and predictable therapy. Several xenogeneic biomaterials of different biologic origin have been used as valid and predictable alternatives to autogenous bone. This multicenter randomized controlled double-blind prospective clinical trial aimed to compare histomorphometrically two xenogeneic grafting materials used for sinus elevation with simultaneous implant placement.* ***Materials and Methods:*** *Seven private practices in Italy were involved. Patients presenting at least one site with a residual bone crest height between 2 and 4 mm were treated. Control sites were grafted with 100% deproteinated particulated bovine bone (DPBB), while test sites were grafted with prehydrated corticocancellous porcine bone (PCPB). Root-form implants were placed simultaneously. Insertion torque and clinical stability were assessed and recorded. At 6 months, a biopsy specimen was harvested from each site, and histomorphometric analyses were performed.* ***Results:*** *Thirty-seven patients received 42 sinus elevations (24 test and 18 control). Eighty-two implants with adequate primary stability were placed. Fifty-five implants were placed in residual bone crests greater than 2 mm but less than 4 mm (average 2.7 mm) and achieved an average insertion torque of 22.8 ± 11.3 N/cm. Nineteen implants were placed in ridges greater than 3 mm but less than 5 mm, and eight were placed in ridges with more than 5 mm remaining. After 6 months, three implants had failed to integrate, leading to a survival rate of 96.34%. Forty-two specimens were analyzed histomorphometrically. No significant differences in total bone volume (PCPB 37.43%, DPBB 37.52%) or residual grafting material (PCPB 13.55%, DPBB 16.44%) were detected.* ***Conclusions:*** *In this study, PCPB compared well with DPBB as a grafting material for lateral sinus elevation.* Int J Oral Maxillofac Implants 2013;28:543–549. doi: 10.11607/jomi.2647

Key words: *bovine bone substitute, porcine bone particles, posterior maxilla, simultaneous implant position, sinus elevation*

Rehabilitation of the atrophic posterior edentulous maxilla is challenging because of the significant resorption of the alveolar process that occurs following extraction, coupled with pneumatization of the maxillary sinus.[1] Sinus floor elevation to overcome alveolar bone height deficiency was introduced and described by Boyne and James[2] and Tatum.[3] The earliest approaches to this surgery involved lateral access to the sinus antrum and filling of the cavity with autogenous bone graft. Although autogenous bone is still considered the gold standard for bone regenerative procedures,[4] in the past 25 years a number of different bone substitutes, including allografts, xenografts, and alloplastic materials, either alone or in various combinations, have been used in sinus elevation. Autogenous bone is a unique grafting material with osteoconductive, osteoinductive, and osteogenic properties.[5] Unfortunately, extraoral donor sites are often needed to acquire an adequate amount of bone to fill the elevated sinus, with a resultant significant increase in patient morbidity. Intraoral sites such as the symphysis may not provide adequate graft

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volume to fill the antrum and may be associated with neurologic disturbances such as transient or permanent paresthesia of the lip and mandibular incisors.[6–8]

Because of the reduced patient morbidity during sinus grafting, composite grafts have become favored over autogenous bone as the sole grafting material. In this technique, autogenous bone is mixed or even completely replaced by other bone substitutes such as deproteinized (bovine or porcine) bone matrix,[9,10] reabsorbable hydroxyapatite,[11] porous hydroxyapatite,[12] tricalcium phosphates,[13,14] and bioactive glass particles.[15,16] All these materials are considered osteoconductive and share the same biologic mechanism, as they work as a scaffold to permit outgrowth of osteogenic cells from existing bone surfaces into adjacent graft particles. This substrate scaffold supports also vessel ingrowth, so that over time the spaces between particles are colonized by newly formed bone. Histologic studies have shown that bone substitute particles are replaced to some extent by osteoclastic activity directed to the grafting granules that takes place at the time of the osteogenic process occurring inside the grafted area.

One of the most widely investigated bone substitutes is a deproteinated particulated bovine bone (DPBB) (Bio-Oss, Geistlich). Because of the overwhelming amount of published clinical, histologic, and histomorphometric data, this biomaterial may well be considered as a reference for any other nonautogenous bone grafting material. DPBB may be obtained from two different bone types (cortical and cancellous bone), is a calcium-deficient carbonate apatite with a crystal size of approximately 10 nm, and is chemically and physically identical to human bone.[17] The osteoconductive properties of DPBB have been studied in animal trials[18,19] and documented in well-designed clinical studies, especially sinus floor elevation procedures.[20–24] It is still not clear whether DPBB undergoes complete resorption at least within a year.[25] In human grafted sinuses, DPBB alone or mixed with other materials[8,16] has shown excellent histomorphometric, radiographic, and clinical results.

Recently, a new grafting material from a different porcine origin, particulated cortical porcine bone (PCPB) (OsteoBiol mp3, Tecnoss), was introduced into clinical practice. This PCPB has a porosity ranging from 600 to 1,000 μm,[26] and the prehydrated form is supplemented with collagen. Nannmark and Sennerby[27] reported on the optimal biocompatibility and osteoconductive properties of porcine bone alone and after the addition of collagen to the bone preparation. Its microstructure resembles that of human bone, with pore sizes ranging from 0.25 to 1 mm.[28]

This two-armed study was designed with two different experimental goals: *(1)* to report implant survival at 6, 12, and 24 months after placement simultaneously with sinus elevation with 100% xenogeneic bone substitute, and *(2)* to compare histomorphometrically two different xenografts in sinus elevation. The present paper will report the histomorphometric findings of the grafting materials, while implant survival data will be presented elsewhere.

MATERIAL AND METHODS

Randomization Method and Sample Size Definition

This multicenter double-blind prospective clinical trial involved seven private practice centers; at each center, a surgical operator and a data collector were identified.

Two bone substitutes were involved in the trial: PCPB and DPBB. An independent randomization center provided each center with sealed envelopes (each one was labeled with a center code and a progressive number) that indicated which material (test = PCPB, control = DPBB) would be used. The day before surgery, the independent randomization center matched envelopes with patients. During surgery and only after the lateral window had been elevated, the envelope was torn off and the graft material assigned to the case. The study design followed the CONSORT guidelines for randomized clinical trials and was carried out in accordance with the 2008 principles of the Declaration of Helsinki. The histologic assessor was blinded to the material examined, and the results were then correlated with the predetermined center/patient codes.

Patient Selection and Baseline Consultation

Patient inclusion criteria were: *(1)* age over 18 years; *(2)* full-mouth plaque score and full-mouth bleeding score < 25% and good general health at the time of surgery; *(3)* no signs or symptoms of maxillary sinus disease; and *(4)* insufficient bone volume in edentulous or partially edentulous lateral-posterior maxilla, with a residual bone crest height (RBCH) between 2 and 5 mm, as measured in cross-sectional reconstructions from computed tomographic (CT) scans. Exclusion criteria were: *(1)* RBCH > 5 mm in the lateral-posterior maxilla, which would allow a crestal approach to the sinus; *(2)* smoking (more than 10 cigarettes per day); *(3)* severe renal and/or liver disease; *(4)* a history of radiotherapy in the head and neck region; *(5)* chemotherapy for treatment of malignant tumors at the time of the surgical procedure; *(6)* uncontrolled diabetes; *(7)* active periodontal disease involving the residual dentition; *(8)* presence of mucosal disease, such as lichen planus, in the areas to be treated; *(9)* poor oral hygiene; and *(10)* noncompliance with the study protocols.

Initial consultation included careful review of medical and dental history, intra and extraoral examination, periodontal probing and full mouth series of radiographs. Periodontally affected patients underwent initial periodontal preparation to meet the inclusion criteria. For all patients a surgical and prosthetic treatment plan was defined. The nature and goals of the study were thoroughly discussed with each patient, and their availability for recalls in the first 2 years after surgery was specifically confirmed before they gave written consent to participate in the study.

Treatment Protocol

A panoramic radiograph and CT scan of the maxilla were obtained preoperatively for each patient. Implant positions were determined prior to surgery using a prosthetic radiopaque diagnostic guide. CT cross-sectional reconstructions were evaluated. At least one residual bone area in the lateral-posterior segments of the edentulous maxilla had to have a RBCH between 2 and 3 mm. Furthermore, average residual bone width had to be at least 5 mm, as measured on CT scans.

All patients underwent the same surgical protocol. Antibiotic prophylaxis (2 g amoxicillin, VELAMOX 1 g, Mediolanum Farmaceutici) was given 1 hour preoperatively, and 1 g was given twice a day for 1 week. Anti-inflammatory medication (nimesulide 100 mg, Mylan Generics) was administered immediately after surgery and continued twice a day for the first 2 to 3 days post-surgery as needed.

Root-form implants (SPI CONTACT, Thommen) were placed simultaneously with sinus elevation. To confirm primary implant stability, each center used the same surgical unit (Implantmed, W&H), which was digitally preset in terms of torque control by the manufacturer. The bony sinus windows were covered with a reabsorbable collagen membrane (Evolution, Tecnoss; or BioGide, Geistlich) according to the surgeon's preference.

Six months later, during stage-two surgery, a biopsy specimen was harvested. According to the clinical scenario, the bone specimen could be obtained with a 2-mm trephine, either between the implants or distally to the most distal implant, provided that the site had no more than 3 mm of RBCH. A bone specimen at least 8 mm long had to be harvested to ensure adequate histologic material.

All patients were treated with maxillary sinus floor elevation via a lateral approach, as described by Boyne and James.[2] One of the two xenografts was used as the sole grafting material. With the patient under local anesthesia (Ubistesin, 3M), a full-thickness mucoperiosteal flap was raised and the maxillary lateral wall was exposed. Vertical releasing incisions at the mesial and distal aspect were carried out according to surgical need. A small round diamond bur mounted on a high-speed or a piezoelectric insert was used to outline the osteotomy window. After the bony window was mobilized, the antral mucosa was carefully elevated using dedicated surgical curettes. The bony window was then gently pulled inward and upward, and the mucosa's integrity was checked. Upon completion of membrane elevation, implant sites were prepared with twist drills and dedicated shaping drills. Care was taken to underprepare the osteotomy sites to ensure the highest possible primary stability upon implant tapping. A custom-made measuring device was used to record the RBCH at any implant site. After this, the indicated graft material was packed into the cavity to partially fill the space. After implant insertion, any residual voids were grafted. The bony sinus window was then covered with a reabsorbable collagen membrane. Vertical interrupted mattress sutures were used to achieve primary flap closure. Periosteal releasing incisions were used if needed to achieve tension-free flap closure.

Stage-two surgery was performed at 6 months. All the implants were uncovered and the biopsy specimens harvested. Again under local anesthesia, a full-thickness flap was raised, and a 2-mm internal-diameter trephine mounted on a low-speed handpiece under abundant cooling solution was used to harvest the specimen. All the implants were loaded with fixed provisional restorations within 2 months of uncovering.

Histomorphometric Analysis and Tissue Processing

All specimens were processed and analyzed at the Institute for Biomedicine, University of Göteborg, Sweden. After being harvested, the specimens were carefully rinsed with sterile solution and immediately placed in a 4% paraformaldehyde solution for fixation. Specimens were decalcified in ethylenediaminetetraacetic acid (1%) for a period of 2 weeks and radiographed to verify that decalcification was complete. After dehydration in a graded series of ethanol, the specimens were embedded in paraffin, sectioned (3- to 5-mm sections), and stained with both hematoxylin-eosin and modified Mallory aniline blue.

Examinations were performed with a Nikon Eclipse 80i microscope (Teknooptik) equipped with an Easy Image 2000 System (Teknooptik) using ×4 to ×40 objectives for descriptive evaluation and morphometric measurements. Histomorphometric measurements were performed blindly for each specimen, and the following parameters were recorded: *(1)* total bone volume (TBV), expressed as a percentage; *(2)* amount of residual grafting material (GMR); and *(3)* amount of osteoid surface (OS), ie, soft tissue components including marrow spaces and connective tissue.

Table 1 Histomorphometric Findings of the Grafting Materials

Material/parameter	Mean (%)	Range (%)
DPBB (Bio-Oss)		
TBV	37.52	15.39–83.30
GMR	16.44	0–36.34
OS	46.02	30.85–74.48
PCPB (Osteobiol mp3)		
TBV	37.43	0–93.98
GMR	13.53	0–42.65
OS	49.03	0–93.00

One histologic specimen was recognized as not reliable in terms of histomorphometric analysis and represented as 0% in the range data.

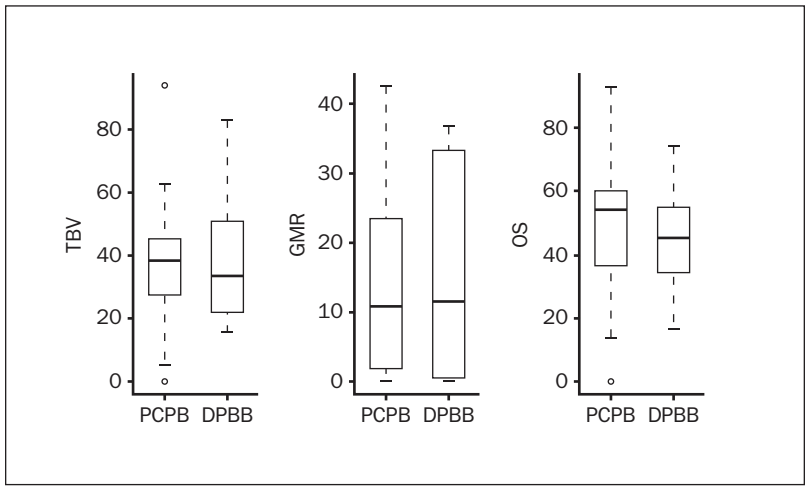

Fig 1 Box plots describing the statistical distribution of the results. The thick horizontal bars indicate median values, the upper and lower boundaries of the boxes indicate 75th and 25th percentiles of the empirical distribution for the corresponding treatment. Whiskers depict the full range of observed values in the sample.

RESULTS

Thirty-seven patients (age range, 35 to 68 years) were included in the study, and 42 sinuses (six from each center) were successfully treated with sinus elevation and simultaneous implant placement. Twenty-four sinuses were randomly grafted with PCPB (test) and 18 with DPBB (control). Eighty-two implants with adequate primary stability were placed. Fifty-five implants were placed in residual bone crests greater than 2 mm but less than 4 mm (average 2.7 mm) and achieved an average insertion torque of 22.8 ± 11.3 N/cm. Nineteen implants were placed in ridges greater than 3 mm but less than 5 mm, and eight were placed in ridges with more than 5 mm remaining. In all cases, healing was uneventful and no membrane perforations or sinus infections were reported by any center.

A total of 42 vertical biopsy specimens (24 test and 18 control) were harvested and available for histomorphometric analysis. Data regarding average percentages of TBV, GMR, and OS calculated are shown in Table 1.

The three box plots of Fig 1 compare the two treatments in terms of TBV, GMR, and OS percentages, respectively, on the basis of the full set of 42 sample units. An inspection of Table 1 suggests that PCPB showed a slightly higher median TBV and a slightly lower median GMR compared to DPBB. However, the mean TBV percentage for PCPB was 37.43% compared to a mean of 37.52% for DPBB, a difference that failed to achieve statistical significance ($P = .99$; t test). No striking asymmetries were evident in the empirical distribution of TBV percentage; therefore, the mean values are representative measures of central tendencies.

The mean GMR percentage for PCPB was 13.53%, compared to a mean of 16.44% for GMR percentage in DPBB; this difference also failed to achieve statistical significance ($P = .57$, t test). No striking asymmetries were evident in the empirical distribution of GMR percentage, so that mean values are representative measures of central tendency.

No significant difference in OS was detected between the two treatment groups ($P = .64$, t test).

Eighty-two implants were positioned at the time of sinus surgery. Implants were 4 or 4.5 mm in diameter, and lengths ranged from 9.5 to 11.5 mm. At 6 months, three implants had not osseointegrated and were removed, leading to a survival rate of 96.34%.

DISCUSSION

The present experimental randomized clinical trial was designed to evaluate the histologic behavior of two xenogeneic bone substitutes with different biologic origin used in sinus floor augmentation procedures via the lateral approach. At the same time, the survival rate of implants placed simultaneously with sinus elevation in severely resorbed bone crests (patients presenting at least one site with a residual bone crest height between 2 and 4 mm) was assessed. The two materials compared were DPBB and PCPB.

Although autogenous bone remains the gold standard for regenerative procedures, there is no evidence to either support or refute the superiority, with regard to implant survival, of autogenous bone over other graft materials.[8,9] Furthermore, at least for sinus elevation, it is still unclear whether a minimal TBV is required to ensure implant osseointegration.[29] In general, bone substitutes have allogeneic or xenogeneic origins or are created synthetically from calcium-based materials. Xenogeneic biomaterials are interesting as bone substitutes, as they display a morphology that is similar to that of human bone and have the potential for being resorbed in conjunction with providing a scaffold for osteoregeneration. Autogenous bone possesses osteoconductive, osteoinductive, and osteogenic properties[5]; unfortunately, the harvest of a sufficient quantity of bone graft to fill an augmented sinus usually requires the involvement of major donor sites, such as the iliac crest, chin, tibia, or calvarium, which is associated with a severe increase in patient morbidity. Among these osteoconductive bone substitutes, DPBB is a very well-documented material to which all different xenografts materials should be compared in terms of clinical handling, histomorphometric results, and surgical approach. Several clinical and experimental studies have demonstrated its biocompatibility and osteoconductive properties in different regenerative procedures. A rather interesting histologic finding is the persistence of DPBB granules within the grafted area, even after 6 and 10 years.[30]

PCPB is a newer xenogeneic biomaterial characterized by the addition of a collagen gel to the bone matrix.[27,31] From a clinical standpoint, this improves its handling properties, while histologically a high resorption rate of the collagenated PCPB granules has been reported, even after only 5 months.[26,27] PCPB has also demonstrated optimal biocompatibility and good osteoconductive properties for all bone regeneration procedures, particularly as the sole grafting material in lateral sinus elevation procedures.[32] In the present randomized clinical trial, the osteoconductive behaviors of PCPB and DPBB were compared as the sole grafting materials for lateral sinus floor augmentation procedures. The histomorphometric analysis failed to show any significant difference between the two grafting materials in terms of TBV (37.43% for PCPB versus 37.52% for DPBB) or for residual grafting material (PCPB GMR: 13.55%; DPBB GMR: 16.44%). From a biologic standpoint, the osteoconductive behavior of the two materials shows some microscopic differences that can be identified in high-magnification images (Fig 2). It has recently been shown in other studies[27,32] as well as in the present study that PCPB appears to activate bone metabolic units by deposition of new matrix and subsequent mineralization. This is a consequence of the resorption leading to apposition of new bone. The main reason for resorption is not yet known, but the authors suggest that collagen influences both cellular and molecular activity. Because little to no resorption takes place of the DPBB particles, a limitation of bone-forming capacity at sites grafted with DPBB could be speculated. Furthermore, the higher resorption rate suggests that with time, all other things being equal, the amount of bone might differ in favor of PCPB-grafted areas. However, in the present study, no obvious differences in the amount of bone, neovascularization, or soft tissue appearance were seen.

Figures 2a and 2b show the two studied biomaterials at low magnification. Both materials showed a relatively high degree of growth of new bone in between the particles. Also, soft tissue, most likely undefined bone marrow, could be seen. Remaining particles were surrounded by autogenous bone and newly vascularized tissues. Figures 2c and 2d show the different biomaterials at a higher magnification. In the PCPB specimens, signs of active resorption were apparent and the bone/biomaterial interface was more difficult to distinguish, in contrast to the DPBB sections.

To the authors' knowledge, this is the first multicenter randomized double-blind clinical trial to compare a new generation of porcine-derived xenograft to DPBB for sinus augmentation with simultaneous

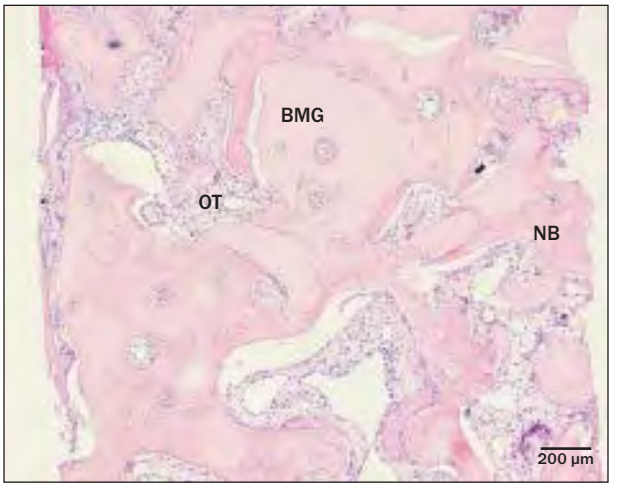

Fig 2a Low-magnification image (×4) of OsteoBiol mp3 (PCPB). NB = new bone; OT = osteoid tissue; BMG = biomaterial granule.

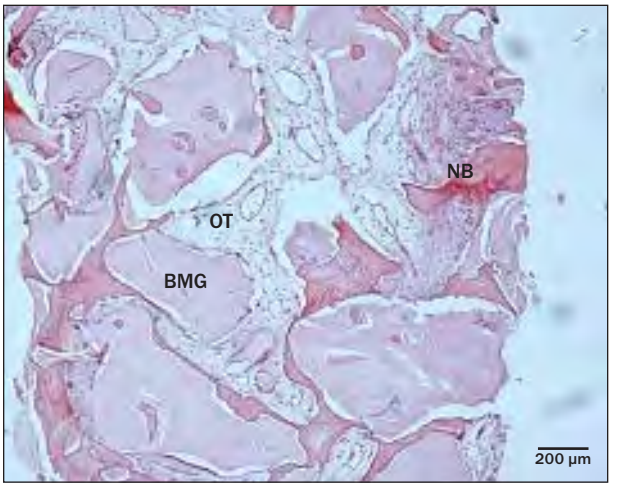

Fig 2b Low-magnification view (×4) of Bio-Oss (DPBB). NB = new bone; OT = osteoid tissue; BMG = biomaterial granule.

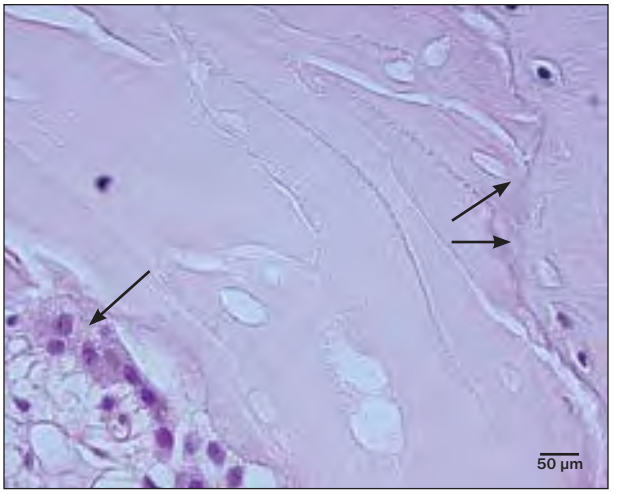

Fig 2c High-magnification image of PCPB. Signs of active resorption are apparent in the lower left corner (*arrow*), where osteoclasts have started to degrade the particles. The bone/biomaterial interface *(upper right arrow)* is difficult to distinguish in some areas (hematoxylin-eosin; magnification ×40).

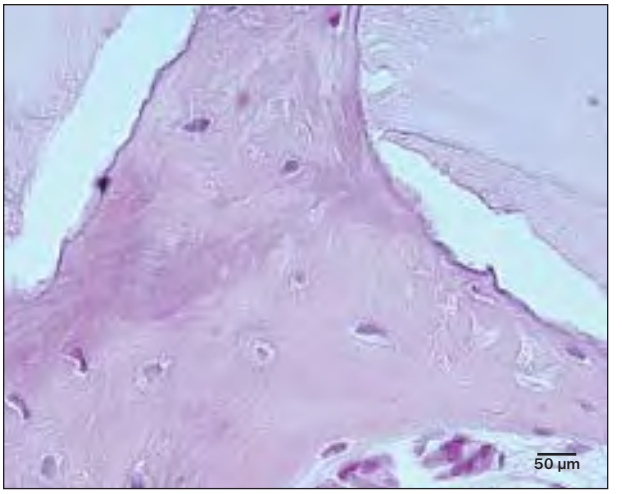

Fig 2d High-magnification image (×40) of DPBB. This specimen does not show the signs of active resorption that were apparent in the PCPB samples (hematoxylin-eosin; magnification ×40).

implant placement. The present data are in agreement with those reported by other authors[29,32] demonstrating that PCPB has a good osteoconductivity, and the data compare well to one of the better studied and most commonly used biomaterials (DPBB).

CONCLUSION

The histomorphometric data presented in the present experimental randomized clinical trial suggested that particulated cortical porcine bone is an excellent osteoconductor and compares well to deproteinated particulated bovine bone. The results of this study suggest that simultaneous implant placement along with sinus elevation by the lateral technique, even in cases of severely reduced bone crest height (2 to 4 mm), may be possible. The association of an experienced and well-trained surgeon and the efficiency of implant equipment may be a relevant parameter for successful implant therapy in sinus augmentation procedures with simultaneous implant positioning in terms of implant survival rate, provided that adequate primary implant stability is achieved. Long-term analysis of success and survival rates in this group of implants is underway.

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REFERENCES

1. Sharan A, Madjar D. Maxillary sinus pneumatization following extractions: A radiographic study. Int J Oral Maxillofac Implants 2008;23: 48–56.
2. Boyne PJ, James RA. Grafting of the maxillary sinus floor with autogenous marrow and bone. J Oral Surg 1980;38:613–616.
3. Tatum H Jr. Maxillary and sinus implant reconstructions. Dent Clin North Am 1986;30:207–229.
4. Misch CE. Maxillary sinus augmentation for endosteal implants: Organized alternative treatment plans. Int J Oral Implants 1987; 14:49–58.
5. Galindo-Moreno P, Avila G, Fernandez-Barbero JE, Mesa F, O'Valle-Ravassa F, Wang HL. Clinical and histologic comparison of two different composite grafts for sinus augmentation: A pilot clinical trial. Clin Oral Implants Res 2008;19:755–759.
6. Nkenke E, Radespiel-Troger M, Wiltfang J, Schultze-Mosgau S, Winkler G, Neukam FW. Morbidity of harvesting of retromolar bone grafts: A prospective study. Clin Oral Implants Res 2002;13:514–521.
7. Nkenke E, Schultze-Mosgau S, Radespiel-Troger M, Kloss F, Neukam FW. Morbidity of harvesting of chin graft: A prospective study. Clin Oral Implants Res 2001;12:495–502.
8. Nkenke E, Stelzle F. Clinical outcomes of sinus floor augmentation for implant placement using autogenous bone or bone substitutes: A systematic review. Clin Oral Implants Res 2009 Sep;20(suppl 4): 124–133.
9. Del Fabbro M, Testori T, Francetti L, Weinstein R. Systematic review of survival rates for implants placed in the grafted maxillary sinus. Int J Periodontics Restorative Dent 2004;24:565–577.
10. Artzi Z, Nemcovsky CE, Tal H, Dayan D. Histopathological morphometric evaluation of 2 different hydroxyapatite-bone derivatives in sinus augmentation procedures: A comparative study in humans. J Periodontol 2001;72:9–11.
11. Wagner JR. A 3 1/2-year clinical evaluation of resorbable hydroxylapatite OsteoGen (HA Resorb) used for sinus lift augmentations in conjunction with the insertion of endosseous implants. J Oral Implantol 1991;17(2):152–64.
12. Smiler DG, Holmes RE. Sinus lift procedure using porous hydroxyapatite: A preliminary clinical report. J Oral Implantol 1987;13(2):239–253.
13. Saffar JL, Colombier ML, Detienville R. Bone formation in tricalcium phosphate-filled periodontal intrabony lesions. Histological observations in humans. J Periodontol 1990;61(4):209–16.
14. Esposito M, Grusovin MG, Coulthard P, Worthington HV. The efficacy of various bone augmentation procedures for dental implants: A Cochrane systematic review of randomized controlled clinical trials. Int J Oral Maxillofac Implants 2006 Sep–Oct;21(5):696–710.
15. Tadjoedin ES, de Lange GL, Lyaruu DM, Kuiper L, Burger EH. High concentrations of bioactive glass material (Biogran) vs autogenous bone for sinus floor elevation. Clin Oral Implants Res 2002;13:428–436.
16. Tadjoedin ES, de Lange GL, Holzmann PJ, Kulper L, Burger EH. Histological observations on biopsies harvested following sinus floor elevation using a bioactive glass material of narrow size range. Clin Oral Implants Res 2000;11:334–344.
17. Hürzeler MB, Quiñones CR, Kirsch A, et al. Maxillary sinus augmentation using different grafting materials and dental implants in monkeys. Part I. Evaluation of anorganic bovine-derived bone matrix. Clin Oral Implants Res 1997 Dec;8:476–486.
18. Klinge B, Alberius P, Isaksson S, Jönsson J. Osseous response to implanted natural bone mineral and synthetic hydroxylapatite ceramic in the repair of experimental skull bone defects. J Oral Maxillofac Surg 1992;50:241–249.
19. Spector M. Anorganic bovine bone and ceramic analogs of bone mineral as implants to facilitate bone regeneration. Clin Plast Surg 1994;21:437–444.
20. Valentini P, Abensur D, Densari D, Graziani JN, Hammerle CHF. Histological evaluation of Bio-Oss in a 2-stage sinus floor elevation and implantation procedure. Clin Oral Implants Res 1998;9:59–64.
21. Piattelli M, Favero GA, Scarano A, Orsini G, Piattelli A. Bone reactions to anorganic bovine bone (Bio-Oss) used in sinus procedures: A histologic long-term report of 20 cases in humans. Int J Oral Maxillofac Implants 1999;14:835–840.
22. Valentini P, Abensur D. Maxillary sinus floor elevation for implant placement with demineralized freeze-dried bone and bovine bone (Bio-Oss): A clinical study of 20 patients. Int J Periodontics Restorative Dent 1997;17:233–241.
23. Froum SJ, Wallace SS, Cho SC, Elian N, Tarnow DP. Histo- morphometric comparison of a biphasic bone ceramic to anorganic bovine bone for sinus augmentation: 6- to 8-month postsurgical assessment of vital bone formation. A pilot study. Int J Periodontics Restorative Dent 2008;28:273–281.
24. Sbordone L, Levin L, Guidetti F, Sbordone C, Glikman A, Schwartz-Arad D. Apical and marginal bone alterations around implants in maxillary sinus augmentation grafted with autogenous bone or bovine bone material and simultaneous or delayed dental implant positioning. Clin Oral Implants Res 2011 May;22:59–64.
25. Skoglund A, Hising P, Young C. A clinical and histologic examination in humans of the osseous response to implanted natural bone mineral. Int J Oral Maxillofac Implants 1997;12:194–199.
26. Barone A, Crespi R, Aldini NN, Fini M, Giardino R, Covani U. Maxillary sinus augmentation: Histologic and histomorphometric analysis. Int J Oral Maxillofac Implants 2005;20:519–525.
27. Nannmark U, Sennerby L. The bone tissue responses to prehydrated and collagenated cortico-cancellous porcine bone grafts: A study in rabbit maxillary defects. Clin Implant Dent Relat Res 2008;10:264–270.
28. Kim SH, Shin JW, Park SA, et al. Chemical, structural properties, and osteoconductive effectiveness of bone block derived from porcine cancellous bone. J Biomed Mater Res B Appl Biomater 2004;68:69–74.
29. Klijn RJ, Meijer GJ, Bronkhorst EM, Jansen JA. A meta-analysis of histomorphometric results and graft healing time of various biomaterials compared to autologous bone used as sinus floor augmentation material in humans. Tissue Eng Part B Rev 2010;16:493–507.
30. Sartori S, Silvestri M, Forni F, Icaro Cornaglia A, Tesei P, Cattaneo V. Ten-year follow-up in a maxillary sinus augmentation using anorganic bovine bone (Bio-Oss). A case report with histomorphometric evaluation. Clin Oral Implants Res 2003;14:369–372.
31. Orsini G, Searano A, Piattelli M, Piccirilli M, Caputi S, Piattelli A. Histologic and ultrastructural analysis of regenerated bone in maxillary sinus augmentation using a porcine bone-derived biomaterial. J Periodontol 2006;77:1984–1990.
32. Barone A, Ricci M, Covani U, Nannmark U, Azarmehr I, Calvo-Guirado JL. Maxillary sinus augmentation using prehydrated cortico-cancellous porcine bone: Histomorphometric evaluation after 6 months. Clin Implant Dent Relat Res 2012 Jun;14:373–379.