A Prospective Multicenter Randomized Clinical Trial of Autogenous Bone Versus β-Tricalcium Phosphate Graft Alone for Bilateral Sinus Elevation: Histologic and Histomorphometric Evaluation

György Szabó, MD, DDS, PhD[1]/Luc Huys, DDS[2]/Paul Coulthard, MD, DDS[3]/Carlo Maiorana, MD, DDS[4]/
Umberto Garagiola, DDS[5]/József Barabás, MD, DDS, PhD[6]/Zsolt Németh, MD, DDS[7]/
Károly Hrabák, MD[8]/Zsuzsanna Suba, MD, DDS, PhD[9]

Purpose: *Two different graft materials, β-tricalcium phosphate (Cerasorb) and autogenous bone, were used in the same patient. The objective was to determine whether donor site morbidity could be avoided by using pure-phase β-tricalcium phosphate (Cerasorb).* ***Materials and Methods:*** *Bilateral sinus grafting was performed on 20 selected patients; Cerasorb was used on the experimental side, and autogenous bone was used on the control side. In each patient, one side was randomly designated the experimental side. In 10 of the 20 patients, the maxilla reconstruction included sinus grafting and onlay bone grafting. Implants were placed 6 months after the procedure. In addition to routine panoramic radiographs, in 10 of the 20 patients, 2- and 3-dimensional computerized tomographic examinations were performed pre- and postoperatively and after implantation. Eighty bone biopsy specimens were taken at the time of implant placement.* ***Results:*** *Histologically and histomorphometrically, there was no significant difference between the experimental and control grafts in terms of the quantity and rate of ossification. For each histologic sample, the total surface area, the surface area that consisted of bone, and the surface area that consisted of graft material were measured in mm^2, and bone and graft material were analyzed as percentages of the total. The mean percentage bone areas were 36.47% ± 6.9% and 38.34% ± 7.4%, respectively; the difference was not significant (P = .25).* ***Discussion and Conclusion:*** *Comparisons with other studies reveal that β-tricalcium phosphate (Cerasorb) is a satisfactory graft material, even without autogenous bone.* Int J Oral Maxillofac Implants 2005;20:371–381

Key words: *autogenous bone, donor site morbidity, sinus elevation, β-tricalcium phosphate*

[1]Professor and Chairman, Department of Oral and Maxillofacial Surgery, Semmelweis University, Budapest, Hungary.
[2]Private Practice in Periodontology, Oral Implantology, Dento-alveolar Surgery, Brugge, Belgium.
[3]Senior Lecturer and Honorary Consultant, Department of Oral and Maxillofacial Surgery, University Dental Hospital of Manchester, United Kingdom.
[4]Professor, Odontologic and Stomatologic Clinic, University of Milan, Milan, Italy.
[5]Senior Lecturer and Honorary Consultant, Odontologic and Stomatologic Clinic, University of Milan, Milan, Italy.
[6]Associate Professor, Department of Oral and Maxillofacial Surgery, Semmelweis University, Budapest, Hungary.
[7]Senior Lecturer, Department of Oral and Maxillofacial Surgery, Semmelweis University, Budapest, Hungary.
[8]University Assistant, Department of Otorhinolaryngology and Head and Neck Surgery, Semmelweis University, Budapest, Hungary.
[9]Associate Professor, Department of Oral and Maxillofacial Surgery, Semmelweis University, Budapest, Hungary.

Correspondence to: Dr György Szabó, Department of Oral and Maxillofacial Surgery, Semmelweis University, Mária u. 52, Budapest H-1085, Hungary. Fax: +36 1 2660 456. E-mail: szabo@szajseb.sote.hu

One of the most important conclusions of a consensus conference on sinus grafting held several years ago[1] was that, "retrospective analyses did not reveal any bone substitute material that was equivalent to autogenous spongiosa... Accordingly, many participants believed that autografts were the most efficacious... [but] the doubts raised revealed the need for controlled prospective multicenter clinical trials." Therefore, since the present authors had achieved good results with various bone-substitute materials (especially β-tricalcium phosphate [β-TCP]), a prospective multicenter study was initiated to shed more light on this question.

In a preliminary study[2] involving bilateral sinus elevation in 4 patients in 2001, β-TCP was used on one side and autogenous bone on the other. Sixteen bone biopsy specimens were taken at the time of implant placement. It was concluded that the implantation of β-TCP was followed by the formation

of new bone of similar quality and quantity to that observed after grafting with autogenous bone. The histologic and histomorphometric results indicated that when new bone formation was slow, it was slow on both the β-TCP side and the autogenous bone side, and when it was rapid, it was rapid on both sides. Individual patient factors strongly influenced the results.

In essence, the present study is a continuation of that previous work, but on a broader basis. A prospective, multicenter study of 20 patients was organized to confirm the findings of the initial study of 4 patients and to examine whether β-TCP alone is a suitable graft material for sinus elevation.

A number of articles have examined the significance of pure-phase β-TCP[3–6] and other alloplastic materials[7–18] as bone substitute materials. However, very few studies have involved bilateral sinus elevation with 2 different materials in the same patient.

Tadjoedin and associates[19] applied autogenous bone mixed with bioactive glass on the experimental side and autogenous bone alone on the control side. They noted that "bioactive glass particles in the size range 300 to 355 μm clearly show a bone-augmenting capacity, and the cotransplantation of autogenous bone may not be necessary for sinus floor augmentation." This was somewhat contradicted by 2 publications by Yildirim and colleagues,[20,21] who used a xenogenic bone-substitute material, Bio-Oss, first in combination with venous blood and later with autogenous intraoral bone. The combination of osteoconductive Bio-Oss and osteoinductive autogenous bone proved better for sinus floor augmentation than did venous blood and Bio-Oss. In animal experiments, McAllister and coworkers[18] demonstrated radiographic evidence that bone density and height stability were maintained for 1.5 years after sinus grafting with Bio-Oss. Valentini and Abensur[22] retrospectively evaluated the rates of survival of 2 different types of implants in sinuses grafted with inorganic bovine bone alone or with inorganic bovine bone mixed with a demineralized freeze-dried bone allograft. They concluded that inorganic bovine bone used alone appeared to be a suitable material for sinus floor augmentation. A meta-analysis by Wallace and Froum[23] showed that there was no difference in regard to implant survival between grafting with 100% autogenous bone or grafting with composites that included autogenous bone as a component. In a pilot study, Schmelzeisen and associates[24] used tissue-engineered bone for sinus floor augmentation. Their results suggested that periosteum-derived osteoblasts on a suitable matrix form lamellar bone within 4 months, which allows reliable implantation.

Despite this encouraging research, in everyday practice most surgeons believe that no matter what bone-substitute material is used, the results are always better if autogenous bone is added. Since the autogenous bone must be taken from somewhere, a second operation is necessary, which puts the patient at risk of donor site morbidity. This study examined whether donor site morbidity can be avoided by using synthetic bone substitutes.

MATERIALS AND METHODS

Study Centers and Patient Selection

Twenty edentulous patients were scheduled for bilateral sinus floor grafting at the following 4 centers:

- Periodontology, Oral Implantology, Dento-Alveolar Surgery, Brugge, Belgium
- Semmelweis University, Department of Oral and Maxillofacial Surgery, Budapest, Hungary
- Department of Oral and Maxillofacial Surgery, Manchester Royal Infirmary, Manchester, United Kingdom
- Odontologic and Stomatologic Clinic, University of Milan, Italy

At each center, identical protocols were followed for patient selection, preoperative examinations, surgical procedure, implantation, biopsy specimen removal, postoperative treatment, and patient follow-up. In 10 cases, the operation was combined with onlay bone grafting.

All of the patients had conventional denture retention problems because of severe anterior and posterior maxillary alveolar ridge atrophy. All had a residual sinus floor less than 5 mm high (using the Cawood and Howell classification,[25] bone loss was 3 to 4 in 3 of the 20 patients, 5 in 7 patients, and 5 to 6 Howell class in the other 10 patients). In 10 patients, the maxilla was atrophied to such an extent that sinus grafting alone was insufficient; in these cases, a large section of the residual alveolar arch had thinned to a knife edge in the horizontal and sagittal directions. The residual sinus floor of such a patient is illustrated in Figs 1a and 1b.

The patient population consisted of 9 men and 11 women who ranged in age from 38 to 67 years (mean 52 years). After routine oral and physical examinations, the patients were selected and bone reconstruction procedures were planned. In 10 patients, the reconstruction included only bilateral sinus floor grafting; in the other 10 patients, bilateral sinus grafting was performed, with onlay bone grafting in the anterior and part of the posterior maxilla, followed by implant placement 6 months later.

All of the patients were healthy, with no disease that might influence the treatment outcome. The patients were fully informed about the procedures, including the surgery, bone-substitute material, and implants. They were asked for their cooperation during treatment and research; all gave their written informed consent. The ethics committees of the various institutions approved the research protocol.

Radiographs and Computerized Tomograms

Routine panoramic radiographs were obtained in all cases pre- and postoperatively, 6 months after the first surgery (prior to implant placement), and immediately after implant placement. Additional panoramic radiographs were taken at 6-month intervals after implant placement. Moreover, in the 10 patients in which onlay bone grafting was performed, 2D and 3D CT examinations were performed pre- and postoperatively and 6 months after implant placement, using a General Electric Pro-Speed Plus (General Electric Medical Systems, Milwaukee, WI). The later exposures were taken in the same plane and direction as the preoperative ones. (For further technical details related to these procedures, the reader is referred to an earlier publication.[26])

Surgery

In all 20 patients, surgery was performed under general anesthesia. Before or at the time of sinus grafting, 5 to 6 cm^3 of spongious bone were harvested from the left iliac crest by a second team of surgeons. In the cases that included onlay grafting, the spongiosa was removed together with a piece of cortical bone about 3 cm wide and 4 to 6 cm long.

The bilateral sinus grafting procedure followed Tatum's classical description.[27] On one side, the sinus-elevation space was filled only with 1.5 to 2 g of β-TCP (Cerasorb; Curasan AG, Kleinostheim, Germany) (particle size 1,000 μm); on the other side, it was filled with 3 to 4 cm^3 of autogenous bone. The Cerasorb side was the experimental side; the autogenous bone side was the control side. The choice of sides was randomized using the coin-toss method. In 12 of the 20 patients, the experimental side was on the right; in 8, it was on the left.

Onlay Bone Grafting

In 10 of the 20 patients, it was necessary to widen the alveolar crest, which had become extremely thin in places. This was performed at the same time as the bilateral sinus grafting. The harvested cortical bone was attached to the buccal side of the compromised maxilla using microscrews. Next, the uneven bone edges were smoothed with spongiosa, the buccal and labial periosteum was extended in the customary way, and the wound was closed in a tension-free manner. No membrane was used to cover the bone.

The sutures were removed 7 to 10 days later. The following postoperative regime was applied to avoid infection: ciprofloxacin (Ciprobay; Bayer, Leverkusen, Germany) 500 mg 2 times daily for 5 days and ibuprofen (Klinge Pharma, Killorglin, Ireland) 400 mg 3 times daily to reduce pain and swelling. The patients were instructed not to wear removable prostheses for 30 days and not to blow their noses for 7 days.

Implant Placement Surgery

After 6 months of healing, the patients received implants. Eighty cylindric bone biopsy specimens were taken from the grafted posterior maxilla (2 from the experimental side and 2 from the control side in every patient) using a trephine bur (Straumann, Waldenburg, Switzerland) with an inner diameter of 2 mm and an outer diameter of 3 mm. After biopsy specimen removal, osteotomy sites were prepared for implant placement.

In 4 patients, 16 Protetim (Hódmezo'vásárhely, Hungary) implants were placed at the sinus elevation sites. In the other 16 patients, 64 Ankylos (Dentsply Friadent Ceramed, Lakewood, CO) implants were used. In addition to the 80 implants placed at the sites of the Cerasorb or autogenous bone grafts, many more implants were required for the complete rehabilitation of the edentulous maxillae of the 20 patients, but the remaining implants were not directly related to this study.

Histology and Histomorphometry

The bone biopsy samples contained both the grafted area and the previously existing area of sinus floor, but the residual native crestal bone was not included in the histologic and histomorphometric examinations. Cortical bone in samples from patients with onlay grafts was not included either.

Biopsy samples from all 4 centers were fixed in 4% formaldehyde and then submitted for histologic examination to the oral pathology unit of the Department of Oral and Maxillofacial Surgery of Semmelweis University. The bone samples were processed and stained as reported earlier.[2] Briefly, they were fixed in 4% formaldehyde in phosphate buffer, dehydrated in an ascending series of graded alcohols, and embedded in methylmethacrylate resin at 4°C. Five-μm-thick histologic sections were cut in the longitudinal plane with a diamond knife and stained with toluidine blue and hematoxylin-eosin. Goldner's trichrome method was used for light microscopy.

Histomorphometry

Morphometric studies were performed according to the principles of Parfitt and colleagues.[28] Sections of each sample were taken for histomorphometry from 4 levels at 150-µm intervals. The samples were measured semiautomatically using an Olympus microscope (Olympus, Tokyo, Japan) connected to a computer using AnalySIS software (Soft Imaging System, Münster, Germany). The total surface area of each sample, the surface area that consisted of bone, and the area that consisted of graft material were measured in mm^2, and bone and graft material were analyzed as a percentage of the total. Bone from the original sinus floor was not involved in the bone area measurement.

Statistical Analysis

The Student *t* test was used to determine statistical significance. Values of $P < .05$ were considered significant.

RESULTS

Clinical Observations

After sinus elevation, no postoperative complications occurred in any of the patients. Normal wound healing was observed after both the first and second operations (graft harvesting/sinus elevation and implant placement surery). Minor nosebleeds occurred in 3 patients.

One patient had permanent sensory loss in the distribution of the lateral femoral cutaneous nerve, and 2 patients had prolonged wound drainage (2 to 3 weeks). No other postoperative complications were observed in conjunction with the donor sites.

Radiology

The 2D and 3D CT investigation was discussed in some detail in a previous publication.[2] Only the most important results are summarized here.

Panoramic Radiograph. Three panoramic radiographs were compared for every patient: 1 taken shortly after graft implantation surgery, 1 taken at 6 months postoperatively (ie, at implantation), and 1 taken 12 months postoperatively (ie, at suprastructure fabrication). These radiographs clearly showed the positions of both types of graft material and the height of the new sinus floor.

The autogenous bone was initially less visible than the β-TCP, but new bone formation was clearly observed for both materials. The consecutive images also revealed changes in the graft materials and their incorporation. β-TCP was markedly more radiopaque than autogenous bone.

After 6 months, the β-TCP had changed slightly in the radiographs: The contour of the bone around the graft became more defined. After 12 months, the graft was similar to bone because of absorption of the β-TCP and the simultaneous formation of new bone.

Computerized Tomography. A comparison of the panoramic radiographs and CT images in 10 patients revealed the advantages of supplementing the panoramic radiographs with 2D CT images. In planning the surgery, the thickness and width of the alveolar bone and the process of new bone formation could be better assessed in this way. The 3D CT reconstruction best revealed the postoperative sinus graft height and new sinus floor, as well as the ossification process (Figs 1c to 1f and 2a to 2e).

Histology

Experimental Side. In the biopsies from the experimental side, the β-TCP graft was identified as achromatic rounded or scalloped granules, depending on the phase of resorption. They were partially embedded in newly formed bone, which was predominantly lamellar bone (Fig 3a).

Bone formation was preceded by the abundant proliferation of a cell-rich osteogenic mesenchyme and a new capillary network in the pores of the resorbing granules (Fig 3b). Newly formed bone replaced the resorbing β-TCP particles continuously. Bone deposition characteristically occurred along the surface and in the pores of the disintegrated graft material. There was no foreign body-type giant cell reaction in the grafted samples. In 1 sample, there was a focal lack of bone formation and an intense inflammatory reaction, suggesting a local infection.

Control Side. The majority of the biopsy samples from the control side contained mature lamellar bone (Fig 4a). The bone trabeculae contained osteocytes in their lacunae. Signs of dynamic bone formation with osteoblast activity or lacunar osteoclastic resorption were rare. The remnants of the autogenous bone grafts could be seen in several foci as homogeneous tissue fragments that stained like living bone (Fig 4b). In these samples, there was intimate contact between the graft particles and new bone.

Several samples were typified by torpid bone formation, a predominantly fibrous bone marrow, and a diffuse, thin network of bone trabeculae.

Fig 1 Radiographic studies of patient H5.

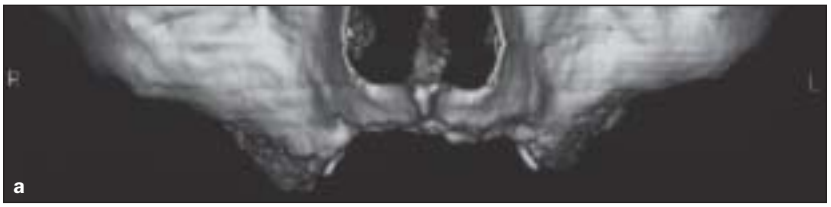


Fig 1a Preoperative 3-dimensional (3D) computerized tomogram (CT) demonstrating that a large part of the alveolar crest has atrophied.

Fig 1b Preoperative 2-dimensional (2D) CT. Using the classification of Cawood and Howell,[25] the bone loss grade was 6 (ie, the height of the residual sinus floor was less than 2 mm).

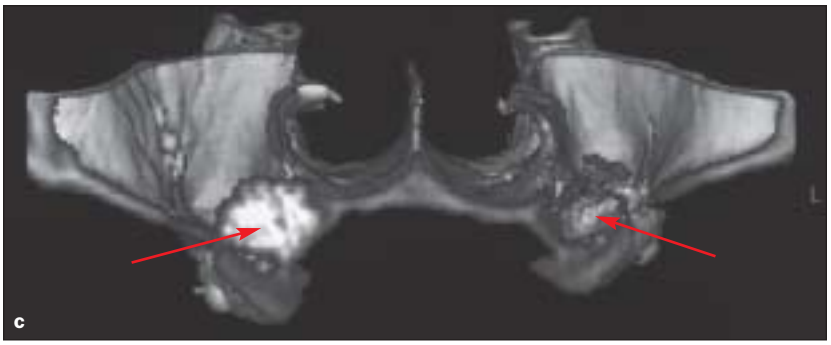


Fig 1c Postoperative 3D CT. The bilateral sinus grafts are clearly visible (β-TCP in the right maxilla and autogenous bone in the left maxilla).

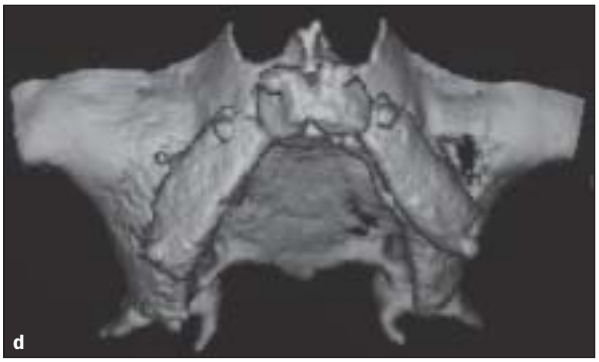


Fig 1d 3D CT reconstruction. The onlay bone grafting is clearly visible.

Fig 1e Panoramic radiograph 6 months after the sinus grafting. Ankylos implants were placed.

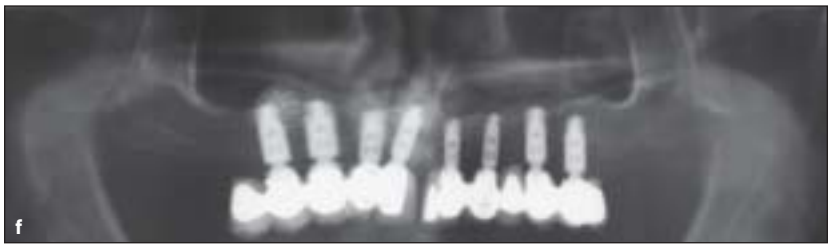
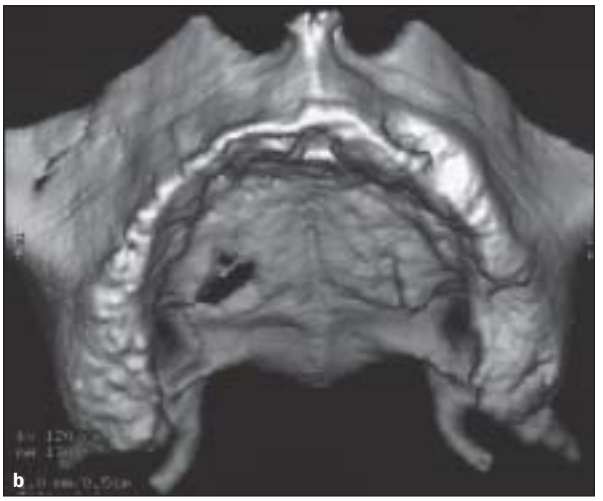


Fig 1f One year after sinus grafting, after prosthetic rehabilitation. The Cerasorb graft *(right)* appeared similar to bone.

Fig 2 Radiographic studies of patient H4.



Figs 2a and 2b Preoperative *(a)* 2D and *(b)* 3D CT scans. The right side of the residual alveolar crest has thinned to a knife edge in the horizontal and sagittal directions. The 2D CT clearly reveals the situation of the residual sinus floor. According to the classification of Cawood and Howell, the bone loss grade is 3 to 4.

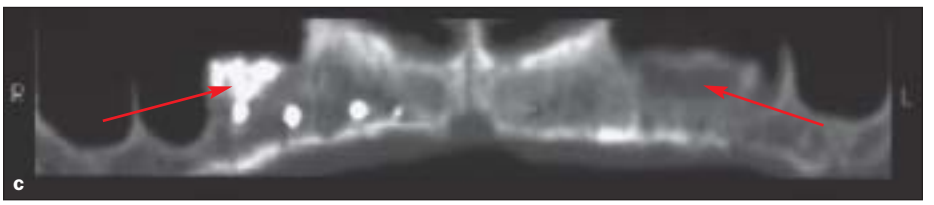


Fig 2c After sinus grafting and onlay bone graft. The heads of the microscrews are visible in the right and middle parts of the maxilla.

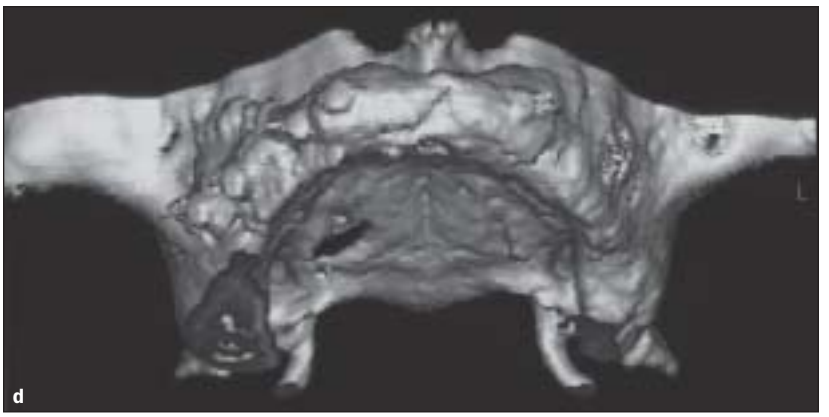


Fig 2d Three-dimensional CT 6 months after onlay bone grafting; bone integration is clearly visible.

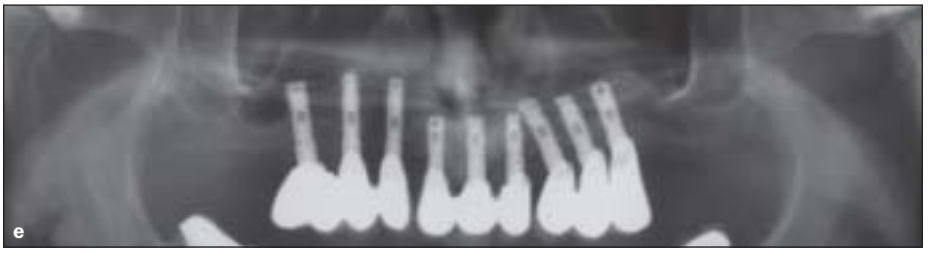


Fig 2e Twelve months after the first surgery, prosthetic rehabilitation of the Protetim implants was completed. With absorption of the β-TCP and the simultaneous formation of new bone, the grafted areas have become similar to bone.

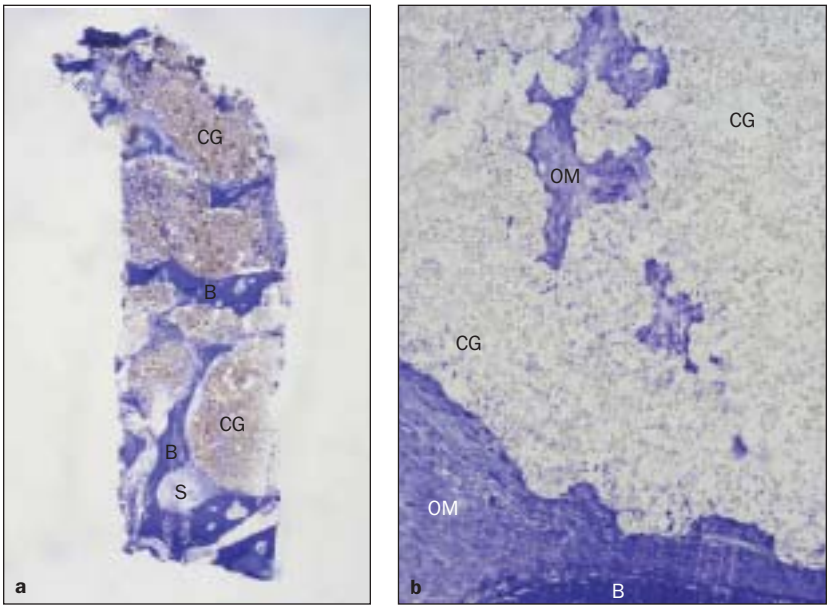


Fig 3a β-TCP graft and new bone formation. CG = Cerasorb granule; B = new bone; S = soft tissue (toluidine blue; original magnification ×2).

Fig 3b Osteogenic mesenchyme growing on the surface and in the pores of a Cerasorb granule. B = bone, CG = Cerasorb granule, OM = osteogenic mesenchyme (toluidine blue; original magnification ×25).

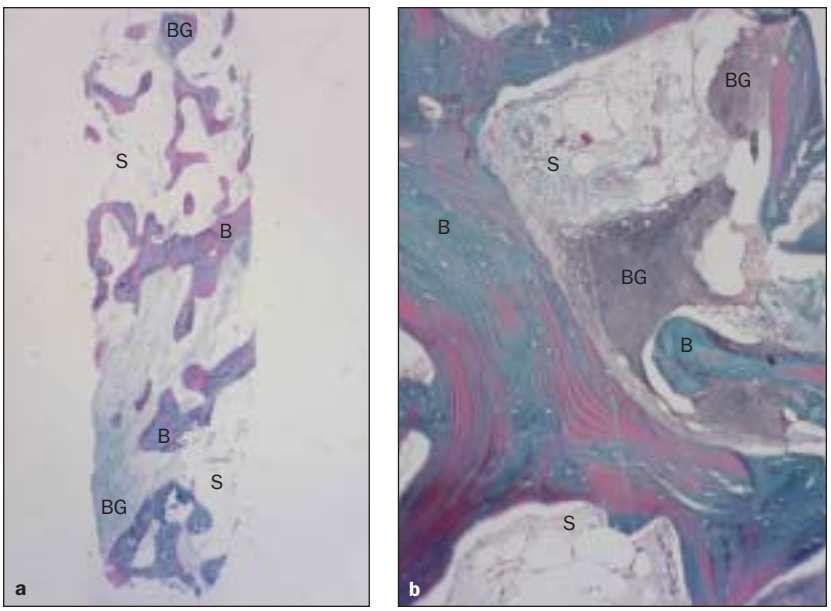


Fig 4a Autogenous bone graft and newly formed lamellar bone. B = bone, BG = bone graft, S = soft tissue (Goldner's trichrome; original magnification ×2).

Fig 4b Bone graft focus and newly formed lamellar bone. B = bone, BG = bone graft, S = soft tissue (Goldner's trichrome, original magnification ×25).

Histomorphometry

The mean percentage of bone area for the 20 patients was 36.47% ± 6.9% on the experimental side and 38.34% ± 7.4% on the control side; the difference was not significant ($P = .25$).

In a majority of the patients (n = 13), the intensity of new bone formation was similar on both sides. When the volume occupied by the graft remnants was considered, these data suggest that the bone density was sufficient on both sides (Table 1). Nevertheless, the new bone was markedly less dense on the experimental side in 4 of the 20 cases compared to the control side (H2, B2, B4, I1). In 1 of these patients, the lethargic bone formation process could be explained by a local inflammatory reaction. In the other 3 cases, the percentage of the graft area was quite high (H2 25.9%, B4 25.6%, I1 21.1%), ie, the graft material took up too much space in the bone samples.

The bone-forming capacity on the control side was more sluggish than on the experimental side in 3 cases (H5, H7, B3). In these cases, no inflammatory reaction or delayed graft resorption hampered bone

Table 1 Histomorphic Values: Total Biopsy Area (mm^2), Area (mm) and Density (%) of New Bone, and Area (mm^2) and Density (%) of Graft Area

	Total area		New bone		Residual graft	
Cases	mm^2	%	Area	Density	Area	Density
H1						
Experimental side	11.59	100	2.91	25.55	0.93	7.90
Control side	12.15	100	2.86	23.95	1.06	8.67
H2						
Experimental side	7.01	100	1.23	16.62	1.72	25.92
Control side	10.00	100	4.17	41.70	0.86	8.55
H3						
Experimental side	10.14	100	3.51	34.40	0.91	9.01
Control side	7.09	100	3.09	42.98	0.61	8.91
H4						
Experimental side	10.74	100	4.37	40.89	1.41	10.41
Control side	9.79	100	3.83	39.45	0.66	6.75
H5						
Experimental side	7.13	100	2.68	37.50	0.87	12.20
Control side	8.34	100	2.65	28.20	0.56	6.71
H6						
Experimental side	8.16	100	3.31	40.55	0.90	11.02
Control side	7.19	100	2.78	38.64	0.48	6.67
H7						
Experimental side	8.55	100	3.12	36.45	1.61	18.88
Control side	8.38	100	2.25	26.85	0.45	5.01
H8						
Experimental side	8.36	100	3.62	43.30	0.93	11.12
Control side	11.20	100	4.62	41.25	0.92	8.21
H9						
Experimental side	7.12	100	2.98	41.85	0.78	10.95
Control side	10.35	100	4.06	39.22	0.82	7.92
H10						
Experimental side	10.92	100	4.23	38.74	1.23	11.26
Control side	7.63	100	3.16	41.42	0.66	8.65
B1						
Experimental side	6.65	100	1.83	27.47	0.61	9.19
Control side	9.52	100	2.80	28.17	0.46	4.62
B2						
Experimental side	8.12	100	2.75	33.87	0.98	12.11
Control side	7.98	100	4.18	52.39	0.85	10.59
B3						
Experimental side	7.00	100	2.82	40.21	0.68	10.30
Control side	11.34	100	3.43	30.23	1.59	7.10
B4						
Experimental side	13.75	100	4.05	32.77	3.52	25.63
Control side	6.12	100	2.67	43.67	1.20	19.53
B5						
Experimental side	14.61	100	6.29	43.07	1.91	13.04
Control side	6.69	100	2.59	38.65	0.78	11.67
B6						
Experimental side	9.74	100	4.47	45.90	1.70	17.40
Control side	7.26	100	3.58	49.31	0.56	7.61
E1						
Experimental side	6.18	100	2.37	38.44	1.15	18.61
Control side	9.14	100	3.66	40.03	0.79	8.69
E2						
Experimental side	11.80	100	4.33	36.67	1.28	10.84
Control side	9.67	100	3.77	39.03	0.52	5.35
I1						
Experimental side	6.86	100	2.33	33.92	1.45	21.12
Control side	11.63	100	4.92	42.27	1.23	10.59
I2						
Experimental side	9.30	100	3.81	40.96	1.13	12.15
Control side	8.33	100	3.28	39.37	0.61	7.32

H = Hungarian patient; B = Belgian patient; E = English patient; I = Italian patient.

regeneration. In 2 cases (H1 and B1), the ossification process was uniformly weak on both sides; the respective percentages of newly formed bone were 25.6% and 27.5% on the experimental side and 24.0% and 28.1% on the control side. In these 2 cases, the new bone trabeculae were uniformly thin, with no focal inflammatory lesion.

The rate of graft resorption was generally lower on the experimental side than on the control side. The mean graft area percentages were 13.95% ± 5.38% and 8.47% ± 3.17%, respectively, and the difference was highly significant ($P < .001$).

The mean areas of the biopsy samples taken from the 2 sides were quite similar: 9.18 ± 2.42 mm^2 on the experimental side and 8.98 ± 1.76 on the control side.

Failed Implants

In the 6-month period between implantation and loading of the implants, 2 of the 80 implants were lost (both Ankylos); 1 on the experimental side and 1 on the control side. Both were replaced, but delivery of the definitive restoration was delayed by 3 to 6 months.

DISCUSSION

The primary aim of this work was to compare the implanted graft material using clinical, radiologic, and histologic studies. In this study, the medium- or long-term stability of the implants was not the interest focus, since such an investigation would have required a much longer study period. Such an investigation will be undertaken by the authors in the future.

Two of the 80 implants (2.5%) were lost, 1 from each side, suggesting the equivalence of the 2 materials. The comparison of the bone-forming activity of β-TCP and autogenous bone confirmed earlier findings. New bone production was similar on both sides; the difference between the 2 sides was not significant. These results support the view that β-TCP can be a satisfactory graft material, even without the addition of autogenous bone.

Radiologic examinations indicated that the grafted area changed in contour during the period of study (from sinus floor augmentation to definitive prosthetic rehabilitation). The vertical height of the grafts was not analyzed in the present study. This will be the subject of an investigation covering a longer period.

Several factors can influence new bone formation, in addition to the nature of the graft. In 2 cases (H1 and B1), the rate of new bone formation was low on both sides. This might be the result of general factors, such as old age, hormonal dysfunction, or disturbances in calcium metabolism.

Local factors can explain 1-sided lethargic bone formation. Disturbances in the blood supply or inflammation at the site of surgery can also delay bone regeneration. In the present study, unilateral lower rates of bone formation were seen on the experimental and control sides in different patients, which supports the important role of local factors.

The size of the biopsy sample can also influence the quantitative comparison of the effects of the graft materials. The greater the area of the bone sample, the more representative the quantitative measurement. In the present study, the areas of the bone samples derived from the 2 sides did not differ significantly.

In the introduction, the question was posed whether, under certain conditions, a bone-substitute material can be equivalent to the patient's own spongiosa. These results suggest a positive answer to this question. In sinus elevation surgery, Cerasorb can be as effective as autogenous bone. Naturally, this does not necessarily hold true for other operations. For instance, onlay grafting should still be performed with autogenous bone.

This study investigated 20 patients. Strict patient selection was necessary, mainly for ethical reasons. In the 10 onlay grafting cases, which required autogenous bone, use of the control material could be justified. However, in those cases with no onlay grafting, the question was not so clear-cut. The number of cases had to be restricted to the minimum number necessary to draw reliable conclusions. The examination of the 80 biopsy samples taken from the 20 patients led to unambiguous findings. The conclusions drawn appear to be supported by the clinical and radiologic data.

Initially, more working groups had been planned. However, 2 groups were forced to withdraw from participation in the investigation because patients did not agree to the excision of autogenous bone. This further demonstrates the importance of having a suitable bone-substitute material.

Onlay grafting was necessary in 10 of the 20 patients. In these cases, the alveolar crest of the maxilla was so thin at many sites bilaterally that stability of the implants could not have been ensured by sinus elevation alone. The vertical augmentation had to be supplemented with horizontal augmentation. A porous bone substitute is not very suitable for this purpose; on the other hand, cortical bone taken from the hip is integrated into the outer surface of the maxilla within a few months (Fig 2d). Onlay bone grafting clearly has no effect on the healing process following sinus elevation, as one of the processes occurs on the outer surface of the maxilla, while the other proceeds internally.

Regarding the question of spongiosa as the gold standard, while it is true that the quality of new bone obtained using any of the bone substitutes may be compared with this as a standard, this standard does have disadvantages. The most important of these are donor site morbidity, the relatively high number of complications, the need for general anesthesia, and the high costs of hospitalization.[29] Niedhart and associates[29] have given a clear picture of the cost: Removal of the bone requires an average of 30 minutes, a second surgical team, and an anesthesiologist. These costs far exceed the price of the bone substitute. With careful surgical techniques, the rate of complications may be reduced; nevertheless, it generally ranges from 20% to 30%. When all these factors are taken into consideration, it appears important to avoid the excision of autogenous bone whenever possible.

Mention must be made of the membrane question. On the basis of more than 40 publications, Wallace and Froum[23] performed a comparative meta-analysis of the use of barrier membranes over the lateral window. They found that implant survival rates were higher when a membrane was applied.

A long-term clinical, histologic, histomorphometric, and radiographic study of the sinus elevation procedure led Tarnow and coworkers[30] to the following conclusions:

- Application of a barrier membrane tends to increase vital bone formation.
- Application of a barrier membrane has a positive effect on implant survival.
- Membrane application should be considered for all sinus elevation procedures.

As these findings were accepted, no membrane was used in the present study. In 10 of the 20 patients, an onlay graft was applied on the lateral wall of the sinuses. This autogenous bone served as a barrier to soft tissue invasion. In the interest of comparison, in the other 10 cases no membrane was applied over the lateral window.

The tissue-engineering procedures mentioned in the introduction, which also aim to minimize donor site morbidity, may be the procedures of choice in the future. Obviously, if the application of tissue-engineered bone becomes as routine as the use of skin or mucosa, the debate over graft materials will become less relevant. This may take considerable time, and at present, materials are needed that avoid the excision of autogenous bone.

In addition, with regard to the publications by Skoglund and associates,[16] Tadjoedin and associates,[19] and Yildirim and colleagues,[20,21] which consider natural bone mineral, bioactive glass, and so on, the present work did not set out to compare and contrast individual graft materials. If "remodeling" is considered, pure-phase β-TCP used alone appears to be a suitable material for sinus floor augmentation.

CONCLUSION

Comparisions with other studies reveal that β-TCP (Cerasorb) is a satisfactory graft material, even without autogenous bone.

REFERENCES

1. Jensen OT, Shulman LB, Block MS, Iacono VJ. Report of the Sinus Consensus Conference of 1996. Int J Oral Maxillofac Implants 1998;13(suppl):11–45.
2. Szabó G, Suba Z, Hrabák K, Barabás J, Németh Z. Autogenous bone versus beta-tricalcium phosphate graft alone for bilateral sinus elevations (2- and 3-dimensional computed tomographic, histologic, and histomorphometric evaluations): Preliminary results. Int J Oral Maxillofac Implants 2001;16:681–692.
3. Gruber AAJ. Practical applications of a bone substitute—Beta-tricalcium phosphate in hand surgery. Trauma Line 1999;2: 50–58.
4. Foitzik C, Staus H. Phasenreines β-Tricalcium Phosphat zum Knochenersatz bei parodontaler Indikation. Quintessenz 1999:50:1049–1058.
5. Ghazal G, Prein J. Bone defect filling material in jawbones using tricalcium phosphate [in German]. Swiss Dent 1992; 13(1):15–18.
6. Reinhardt C, Kreusser B. Retrospective study of dental implantation with sinus lift and Cerasorb augmentation. Dent Implantol 2000;4:18–26.
7. Becker W, Becker BE, Caffesse R. A comparison of demineralized freeze-dried bone and autologous bone to induce bone formation in human extraction sockets. J Periodontol 1994; 65:1128–1133 [erratum 1995;66:309].
8. Bereiter H, Melcher GA, Gautier E, Huggler AH. Erfahrungen mit Bio-Oss, einem bovinen Apatit, bei verschiedenen klinischen Indikationsbereichen. In: Huggler, AH, Kuner EH (eds). Aktueller Stand beim Knochenersatz. Hefte zur Unfallheilkunde. Berlin: Springer, 1991:117–126.
9. Boyne PJ, James RA. Grafting of the maxillary sinus with autogenous marrow and bone. J Oral Surg 1980;38:613–616.
10. Boyne PJ. Comparison of Bio-Oss and other implant materials in the maintenance of the alveolar ridge of the mandible in men. In: Huggler AH, Kuner EH (eds). Aktueller Stand beim Knochenersatz. Hefte zur Unfallheilkunde. Berlin: Springer, 1991:98–103.
11. Donath K. Integration of bone substitutes in the jawbone. Morphologic findings [in German]. Dtsch Zahnärztl Z 1988;43:16–21.
12. Jensen SS, Aaboe M, Pinholt EM, Hjorting-Hansen E, Melsen F, Ruyter E. Tissue reaction and material characteristics of four bone substitutes. Int J Oral Maxillofac Implants 1996;11:55–66.

13. Kasperk CH, Ewers R. Tierexperimentelle Untersuchungen zur Einheilungstendenz synthetischer, koralliner und aus Algen gewonnener (phykogener) Hydroxylapatit-materialien. Z Zahnärztl Implantologie 1986;2:242–248.
14. Terheyden H, Jepsen S, Möller B, Tucker MM, Rueger DC. Sinus floor augmentation with simultaneous placement of dental implants using a combination of deproteinized bone xenografts and recombinant human osteogenic protein-1. A histomorphometric study in miniature pigs. Clin Oral Implants Res 1999;10:510–521.
15. Schlegel AK. Bio-Oss bone replacement materials. Long-term results with Bio-Oss bone replacement material [in French, German]. Schweiz Monatsschr Zahnmed1996;106:141–149.
16. Skoglund A, Hising P, Young C. A clinical and histological examination in humans of the osseous response to implanted natural bone mineral. Int J Oral Maxillofac Implants 1997;12:194–199.
17. Moy PK, Lundgren S, Holmes RE. Maxillary sinus augmentation: Histomorphometrical analysis of graft materials for maxillary sinus floor augmentation. J Oral Maxillofac Surg 1993;51:857–862.
18. McAllister BS, Margolin MD, Cogan AG, Buck D, Hollinger JO, Lynch SE. Eighteen-month radiographic and histologic evaluation of sinus grafting with anorganic bovine bone in the chimpanzee. Int J Oral Maxillofac Implants 1999;14:361–368.
19. 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.
20. Yildirim M, Spiekermann H, Biesterfeld S, Edelhoff D. Maxillary sinus augmentation using xenogenic bone substitute material Bio-Oss in combination with venous blood. A histological and histomorphologic study in humans. Clin Oral Implants Res 2000;11:217–229.
21. Yildirim M, Spiekermann H, Handt S, Edelhoff D. Maxillary sinus augmentation with the xenograft Bio-Oss and autogenous intraoral bone for qualitative improvement of the implant site: A histologic and histomorphometric clinical study in humans. Int J Oral Maxillofac Implants 2001;16:23–33.
22. Valentini P, Abensur DJ. Maxillary sinus grafting with anorganic bovine bone: A clinical report of long-term results. Int J Oral Maxillofac Implants 2003;18:556–560.
23. Wallace SS, Froum SJ. Effect of maxillary sinus augmentation on the survival of endosseous dental implants. A systematic review. Ann Periodontol 2003;8:328–343.
24. Schmelzeisen R, Schimming R, Sittinger M. Making bone: Implant insertion into tissue-engineered bone for maxillary sinus floor augmentation—A preliminary report. J Craniomaxillofac Surg 2003;31:34–39.
25. Cawood JI, Howell A. Reconstructive preprosthetic surgery. I. Anatomical considerations. Int J Oral Maxillofac Surg 1991;20:75–82.
26. Hrabák K, Szabó G, Ewers R, Gyulai-Gaál SZ. 2D and 3D computer tomography and sinus graft analysis with various graft materials. J Long Term Eff Med Implants 1999;9:223–233.
27. Tatum H Jr. Maxillary and sinus implant reconstructions. Dent Clin N Am 1986;30:207–229.
28. Parfitt AM, Drezner MK, Glorieux FH, et al. Bone histomorphometry: standardization of nomenclature, symbols, and units. Report of the ASBMR Histomorphometry Nomenclature Committee. J Bone Miner Res 1987:2:6:595–610.
29. Niedhart C, Pingsmann A, Jürgens C, Marr A, Elatt R, Niethard FU. Complications after harvesting of autologous bone from the ventral and dorsal iliac crest—A prospective, controlled study [in German]. Z Orthop Ihre Grenzgeb 2003;141:481–486.
30. Tarnow DP, Wallace SS, Froum SJ, Rohrer MD, Cho SC. Histologic and clinical of bilateral sinus floor elevations with and without barrier membrane placement in 12 patients: Part 3 of an ongoing prospective study. Int J Periodontics Restorative Dent 2000;20:117–125.