A Prospective 1-Year Clinical and Radiographic Study of Implants Placed after Maxillary Sinus Floor Augmentation with Synthetic Biphasic Calcium Phosphate or Deproteinized Bovine Bone

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ABSTRACT

Background: The technique of using bone grafts or different biomaterials for augmentation of the maxillary sinus prior to implant placement is well accepted by clinicians. However, clinical documentation of some bone substitutes is still lacking.

Purpose: This prospective study was designed to evaluate the success rate of implants placed after maxillary sinus augmentation with a novel synthetic biphasic calcium phosphate (BCP) or deproteinized bovine bone (DBB), the latter acting as control.

Material and Methods: Nine edentulous patients and two partially edentulous patients with a mean age of 67 years with a bilateral need for sinus augmentation, <5 mm residual bone in the floor of the sinus and a crestal width \geq 4 mm, were included in the study. After bilateral elevation of the Schneiderian membrane, all patients were randomized for augmentation with synthetic BCP in one side and DBB in the contralateral side. After 8 months of graft healing, 62 implants with an SLActive surface were placed. Implant survival, graft resorption, plaque index, bleeding on probing, sulcus bleeding index, probing pocket depth, and implant success rate were evaluated after 1 year of functional loading.

Results: After a mean of 118 days, all patients received their fixed prosthetic constructions. One implant was lost in each biomaterial, giving an overall survival rate of 96.8%. Success rates for implants placed in BCP and DBB were 91.7 and 95.7%, respectively. No significant difference in marginal bone loss was found around implants placed in BCP, DBB, or residual bone, respectively. The mean graft resorption was 0.43 mm (BCP) and 0.29 mm (DBB).

Conclusion: In this limited study, implant success rate was not dependent on the biomaterial used for maxillary sinus augmentation. Similar results were found after 1 year of functional loading for implants placed after sinus augmentation using BCP or DBB.

KEY WORDS: augmentation, Bio-Oss®, bone substitutes, BoneCeramic®, dental implants, sinuslift

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INTRODUCTION

Implant placement in the posterior maxilla is often associated with the need for bone grafting.^{1–3} Even though new techniques have been described leading to bone formation without maxillary sinus floor grafting, longterm follow-up data are still missing.^{4,5} Previously, autogenous bone was considered the gold standard for grafting procedures; today, however, it is obvious that some biomaterials can produce results equal to autogenous bone, and are actually recommended as the first choice in sinus augmentation procedures.^{6,7}

With respect to the osteoinductive, osteoconductive and osteogenic properties, and morphology and mechanical characteristics, bone substitutes can vary widely.⁸⁻¹² Some of them are resorbable or slowly degradable and some are nonresorbable.^{13,14} The different properties may be of importance for the final result, such as maintenance of the graft volume over time; therefore, increased knowledge about the biological behavior of these materials in humans is important.

Both deproteinized bovine bone (DBB) and tricalcium phosphate (TCP) are materials that are frequently used and have been well documented.⁷ From a biological point of view, TCP may be superior to DBB, as the material dissolves into phosphorous and calcium ions, which theoretically may stimulate new bone formation;^{15–18} however, one potential drawback is the quick resorption of TCP. On the other hand, a disadvantage with DBB is the fact that it originates from bovine bone, which frequently has been questioned.^{19,20} If equivalent results to those with DBB could be obtained using synthetic biomaterials, this would probably be preferred.

An earlier problem with synthetic materials was to mimic human bone and DBB in its structure and elemental content. During the last few years, Bone-Ceramic (Straumann®, Basel, Switzerland) has been introduced to the market. BoneCeramic® is a biphasic calcium phosphate (BCP) that consists of 60% hydroxyapatite (HA) and 40% TCP. A possible advantage with this biomaterial is that the graft volume will partly remain as only the TCP part will dissolve. The dissolution of TCP might lead to more interparticular space for new bone formation.¹⁷ Furthermore, if the levels of released calcium and phosphorous ions stimulate new bone formation, BCP may be a good substitute to DBB. Today, clinical studies of implants placed in BCP are lacking; nevertheless, interesting results have been found in other fields of surgery.²¹ In a recent histological study of sinus floor augmentation, histomorphometry was performed comparing BCP with deproteinized bone.²² Interestingly, the histology was found to be similar for both materials, although more BCP particles were surrounded by fibrous connective tissue. Whether this may have an impact on implant survival is still to be proven. In a similar study, newly formed bone-to-graft contact was found to be significantly higher for DBB, compared with BCP.23 More soft tissue was found in the BCP group and a significantly lower percentage of remaining graft

material compared with DBB; however, it is not yet known whether these differences have any clinical relevance.

To improve osseointegration of dental implants, efforts to modify the surface properties has been made throughout the years. The Straumann SLA surface was developed in 1994 and was found to reduce the implant healing time significantly.²⁴ In 2006, Straumann's new SLActive implant surface technology was introduced to the market. SLActive is a modification of the SLA surface and showed 60% greater bone formation around the surface compared with SLA surface. Earlier formation of mature bone was also seen in vivo.²⁴

In a clinical study, 383 implants with an SLActive surface (197 immediately loaded and 186 early loaded) were placed in 266 patients. After 1 year follow-up, only four implants failed in the immediate group and six in the early loading group, giving implant survival rates of 98 and 97%, respectively. The conclusions of this multicenter study were that Straumann implants with an SLActive surface are safe and predictable to use even in poor quality bone.²⁵

The purpose of the present clinical investigation was to evaluate the 1-year success rate of SLActive implants placed after sinus augmentation with a novel biphasic synthetic material (BCP) or DBB, the latter serving as control.

MATERIALS AND METHODS

Eleven patients, nine completely edentulous (Figure 1A) and two partially edentulous (six women, five men) with a mean age of 67 years (range 50 to 79 years), referred to the department of Oral and Maxillofacial Surgery, Public Health Service, Gävle, Sweden for maxillary sinus floor augmentation (MSFA), were included in the study. All patients underwent preoperative radiographic examination using Scanora tomograms (Scanora, Soredex Orion Corp Ltd, Helsinki, Finland), and were included in the study if they had <5 mm of residual bone in the floor of the maxillary sinus and a crest width =4 mm. Patients were excluded if they had any severe disease or smoked more than 10 cigarettes/day.

The study was approved by the ethical review board in Uppsala, Sweden. All patients were given written information about the study, and their consent was registered in their charts.



Figure 1 *A*, Preoperative clinical view of an edentulous maxilla in a male patient. *B*, Postsurgical panoramic view showing grafted sinuses, right = biphasic calcium phosphate, left = deproteinized bovine bone. Micro implants in position (blue arrows). *C*, Implants placed using a nonsubmerged protocol. *D*, Panoramic view showing fixed bridges after 1 year of loading. *E*, Clinical photo after 1 year of implant loading.

Surgical Procedure

All 11 patients were treated under local anesthesia, and a prophylactic measure of 1 g penicillin-V (Kåvepenin; Astra, Södertälje, Sweden) was given preoperatively and 3 times daily for 7 days.

MSFA was performed bilaterally in all patients, that is, in a total of 22 surgical sites. In brief, after a crestal incision and vertical releasing incisions, a mucoperiosteal flap was elevated and reflected laterally. An approximately 20-mm wide and 10-mm high window was outlined with a round bur and the Schneiderian membrane was elevated together with the bone window inside the sinus cavity. After randomization, augmentation was performed with BCP (BoneCeramic, Straumann®) in one side of the maxillary sinus floor and with DBB (Bio-Oss®, Geistlich, Biomaterials, Wolhusen, Switzerland) acting as a control at the contralateral side. The particle size was 0.5 to 1.0 mm and 0.25 to 1 mm for BCP and DBB, respectively. One micro implant was inserted in each biomaterial. The micro implants were 10-mm long with a body threaded section 2 mm in diameter and a slotted head (2-mm high). The micro implants were placed vertically and penetrated both the alveolar crest and the grafting material (Figure 1B). A collagenous membrane (BioGide®, Geistlich, Pharma) was used to cover the lateral window of the graft. The wounds were closed using resorbable sutures.

In a second surgical procedure, after a mean graft healing time of 230 days (range: 210 to 250 days), all micro implants were removed with a surrounding bone core using a trephine with a diameter of 3 mm. The micro implants were prepared for histological analysis. The result from the histological analysis was the subject of a separate publication.²²

The trephined holes were used as dental implant sites on each side. Implants with an SLActive[®] surface were placed using a nonsubmerged protocol (Figure 1C).

Prosthetic Procedures

During the first 14 days after the surgical procedure, the patients did not wear removable dentures. Thereafter, the dentures were adjusted and relined with Viscogel[®] (Dentsply, York, PA, USA), which was changed every month during the healing period. All patients were rehabilitated with fixed prosthetic constructions (Figure 1, D and E).

Radiographic Examination

Intraoral radiographs were obtained using both analog (Kodak Ekta Speed Plus; Eastman Kodak, Rochester, NY, USA) and digital Schick sensors (Schick Technologies, Long Island City, NY, USA), and imaged with a Philips Oralix 65 apparatus (Philips, Milano, Italy). The mean marginal bone level from the reference point on the neck of the implants was calculated for all implants placed. The marginal bone level in relation to the implant shoulder was measured on the left and the right side of each implant on the radiographs at baseline (when the fixed prosthetic constructions were fabricated and ready for hand out) and after 1 year of loading. The measurements were carried out using both a lupe (Peak Scale Lupe x7 measurement scale) and a digital ruler in Schick.

To evaluate dimensional changes in height between the grafted materials, measurements from both conven-



Figure 2 Postsurgical panoramic view showing grafted sinuses, right = deproteinized bovine bone, left = biphasic calcium phosphate. Micro implants (blue arrows) in position. Grafted sinus height (red arrows) was measured as the distance from the intraoral marginal bone to the highest point of the grafted area.

tional panoramic X-ray (Kodak Lanex medium; Kodak, Rochester, NY, USA) and digital X-ray panorama (Schick) were carried out using both lupe (Peak Scale Lupe x7 measurement scale, Hacienda Heights, CA, USA) and a digital ruler in Schick. In all measurements, the magnification on conventional panoramic films were taken into consideration (panoramic films \times 1.3). All measurements were made twice.

The grafted sinus height (GSH) was evaluated, defined as the distance from the intraoral marginal bone to the highest point of the grafted area, both at baseline and after 1 year of loading (Figure 2).

Clinical Follow-Up

Clinical recording of implant stability was carried out at the time of abutment connection and bridge connection, as well as after 1 year of functional loading, with the bridge removed before recordings. A rotationally mobile or tender implant was classified as a failure.

The following clinical parameters were registered: plaque index (PLI), bleeding on probing (BPI), sulcus bleeding index (SBI), and probing pocket depth (PPD). All measurements were made at four surfaces of each implant.

Implant survival and success rates were evaluated according to Albrektsson criteria.²⁶ An implant was considered to be successful if the following criteria were met:

• A clinically stable implant, examined after removing the fixed prosthesis and tightening the abutments

- No signs of pathological reaction, pain, or infection in the hard or soft peri-implant tissue
- No peri-implant radiolucency
- Marginal bone loss did not exceed 2 mm after 1 year of functional loading.

An implant was considered a failure if removed for any reason. Implants that were not removed but did not meet the success criteria were regarded as survivals.

Statistics

A Statistical Package for Social Science (SPSS version 17.0, SPSS Inc., Chicago, IL, USA) was used to perform the analyses. Differences between mean bone levels were calculated using the Wilcoxon Signed Rank Test. Comparisons between baseline and 1-year follow-up regarding statistical differences between implants placed in BCP or DBB were made using Fisher's exact test. Oneway analysis of variance was used to analyze differences between clinical findings regarding implants placed in BCP, DBB or in residual bone. PLI, BPI, SBI and PPD were analyzed using descriptive statistics and paired *t*-test.

Analysis of the GSH was performed using a paired *t*-test.

To illustrate whether there were any differences concerning marginal bone resorption between implants placed in DBB or BCP, with the patient as "n" instead of the implants, a dependent *t*-test was carried out. A significant difference was considered if p < .05.

A power calculation with $\beta = 80\%$ and $\alpha = 0.05$ assuming that the differences equals the standard deviation was performed. It was shown with a minimum of 11 (including 10% extra to compensate for dropouts) patients that it will be possible to detect a difference between the two groups.

RESULTS

Clinical Findings

In all 11 patients, the grafts were placed without any complications. The mean implant healing time before functional loading was 118 days (range 97 to 210 days). Sixty two SLActive[®] implants were placed, 24 in sites grafted with BCP, 23 in sites grafted with DBB, and 15 in residual bone close to the augmented areas (Table 1, A–C).

One implant placed in each biomaterial was lost. One placed in DBB was lost only a few weeks after inserTABLE 1 Implants in Different Placements (with Implant Width, Length, and Failures): *A*, 23 Implants Placed in Bio-Oss®; *B*, 24 Implants Placed in BoneCeramic®; *C*, 15 Implants Placed in Residual Bone

	Length			
Width	8 mm	10 mm	12 mm	Failure
Α				
3.3 mm	0	2	9	
4.1 mm	0	4	7	1 (12 mm)
Total	0	6	16	1
В				
3.3 mm	0	1	11	
4.1 mm	0	5	6	1 (12 mm)
Total	0	6	17	1
С				
3.3 mm	1	6	8	
4.1 mm				
Total	1	6	8	0

tion because of lack of initial stability and one placed in BCP was lost after 3 months of functional loading because of infection (see Table 1, A–C). The overall implant survival after 1 year of functional loading was 96.8%; no significant difference was found between the three groups.

PLI was registered at 10.0 and 14.2% for implants in DBB and BCP, respectively. BPI was registered at 11.7% around the implants placed in DBB and 15.8% for implants placed in BCP. SBI was registered as 10 and 14.2% around the implants placed in DBB and BCP, respectively. The mean PPD value was 1.87 ± 1.7 mm (range 0 to 5.8 mm) and 1.95 ± 1.8 mm (range 0 to 5.8 mm) for DBB and BCP, respectively (Figure 3). None of the differences between the groups for PLI, BPI, SBI, or PPD was statistically significant.

Radiographic Evaluations

The mean marginal bone loss from baseline to 1 year of loading was 0.29 ± 0.10 mm (p = .012) and 0.43 ± 0.20 mm (p = .046) for implants placed in DBB and BCP, respectively. Both groups had a boneloss >0 with a *p* value (<.05). Implants placed in residual bone had a mean marginal bone loss from baseline to 1 year of loading at 0.52 ± 0.27 (p = .078). The boneloss was not statistically significant from 0, *p* value (<.05).



Figure 3 Relations between deproteinized bovine bone and biphasic calcium phosphate according to probing pocket depth (PPD) mean value per implant in mm. Bars indicate 95% confidence intervals.

No statistically significant difference between baseline and 1 year of loading was found according to marginal bone levels around the implants placed in DBB, BCP, and residual bone.

However, one implant in the BCP group had a mean marginal bone loss exceeding 2 mm because of periimplantitis, giving a success rate of 91.7% (Figure 4). The success rate was calculated to be 95.7% for all implants

Baseline





Figure 4 Radiographs showing right side augmented with biphasic calcium phosphate and blue arrows showing periimplantitis after 1 year of loading.

in the DBB group because of the one that was lost (Figure 5).

No differences could be seen regarding marginal bone loss around the implants concerning the patient as a dependent variable (Figures 6 and 7).

There were no statistically significant differences between BCP and DBB as a grafting material according to GSH after 1 year of loading (Table 2). The amount of graft resorption for DBB and BCP was 4 and 4.5%, respectively.

DISCUSSION

The present study was designed to be able to evaluate SLActive implants placed 8 months after MSFA with BCP and DBB. The implants were followed for 1 year of functional loading. The choice of DBB as a control was based on its superior documentation compared with other bone substitutes. Furthermore DBB has been suggested to be the standard of choice among biomaterials for augmentation of the maxillary sinus.^{6,7} A graft



Figure 5 Bars showing differences in marginal bone level in mm around the implants within the groups of biphasic calcium phosphate (BCP) and deproteinized bovine bone (DBB). The spread was slightly higher within the BCP group. Four outliers were registered. Implant nr 22 marked with a star in the DBB group was outside the spread in one side. 1Y = 1-year follow up, BL = baseline.

healing time of 8 months was chosen based on experiences from previous studies with Bio-Oss[®].^{2,6,7,27}

SLActive[®] implants were used for this study because of the unique surface characteristics of the material.





Figure 6 Marginal bone loss around the implants between baseline and 1 year. Calculations were made concerning the variation between patients. Each dot represents one patient. Its location in the graph indicates the mean values (mv) for bone resorption around the implants in both materials. BO = deproteinized bovine bone and BC = biphasic calcium phosphate.

Figure 7 Box plot showing small variations of marginal bone loss between baseline and 1 year depending on implant sites. BO1 and BC1 represent the most anterior implants and BO3 and BC3 represent the most posterior implants. Calculations were made concerning the variation between patients. BO = deproteinized bovine bone and BC = biphasic calcium phosphate.

TABLE 2 Table Showing Grafted Sinus Height in mm for Deproteinized Bovine Bone (BO) and Biphasic Calcium Phosphate (BC) Initially after Surgery and after 1 Year of Healing						
Time	Group	n	Mean	Standard Deviation		
Initial	ВО	11	14.8	2.3		
	BC	11	14.7	2.2		
After 1 year	BO	11	14.2	2.8		
	BC	11	14.0	2.8		
Differential initial – 1 year	BO	11	-0.6	0.8		
	BC	11	-0.7	0.6		

SLActive[®] has a chemically modified sandblasted/acid etched surface maintained by storage in isotonic saline. This chemically modified titanium surface displays strongly hydrophilic characteristics.²⁸ Histological observations of SLActive implants in miniature pigs have shown evidence of a significantly higher percentage of bone-to-implant contact compared with implants with SLA surfaces.²⁴ This leads to a possible faster and more predictable integration especially on jaws with poor bone quality.

After 1 year of functional loading one implant, placed in each graft, were lost giving an overall implant survival rate of 96.8%. Of the 62 implants, 15 were placed in residual bone near the edge of the grafted areas. No implants placed in residual bone were lost. Success rates for implants placed in BCP and DBB were 91.7 and 95.7%, respectively. The results for BCP and DBB are in accordance with the general survival rate for current implant treatment. In a study comparing implants placed in ordinary bone with implants placed after sinus augmentation, a decrease in success rate of 5 to 10% was shown.⁷

In another study, an increased implant failure rate in elderly patients over 60, with a history of diabetes mellitus, smokers, postmenopausal patients and patients on hormone replacement therapy, was found, compared with healthy patients.²⁹ Within the limitations of the present study, including 11 patients with a mean age of 67 years, no correlations between implant failure and age were found. One patient with a former history of smoking and bruxism developed an average marginal bone loss exceeding 2 mm for one implant placed in BCP (Figure 5).

As no statistically significant difference in marginal bone level was found in this study for implants placed in BCP, DBB or residual bone, synthetic BCP material seems to be able to function as a possible substitute for autogenous bone and DBB. Because the follow-up period was short, more long-term studies are required to fully study BCP as a bone substitute material.

Even if DBB and materials consisting of HA are considered nonresorbable, whereas TCP resorbs slowly,^{13,14,17,30} no signs of loss of graft height were seen in the BCP group, probably because of the hard sintered mixture of HA and TCP.

From a histological point of view, results from biopsies harvested from the same patient group showed equal degrees of newly formed bone formation around micro implants with an SLA surface placed after MSFA with BCP or DBB after 8 months of healing.²² Bone formation mainly took place between the BCP particles and to a lesser extent on the BCP surfaces compared with the DBB particles, where a statistically significantly higher bone to graft particle contact was found (p = .007). One possible interpretation of the results is that the BCP particles were less attractive for boneforming cells. This conclusion is similar to results from in vitro and experimental studies using TCP.^{13,14,31-34}

In a recent study in minipigs, BCP materials with different ratios of HA/TCP (20/80, 60/40, or 80/20) were compared with deproteinized bovine bone mineral (DBBM) and particulated autogenous bone as control.³⁵ Defects were prepared in the mandibles of the minipigs and the healing times were set to 4, 13, 26, and 52 weeks. BCP (20/80) showed results similar to those of autogenous bone grafts, whereas BCP (60/40) and BCP (80/20) were more equivalent to DBBM. This could indicate that the ratio of HA/TCP (60/40) may not be optimal for bone healing.

Results from the present study show similar implant survival independent of the biomaterial used. This could mean that the statistically significantly lower newly formed bone-to-BCP-particle contact does not affect the osseous integration of the implants when used in the maxillary sinus.

Studying GSH in 3-dimensions instead of 2-dimensions, a computed tomography or cone beam computed tomography can be carried out. However, this is a more expensive radiographic technique that considerably increases the level of radiation for the patients.

More prospective and further controlled studies including long-term follow-ups of loaded implants are needed in order to recommend a preferred biomaterial.

CONCLUSIONS

In this limited study, there was no significant difference in implant success rate for SLActive[®] implants placed in the augmented maxillary sinus with BCP (91.7%) compared with implants placed in DBB (94.7%) following 1-year of functional loading.

REFERENCES

- 1. Wannfors K, Johansson B, Hallman M, Strandkvist T. A prospective randomized study of 1- and 2-stage sinus inlay bone grafts: 1-year follow-up. Int J Oral Maxillofac Implants 2000; 15:625–632.
- 2. Hallman M, Hedin M, Sennerby L, Lundgren S. A prospective 1-year clinical and radiographic study of implants placed after maxillary sinus floor augmentation with bovine hydroxyapatite and autogenous bone. J Oral Maxillofac Surg 2002; 60:277–284.
- Sbordone L, Toti P, Menchini-Fabris G, Sbordone C, Guidetti F. Implant success in sinus-lifted maxillae and native bone: a 3-year clinical and computerized tomographic follow-up. Int J Oral Maxillofac Implants 2009; 24:316–324.
- Lundgren S, Andersson S, Sennerby L. Spontaneous bone formation in the maxillary sinus after removal of a cyst: coincidence or consequence? Clin Implant Dent Relat Res 2003; 5:78–81.
- 5. Thor A, Sennerby L, Hirsch JM, Rasmusson L. Bone formation at the maxillary sinus floor following simultaneous elevation of the mucosal lining and implant installation without graft material: an evaluation of 20 patients treated with 44 Astra Tech implants. J Oral Maxillofac Surg 2007; 65:64–72.
- Aghaloo TL, Moy PK. Which hard tissue augmentation techniques are the most successful in furnishing bony support for implant placement? Int J Oral Maxillofac Implants 2007; 22(Suppl):49–70.
- 7. 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; 21:696–710.

- 8. Urist MR. Bone: transplants, implants, derivatives, and substitutes – a survey of research of the past decade. Instr Course Lect 1960; 17:184–195.
- 9. De Groot K. Effect of porosity and physicochemical properties on the stability, resorption, and strength of calcium phosphate ceramics. Ann N Y Acad Sci 1988; 523:227–233.
- Eggli PS, Muller W, Schenk RK. Porous hydroxyapatite and tricalcium phosphate cylinders with two different pore size ranges implanted in the cancellous bone of rabbits. A comparative histomorphometric and histologic study of bony ingrowth and implant substitution. Clin Orthop Relat Res 1988; 127–138.
- Bouler JM, Trecant M, Delecrin J, Royer J, Passuti N, Daculsi G. Macroporous biphasic calcium phosphate ceramics: influence of five synthesis parameters on compressive strength. J Biomed Mater Res 1996; 32:603–609.
- Berube P, Yang Y, Carnes DL, Stover RE, Boland EJ, Ong JL. The effect of sputtered calcium phosphate coatings of different crystallinity on osteoblast differentiation. J Periodontol 2005; 76:1697–1709.
- Jensen SS, Broggini N, Hjorting-Hansen E, Schenk R, Buser D. Bone healing and graft resorption of autograft, anorganic bovine bone and beta-tricalcium phosphate. A histologic and histomorphometric study in the mandibles of minipigs. Clin Oral Implants Res 2006; 17:237–243.
- Buser D, Hoffmann B, Bernard JP, Lussi A, Mettler D, Schenk RK. Evaluation of filling materials in membrane – protected bone defects. A comparative histomorphometric study in the mandible of miniature pigs. Clin Oral Implants Res 1998; 9:137–150.
- Moore DC, Chapman MW, Manske D. The evaluation of a biphasic calcium phosphate ceramic for use in grafting longbone diaphyseal defects. J Orthop Res 1987; 5:356–365.
- Daculsi G. Biphasic calcium phosphate concept applied to artificial bone, implant coating and injectable bone substitute. Biomaterials 1998; 19:1473–1478.
- Jensen SS, Yeo A, Dard M, Hunziker E, Schenk R, Buser D. Evaluation of a novel biphasic calcium phosphate in standardized bone defects: a histologic and histomorphometric study in the mandibles of minipigs. Clin Oral Implants Res 2007; 18:752–760.
- Daculsi G, Bouler JM, LeGeros RZ. Adaptive crystal formation in normal and pathological calcifications in synthetic calcium phosphate and related biomaterials. Int Rev Cytol 1997; 172:129–191.
- 19. Honig JF, Merten HA, Heinemann DE. Risk of transmission of agents associated with Creutzfeldt-Jakob disease and bovine spongiform encephalopathy. Plast Reconstr Surg 1999; 103:1324–1325.
- 20. Wenz B, Oesch B, Horst M. Analysis of the risk of transmitting bovine spongiform encephalopathy through bone

grafts derived from bovine bone. Biomaterials 2001; 22:1599–1606.

- Bagot d'Arc M, Daculsi G, Emam N. Biphasic ceramics and fibrin sealant for bone reconstruction in ear surgery. Ann Otol Rhinol Laryngol 2004; 113:711–720.
- Lindgren C, Sennerby L, Mordenfeld A, Hallman M. Clinical histology of microimplants placed in two different biomaterials. Int J Oral Maxillofac Implants 2009; 24:1093– 1100.
- Cordaro L, Bosshardt DD, Palattella P, Rao W, Serino G, Chiapasco M. Maxillary sinus grafting with Bio-Oss or Straumann Bone Ceramic: histomorphometric results from a randomized controlled multicenter clinical trial. Clin Oral Implants Res 2008; 19:796–803.
- Buser D, Broggini N, Wieland M, et al. Enhanced bone apposition to a chemically modified SLA titanium surface. J Dent Res 2004; 83:529–533.
- 25. Ganales J, Zöllner A, Jackowski J, Bruggenkate C, Beagle J, Guerra F. Immediate and early loading of Straumann implants with a chemically modified surface (SLActive) in the posterior mandible and maxilla: 1 year results from a prospective multicenter study. Clin Oral Impl Res 2008; 19:1119–1128.
- Albrektsson T, Zarb G, Worthington P, Eriksson AR. The long-term efficacy of currently used dental implants: a review and proposed criteria of success. Int J Oral Maxillofac Implants 1986; 1:11–25.
- Hallman M, Sennerby L, Lundgren S. A clinical and histologic evaluation of implant integration in the posterior maxilla after sinus floor augmentation with autogenous bone, bovine hydroxyapatite, or a 20:80 mixture. Int J Oral Maxillofac Implants 2002; 17:635–643.

- Zhao G, Schwartz Z, Wieland M, et al. High surface energy enhances cell response to titanium substrate microstructure. J Biomed Mater Res A 2005; 74:49–58.
- Moy PK, Medina D, Shetty V, Aghaloo TL. Dental implant failure rates and associated risk factors. Int J Oral Maxillofac Implants 2005; 20:569–577.
- von Arx T, Cochran DL, Hermann JS, Schenk RK, Higginbottom FL, Buser D. Lateral ridge augmentation and implant placement: an experimental study evaluating implant osseointegration in different augmentation materials in the canine mandible. Int J Oral Maxillofac Implants 2001; 16:343–354.
- John A, Varma HK, Kumari TV. Surface reactivity of calcium phosphate based ceramics in a cell culture system. J Biomater Appl 2003; 18:63–78.
- 32. Rice JM, Hunt JA, Gallagher JA. Quantitative evaluation of the biocompatible and osteogenic properties of a range of biphasic calcium phosphate (BCP) granules using primary cultures of human osteoblasts and monocytes. Calcif Tissue Int 2003; 72:726–736.
- Wang C, Duan Y, Markovic B, et al. Phenotypic expression of bone-related genes in osteoblasts grown on calcium phosphate ceramics with different phase compositions. Biomaterials 2004; 25:2507–2514.
- Curran JM, Gallagher JA, Hunt JA. The inflammatory potential of biphasic calcium phosphate granules in osteoblast/ macrophage co-culture. Biomaterials 2005; 26:5313–5320.
- Jensen SS, Bornstein MM, Dard M, Bosshardt DD, Buser D. Comparative study of biphasic calcium phosphates with different HA/TCP ratios in mandibular bone defects. A longterm histomorphometric study in minipigs. J Biomed Mater Res B 2009; 90B:171–181.

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