*Ji Hyun Lee*
*Ui Won Jung*
*Chang Sung Kim*
*Seong Ho Choi*
*Kyoo Sung Cho*

# Histologic and clinical evaluation for maxillary sinus augmentation using macroporous biphasic calcium phosphate in human

**Authors' affiliations:**
*Ji Hyun Lee, Ui Won Jung, Chang Sung Kim*, Department of Periodontology, Research Institute for Periodontal regeneration, College of Dentistry, Yonsei University, Seoul, South Korea
*Seong Ho Choi, Kyoo Sung Cho*, Brain Korea 21 Project for Medical Science, Department of Periodontology, Research Institute for Periodontoal Regeneration, College of Dentistry, Yonsei University, Seoul, South Korea

**Correspondence to:**
*Kyoo Sung Cho*
Brain Korea 21 Project for Medical Science
Department of Periodontology
Research Institute for Periodontoal Regeneration
College of Dentistry
Yonsei University
Seoul
South Korea Tel.: +82-2-2228-3188
Fax: +82-2-392-0398
e-mail: kscho@yuhs.ac

**Key words:** sinus floor elevation, bone substitutes, clinical research, clinical trials

**Abstract**

**Objectives:** This study evaluated both the clinical and histological aspects of bone formation in maxillary sinus augmentation using MBCP as the bone-grafting material.
**Material and methods:** MBCP was used as a primary bone substitute for maxillary sinus augmentation. Fifty-two patients were selected after a medical and dental examination, and were divided into the following three groups: those augmented with MBCP only; MBCP combined with irradiated cancellous bone; and MBCP combined with intraoral autogenous bone. After a healing period (average 6.78 months after surgery), bone cores were harvested for a histological evaluation and the implant fixtures were installed. These bone cores were evaluated via light microscope and implants were followed up for at least six months after loading.
**Results:** Four to ten months after surgery, new vital bone surrounding the MBCP particles was observed in 18 bone biopsies. Two out of the 130 implants installed were explanted due to a failure of osseointegration before the prosthetic procedure. All the remaining implants were functioning for 6 to 27 months (average 12.96 months). The cumulative survival rate of the implants was 98.46%.
**Conclusion:** These results show that MBCP can be used as a grafting material for sinus floor augmentation, whether combined with other bone graft materials or not, and lead to a predictable prognosis for dental implants in the posterior maxillary area where there is insufficient vertical height for fixture installation.

**Date:**
Accepted 19 August 2007

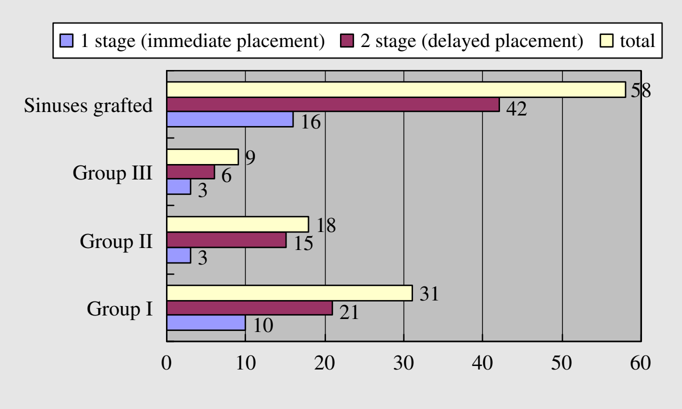
**To cite this article:**
Lee JH, Jung UW, Kim CS, Choi SH, Cho KS. Histologic and clinical evaluation for maxillary sinus augmentation using macroporous biphasic calcium phosphate in human.
*Clin. Oral Impl. Res.* 19, 2008; 767–771
doi: 10.1111/j.1600-0501.2008.01520.x

Maxillary sinus augmentation is an established method that is intended to achieve sufficient vertical bone height on the maxillary posterior region before the placement of an endosseous dental implant. The aim is to restore the resorbed posterior maxilla in order to allow the placement of stable dental implants through the dynamic process of osseointegration. Boyne & James (1980) first reported this technique, which has subsequently been developed and modified by other clinicians.

Autogenous bone is considered to be the gold standard for reconstructing a discontinuity in bone defect and even in sinus floor augmentation (Tadic & Epple 2004). Autogenous bone contains viable cells that can proliferate and contribute to the formation of new bone (Burchardt 1983). However, it has been shown that alloplasts such as hydroxyapatite (HA), β-tricalcium phosphate (β-TCP), bioactive glass have almost equal efficacy in sinus floor augmentation procedures to autogenous bone both clinically and scientifically (Jensen 2006; Wallace et al. 2003).

Recently, some studies have demonstrated the stability and effectiveness of a

***Table 1.*** **Distribution of grafting materials**



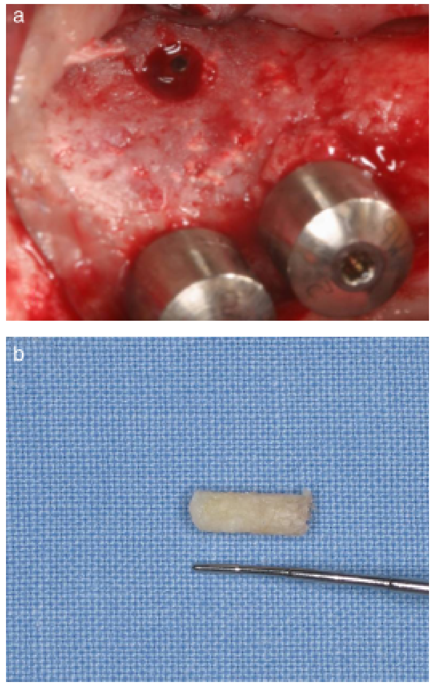




*Fig. 1.* Clinical findings 6 months after sinus graft. (a) Two fixtures are installed successfully. Bone biopsy is harvested from the previous trap door site using trephine drill. (b) Harvested bone core.

mixture of HA and β-TCP for each in sinus floor augmentation (Engelke et al. 2003; Artzi et al. 2004; Suba et al. 2004; Maiorana et al. 2005; Silva et al. 2005). Although HA and its residual crystals provide a good scaffold for the growth of new bone, it has been shown to have poor regeneration potential (Ono et al. 1992; Martin et al. 1993; Kokubun et al. 1994; Ono et al. 2000). β-TCP has been demonstrated to form new bone within the periodontal osseous defects with an unpredictable resorption pattern and rate (Klein et al. 1983). Therefore, the controlled bioactivity with perfect equilibrium between ceramic resorption and bone substitution (Nery et al. 1992; Yamada et al. 1997) has necessitated the judicious mixing of a stable component (HA) and a more bioactive component (β-TCP).

Some studies have suggested an optimum ratio of HA/β-TCP (Hubbard 1974; Ellinger et al. 1986). Nery et al. (1992) have shown that a higher HA ratio causes accelerated new bone formation in osseous defects. A mixture of 60% HA and 40% β-TCP is known to be ideal for biphasic calcium phosphate ceramics as bone substitutes (Ellinger et al. 1986; Yamada et al. 1997).

Macroporous biphasic calcium phosphate (MBCP, Biomatlante Sarl, Nantes, France), with the above-mentioned ratio, has the required porous form for biological exchanges particularly for bone ingrowth and mineralization. Because it is believed that the addition of autogenous bone or osteoinductive agents will induce and facilitate bone formation with the incorporation of bone graft materials (Block & Kent 1997; Misch 2002), frozen irradiated allogenic cancellous bone and marrow [irradiated cancellous bone and marrow (ICB), Rocky mountain tissue bank, USA] was used in this study. The aim of this study was to evaluate the histological and clinical outcomes of three groups of graft materials used in sinus floor augmentation (MBCP only, MBCP combined with ICB, MBCP combined with intraoral autogenous bone).

## Materials and methods

### Study populations

Between March 2004 and August 2005, 52 patients (24 females, 28 males) with insufficient residual bone height (<6 mm) were enrolled in this study. Their ages ranged from 30 to 73 years, with a mean age of 50 years. The inclusion criterion was <6 mm of the alveolar bone remaining on the floor of the sinus, as determined by computed tomography (GE Medical Systems, Milwaukee, WI, USA). All the patients were free from the conditions that would contraindicate dentoalveolar flap surgery or maxillary sinus problems, such as a recent history of acute maxillary sinusitis. A two-stage approach was performed in 42 maxillary sinuses (36 patients). A one-stage approach was performed in 16 sinuses (16 patients) that had sufficient bone height in obtaining initial stability (4–6 mm) (Table 1). A total of 130 implants were installed. Seventy-five implants were the oxidized titanium screw type (TiUnite™, Nobel Biocare, Göteborg, Sweden) and 55 implants were the sand-blasted, large grit, acid-etched type (ITI dental implant system, Straumann, Basel, Switzerland). Only six patients were bilaterally edentulous. The remaining 46 patients were unilaterally edentulous. Information was given about this study and a written informed consent form was signed. The protocol was approved by an Institutional Review Board for Clinical Research in Yonsei Dental Hospital (IRB-2004-02).

### Sinus floor augmentation technique

All surgical procedures were completed under local anesthesia (2% lidocaine, 1 : 100,000 epinephrine, Kwangmyung Pharm., Seoul, Korea). The surgical procedure for the maxillary sinus augmentation has been described elsewhere (Haris et al. 1998). The cavity produced was filled with the graft material with meticulous condensation. The defect of the lateral wall was covered with a collagen membrane (Collatape®, Calcitek, Carlsbad, CA, USA). Implant fixtures, 4 or 5 mm in diameter, were installed, and patients who had undergone a two-stage procedure, installations were done 3–13 months (average 6.68 months) after the augmentation procedure. At the time of implant installation, a lateral biopsy of each side was taken cranially from the dental implant using a hollow trephine drill (3i, West Palm Beach, FL, USA) (Fig. 1). It was possible because

***Table 2.*** **Life table analysis**

| Time | Implant entering interval | Failed in interval | Dropout | Survival rate (%) | Cummulative survival rate (%) |
|---|---|---|---|---|---|
| Placement to loading | 130 | 2 | 0 | 98.46 | 98.46 |
| Loading to 1 year | 128 | 0 | 0 | 100 | 98.46 |

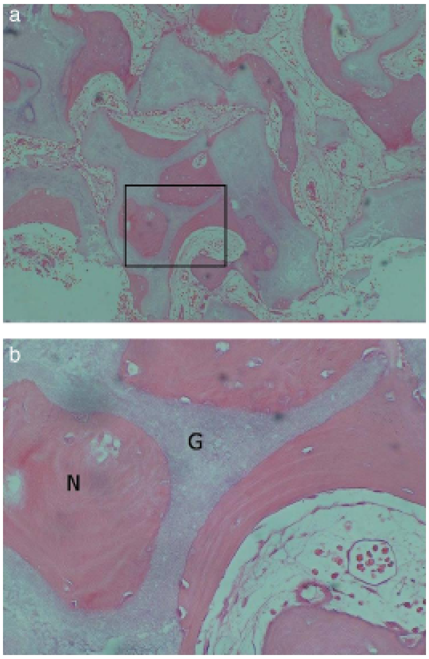



*Fig. 2.* Histologic finding 10 months after surgery (Group I). (a) The macroporous biphasic calcium phosphate particles are fully integrated into new bone and invaginated in woven bone (original magnification × 100). (b) Magnified view of (a): grafted material (G) and vital bone (N) are in close contact and osteocytes are observed. The reversal line in newly formed bone is obvious (original magnification × 400).

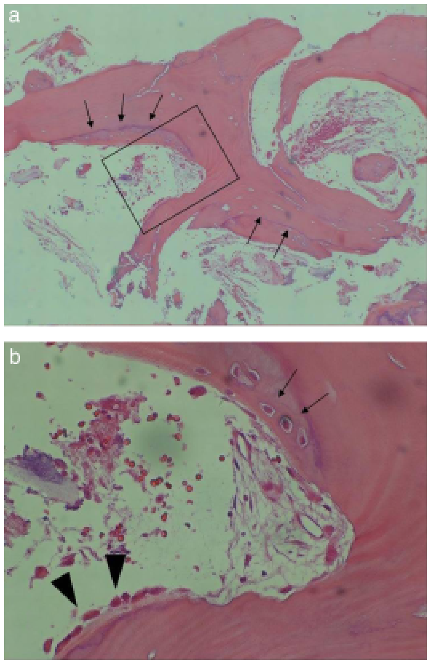



*Fig. 3.* Histologic finding 6 months after surgery (Group II). (a) Show the JCB characterized with empty lacunae, surrounded by newly-formed vital bone whose boundary is well-defined (arrow) (original magnification × 100). (b) Magnified view of (a): osteoblastic cell lining (arrow head) and osteocytes in lacunae, which is the characteristics of vital bone (arrow) (original magnification × 400).

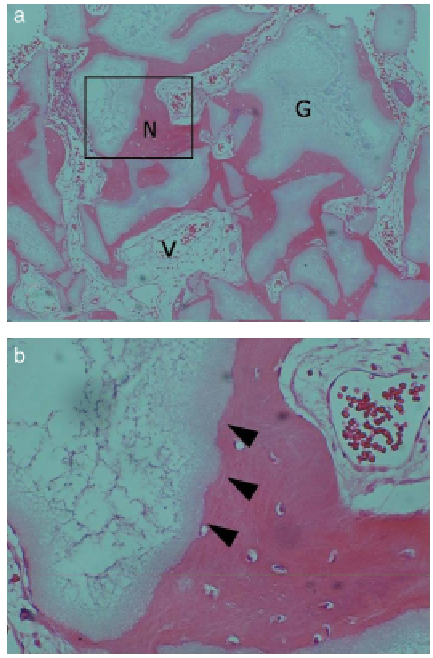



*Fig. 4.* Histologic findings 6 months after surgery (Group III). (a) Macroporous biphasic calcium phosphate (MBCP) particles (G) embedded in newly formed bone (N). Ample marrow space filled with loose connective tissue and abundant blood vessels (V) (original magnification × 100). (b) Magnified view of (a): irregular limit between the new bone and residual MBCP particle shows the progress of bone remodeling (arrow head), which ensures the replacement of grafted material (original magnification × 400).

MBCP particles were remained on the trapdoor site to be observed via naked eyes even though the graft and new bone were well blended with adjacent host bone. Eighteen biopsies in total were harvested 4–10 months (average 6.78 months) after surgery. All the dental implants except for five fixtures showing rotational mobility presented with good initial stability.

#### Bone augmentation materials

The patients were divided into three groups (Table 1): 27 patients received MBCP only for sinus floor augmentation (Group I), 16 patients received MBCP combined with ICB (at a ratio of 50 : 50) (Group II) and the remaining nine patients received MBCP combined with autogenous bone (at a ratio of 80 : 20) for sinus floor augmentation (Group III). Corticocancellous bone of the mandibular ramus or maxillary tuberosity was harvested for the autogenous bone graft. The autogenous block bone was harvested from the mandibular ramus using a trephine drill and particulated using a device (Bone crusher, stainless steel, G. Hartzell & Son. Inc., Concord, CA, USA). Autogenous bone was harvested from the maxillary tuberosity with a bone rongeur (Beyer double action rongeur, ACE Surgical Supply Co. Inc., Brockton, MA, USA).

#### Histological processing

After taking the biopsies, they were immediately fixed in 10% buffered formalin for 10 days. After rinsing in water, the sections were decalcified in 5% formic acid for 14 days and embedded in paraffin. Serial sections, 5 μm thick, were cut along the longitudinal plane. From each bone core, two central sections were selected and stained with hematoxylin and eosin, and examined by optical microscopy coupled to a video camera (Olympus BX50, Olympus Optical Co., Tokyo, Japan). Images of the slides were taken and saved as figure files.

## Results

#### Clinical observation

Healing process after sinus graft procedure was uneventful, even though small tears (< 5 mm) have occurred in five sinuses. None of the patients had influential complications on prognosis of implants such as infection, maxillary sinusitis, and severe sinus membrane perforation. In all three groups, good initial stability was achieved and only five implants showed rotational mobility, which did not correspond to failed implants. It was possible to overcome the poor bone quality through well-known technique such as drilling with smaller diameter and bone compaction using osteotome. Therefore, the fixtures in the 27 sinuses were uncovered at their installation because of good initial stability. Only two fixtures were removed so far, one each from Group I and Group III, just before loading and 1 month after installation surgery, respectively; the failed implants were successfully replaced by wider fixtures. The implants under function were defined as to survive, according to the criteria described by Buser et al (1990). A 100% prosthetic survival rate for 128 implants placed into grafted sinuses was achieved. The cumulative implant success rate after a mean period of 12 months was 98.46% (Table 2).

#### Histological observations

Histologic evaluation could be made of only 18 patients (six from Group I, eight from Group II, and three from Group III), who agreed with harvesting bone core. The gross histology of the retrieved tissues was similar for the three types of graft material. Histologic evaluation at the time of fixture installation revealed new bone formation in conjunction with resorption of graft particles. Most of the MBCP particles were embedded in or surrounded by newly formed bone and it was possible to observe the close contact between graft particles and newly formed bone trabecules (Figs 2 and 4). Newly formed bone was characterized by lacunae containing osteoblast, which seemed to be osteocyte, and had abundant medullary space filled with a well-vascularized connective tissue with no histologic markers of inflammation (i.e., neutrophils and macrophage) or foreign body reaction. The new cancellous bone also exhibited incremental basophilic lines (Figs 2 and 4) .

ICB, used with MBCP in Group II, clearly exhibited differences in comparison with natural bone in spite of similar color they share. In the area of ICB, the osteocyte lacunae were empty and the lamellar layer or reversal line was not obvious and indistinct. As the field of MBCP particle embedded, ICB was surrounded by newly formed bone with close contact. Cells expected to be osteoblastic were lined on boundary of new bone or new bone matrix (Fig. 3). Especially, histologic findings were very similar for Groups I and III because autogenous particles could hardly be distinguished, because they were already resorbed or incorporated with the new bone (Fig. 4).

## Discussion

The present study evaluated the efficacy of MBCP as a grafting material for maxillary sinus augmentation in both one-stage and two-stage approach. Clinically, only two out of 130 implants were lost, and the 1-year survival rate was 98.46%. This result is in agreement with several studies that demonstrated the favorable clinical results in sinus floor augmentation and implant survival with alloplast including HA and β-TCP either alone or an expander (Wheeler et al. 1996; Engelke et al. 2003; Mangano et al. 2003; Szabo et al. 2005). One of the failed implants was removed at 1 month after fixture installation surgery with simultaneous uncovering procedure. It is suspected that premature loading in the most distal site of implant leaded to fail in a month despite good initial stability. The other failed implant was lost during impression taking procedure due to unsuccessful osseointegration.

The aspect to be focused on histologically is the resorptive behavior of MBCP particles (Klein et al. 1983). Bone biopsies taken at 4–10 months after sinus graft (average 6.78 months) show initiation of resorption and newly formed bone in contact with residual MBCP particles without any adverse reaction such as the presence of multinuclear giant cells. Highly magnified view in a light microscope showed that the boundary between MBCP particle and newly formed bone was irregular, suggesting the resorption of MBCP particles with the simultaneous apposition of new bone. It seems to be possible for all MBCP particles to be gradually resorbed completely and substituted by newly formed bone, resulting in alloplastic material not interfering with bone remodeling even on the bone to implant surface. It is obvious that data resulting from even 58 grafts and 18 biopsies cannot be considered conclusive. However, when it is reminded that the bottom line of sinus graft is successful installation of functional dental implants on posterior maxilla with insufficient bone height, it seems to be clear that alloplasts can provide the necessary bone augmentation in the majority of sinus graft cases except extremely resorbed posterior maxilla. This is mainly due to bone conduction ability of alloplasts and the intrinsic bone-growing capacity of the sinus walls (Tong et al. 1998; Tadjoedin et al. 2000; Maiorana et al. 2005; Fugazzotto et al. 2001, Butz et al. 2005).

In conclusion, it can be inferred that MBCP when used as a grafting material for sinus floor augmentation, whether combined with other osteoinductive materials or not, may lead to the predictable results for dental implants on posterior maxillary area with insufficient vertical height for fixture installation.

**Acknowledgements:** This study was supported by the Yonsei University, College of Dentistry Research Fund of 2007.

## References

Artzi, Z., Weinreb, M., Givol, N., Rohrer, M.D., Nemcovsky, C.E., Prasad, H.S. & Tal, H. (2004) Biomaterial resorption rate and healing site morphology of inorganic bovine bone and beta-tricalcium phosphate in the canine: a 24-month longitudinal histologic study and morphometric analysis. *International Journal of Oral & Maxillofacial Implants* **19**: 357–368.

Block, M.S. & Kent, J.N. (1997) Sinus augmentation for dental implants: the use of autogenous bone. *Journal of Oral and Maxillofacial Surgery* **55**: 1281–1286.

Boyne, P.J. & James, R. (1980) Grafting of the maxillary sinus floor with autogenous marrow and bone. *Journal of Oral Surgery* **38**: 613–616.

Burchardt, H. (1983) The biology of bone graft repair. *Clinical Orthopaedics and Related Research* **174**: 28–42.

Buser, D., Bragger, U., Lang, N.P. & Nyman, S. (1990) Regeneration and enlargement of jaw bone using guided tissue regeneration. *Clinical Oral Implants Research* **1**: 22–32.

Butz, S.J. & Huys, L.W. (2005) Long-term success of sinus augmentation using a synthetic alloplast: a 20 patients, 7 years clinical report. *Implant Dentistry* **14**: 36–42.

Ellinger, R.F., Nery, E.B. & Lynch, K.L. (1986) Histological assessment of periodontal osseous defects following implantation of hydroxyapatite and biphasic calcium phosphate ceramics: a case report. *International Journal of Periodontics and Restorative Dentistry* **6**: 22–33.

Engelke, W., Schwarzwaller, W., Behnsen, A. & Jacobs, H.G. (2003) Subantroscopic laterobasal sinus floor augmentation (SALSA): an up-to-5-year clinical study. *International Journal of Oral & Maxillofacial Implants* **18**: 135–143.

Fugazzotto, P.A. & Pikos, M.A. (2001) Guided bone regeneration and sinus augmentation in the absence of autogenous bone grafting. *Implant Dentistry* **10**: 158–161.

Haris, A.G., Szabo, G., Ashman, A., Divinyi, T., Suba, Z. & Martonffy, K. (1998) Five-year 224-patient prospective histological study of clinical applications using a synthetic bone alloplast. *Implant Dentistry* **7**: 287–299.

Hubbard, W. (1974) *Physiological calcium phosphate as orthopedic biomaterials*. PhD thesis, Marquette University, Milwaukee, WI, USA.

Jensen, O.T. (2006) *The Sinus Bone Graft*. Chicago: Quintessence.

Klein, C.P., Driessen, A.A., de Groot, K. & van den Hooff, A. (1983) Biodegradation behavior of various calcium phosphate materials in bone tissue. *Journal of Biomedical Materials Research* **17**: 769–784.

Kokubun, S., Kashimoto, O. & Tanaka, Y. (1994) Histological verification of bone bonding and ingrowth into porous hydroyapatite spinous process spacer for cervical laminoplasty. *Tohoku Journal of Experimental Medicine* **173**: 337–344.

Maiorana, C., Sigurta, D., Mirandola, A., Garlini, G. & Santoro, F. (2005) Bone resorption around dental implants placed in grafted sinuses: clinical and radiologic follow-up after up to 4 years. *International Journal of Oral & Maxillofacial Implants* **20**: 261–266.

Mangano, C., Bartolucci, E.G. & Mazzocco, C. (2003) A new porous hydroxyapatite for promotion of bone regeneration in maxillary sinus augmentation: clinical and histologic study in humans. *International Journal of Oral & Maxillofacial Implants* **18**: 23–30.

Martin, R.B., Chapman, M.W., Sharkey, N.A., Zissimos, S.L., Bay, B. & Shores, E.C. (1993) Bone ingrowth and mechanical properties of coralline hydroxyapatite 1 year after implantation. *Biomaterials* **14**: 341–348.

Misch, C. (2002) *The Maxillary Sinus Lift and Sinus Graft Surgery*. St Louis: Mosby.

Nery, E.B., LeGeros, R.Z., Lynch, K.L. & Lee, K. (1992) Tissue response to biphasic calcium phosphate ceramic with different ratios of HA/beta-TCP in periodontal osseous defects. *Journal of Periodontology* **63**: 729–735.

Ono, I., Ohura, T., Murata, M., Yamaguchi, H., Ohnuma, Y. & Kuboki, Y. (1992) A study on bone induction in hydroxyapatite combined with bone morphogenetic protein. *Plastic and Reconstructive Surgery* **90**: 870–879.

Ono, I., Tateshita, T. & Nakajima, T. (2000) Evaluation of a high density polyethylene fixing system for hydroxyapatite ceramic implants. *Biomaterials* **21**: 143–151.

Silva, R.V., Camilli, J.A., Bertran, C.A. & Moreira, N.H. (2005) The use of hydroxyapatite and autogenous cancellous bone grafts to repair bone defects in rats. *International Journal of Oral and Maxillofacial Surgery* **34**: 178–184.

Suba, Z., Takacs, D., Gyulai-Gaal, S. & Kovacs, K. (2004) Facilitation of beta-tricalcium phosphate-induced alveolar bone regeneration by platelet-rich plasma in beagle dogs: a histologic and histomorphometric study. *International Journal of Oral & Maxillofacial Implants* **19**: 832–838.

Szabo, G., Huys, L., Coulthard, P., Maiorana, C., Garagiola, U., Barabas, J., Nemeth, Z., Hrabak, K. & Suba, Z. (2005) A prospective multicenter randomized clinical trial of autogenous bone versus beta-tricalcium phosphate graft alone for bilateral sinus elevation: histologic and histomorphometric evaluation. *International Journal of Oral & Maxillofacial Implants* **20**: 371–381.

Tadic, D. & Epple, M. (2004) A thorough physicochemical characterisation of 14 calcium phosphate-based bone substitution materials in comparison to natural bone. *Biomaterials* **25**: 987–994.

Tadjoedin, E.S., de Lange, G.L., Holzmann, P.J., Kulper, L. & Burger, E.H. (2000) Histological observations on biopsies harvested following sinus floor elevation using a bioactive glass material of narrow size range. *Clinical Oral Implants Research* **11**: 334–344.

Tong, D.C., Rioux, K., Drangsholt, M. & Beirne, O.R. (1998) A review of survival rates for implants placed in grafted maxillary sinuses using meta-analysis. *International Journal of Oral & Maxillofacial Implants* **13**: 175–182.

Wallace, S.S. & Froum, S.J. (2003) Effect of maxillary sinus augmentation on the survival of endosseous dental implants. A systematic review. *Annals of Periodontology* **8**: 328–343.

Wheeler, SL H.R. & Calhoun, CJ. (1996) Six-year clinical and histologic study of sinus-lift grafts. *International Journal of Oral & Maxillofacial Implants* **11**: 26–34.

Yamada, S., Heymann, D., Bouler, J.M. & Daculsi, G. (1997) Osteoclastic resorption of calcium phosphate ceramics with different hydroxyapatite/beta-tricalcium phosphate ratios. *Biomaterials* **18**: 1037–1041.