Porous Hydroxyapatite for Grafting the Maxillary Sinus: A Comparative Histomorphometric Study in Sheep

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Purpose: This experimental study in adult female sheep examined the value of nonresorbable porous hydroxyapatite (HA) as a grafting material in a single-stage sinus-lift procedure. Materials and Methods: Two titanium plasma-flame-sprayed cylindric implants were placed bilaterally in each of 54 sinuses in 27 adult female sheep. In 2 groups of 18 sinuses each, the subantral hollow space was filled with porous HA or autogenous cancellous bone harvested from the iliac crest, respectively. Eighteen sinuses were not augmented and served as controls. The time course of new bone formation and bone remodeling was evaluated by sequential polyfluorochrome labeling. Observation periods were 12, 16, and 26 weeks after the surgical procedure. Six sinuses per observation period and test group were available for histologic evaluation. Results: All implants were osseointegrated in the local host bone. New bone formation was observed in a triangular area bounded by the implant surface, local buccal antral wall, and submucous connective tissue around all implants. The mean length of bone-implant contact was 3.9 ± 0.3 mm in the control group, 5.7 ± 0.3 mm in the autogenous bone group, and 5.9 ± 0.3 mm in the group augmented with porous HA. During the observation period, the relative length of direct boneimplant contact increased from 20% to 25.1% in the control group, from 30.4% to 35.5% in the autogenous bone group, and from 29.8% to 41.7% in the HA group. At a distance of 1 mm from the implant, the mean bone volume was 29.7 ± 15.7% in the autogenous bone group. In the group augmented with HA the mean bone volume was 11.2 ± 13.0%. Discussion: There was no significant difference between HA and autogenous bone regarding bone-implant contact (P = .89). Conclusions: Both groups showed a significantly greater bone-implant contact (HA: P = .002; autogenous bone: P = .0005) than the empty control group. However, since the results varied widely, the use of HA alone for sinus grafting should be used with discretion in sinus-lift procedures. (INT J ORAL MAXILLOFAC IMPLANTS 2002;17:337–346)

Key words: dental implants, histomorphometry, hydroxyapatites, sinus augmentation

The placement of implants in highly atrophic maxillae continues to be one of the major challenges in implant dentistry. Sinus floor elevation is

one of the preferred options. This involves lifting the sinus floor and packing the inferior part of the sinus with grafting material to provide adequate support for implants.

Ideal grafting materials should meet a number of requirements: they should be osteogenetic (stimulate surviving osteoblasts to form new bone), they should be osteoconductive (serve as a scaffold for the ingrowth of vessels from neighboring bone), and they should be osteoinductive (make pluripotential mesenchymal cells differentiate into osteoblasts). Autogenous bone meets all of these requirements and has therefore been defined as the "gold standard" among grafting materials. It is harvested either intraorally or from the iliac crest. To minimize the demands made on patients and spare them

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Fig 1 Schematic showing access to the buccal wall of the maxillary sinus (*arrow*) and the position of the 2 implants. Projected site of the grafting material is shown in dark gray.

an additional surgical procedure, bone substitutes are increasingly being considered. They are available in unlimited amounts and can be used either alone or in combination with autogenous bone.

Among the bone substitutes, porous hydroxapatite (HA) has been recommended by several authors.^{1,2} Formed by hydrothermal conversion of coral carbonate structures, this calcium compound is characterized by interconnecting pores of a diameter of about 190 to 230 µm and a particle size of about 425 to 1,000 µm.³

The ability of dental implants to survive in sinuses grafted with porous HA has been documented in numerous clinical studies and case reports,4-7 but standardized experimental studies investigating the behavior of HA as a grafting material in such circumstances are scarce. In experimental studies in monkeys, Quinones^{1,8} and Hürzeler² augmented the sinus with porous HA or autogenous bone combined with porous HA and placed titanium plasma-flame-sprayed cylindric implants (IMZ, Interpore International, Irvine, CA) either immediately or in a second procedure. Both approaches enhanced new bone formation and mineralized bone-implant contact in the grafted sinuses. In a study in beagle dogs, Wetzel and associates⁹ examined absorbable HA histologically. They also found new bone formation and direct bone-implant contact in the grafted region. But as the dog sinus is not pneumatized and not lined with Schneiderian membrane, it is not comparable with the sinus in humans.

Sheep proved to be a very useful animal model for single-stage sinus lifts in earlier studies.^{10,11} In these, bovine HA and demineralized freeze-dried bone (DFDB) were used for grafting. The resultant bone-implant interface was examined histologically and compared with that seen after grafting with autogenous bone. The results obtained with bovine HA were equivalent to those obtained with autogenous bone, while those seen with DFDB auto- and heterografts were significantly poorer.^{10,11}

Using an analogous experimental design, the present study was intended to establish the role of porous nonabsorbable HA in improving the boneimplant interface in sinus augmentation procedures.

MATERIALS AND METHODS

The study protocol was examined by the Ethics Commission of the University of Vienna and approved by the Austrian Federal Ministry of Science and Research. All surgical procedures were performed by the same surgeon.

The animals were fasted for 24 hours preoperatively, but were allowed to drink water ad libitum. Anesthesia was induced with thiopental (Hoechst, Vienna, Austria) titrated to its effect. Following orotracheal intubation, anesthesia was maintained with a mixture of nitrous oxide, oxygen, and 0.5% halothane.

Twenty-seven adult female mountain sheep were used. Six maxillary sinuses were studied in each follow-up period (12, 16, and 26 weeks) and in each group. The animals were randomly allocated to the different groups.

Surgical Procedure

The surgical procedure has been described elsewhere.¹⁰ Two titanium plasma-flame-sprayed cylindric implants were placed bilaterally in each of 54 sinuses. Through an extraoral approach, a window 1×1 cm was cut into the bony facial sinus wall. The Schneiderian membrane was carefully elevated, and 2 holes were drilled into the lateral sinus wall distal to the bone window for accommodating the implants (Figs 1 and 2). In 18 sinuses the artificial cavity was packed with porous HA (Interpore-200, Interpore International). Another 18 sinuses were grafted with 4 to 6 mL of autogenous iliac crest bone. Eighteen sinuses were not grafted and served as controls. Titanium plasma-flame-sprayed cylindric implants (Friatec, Friedrichsfeld, Germany) with a diameter of 3.75 mm and a length of 8 mm were placed in the drill holes, completely buried, and covered with the overlying soft tissue. They were thus not exposed to the intraoral environment at any time. Postoperatively, penicillin (20 million IU; Penicillin G Sodium, Biochemie, Kundl, Austria) and oxacillin (1 g; Stapenor, Bayer, Leverkusen, Germany) were administered intramuscularly.

Figs 2a to 2d Intraoperative photographs of the sinus-grafting procedure.



Fig 2a A window is cut into the bony sinus wall.



Fig 2c The grafting material is introduced into the sinus.

The time course of new bone formation and bone remodeling was evaluated by sequential polyfluorochrome labeling.¹² For this purpose the animals were injected with tetracycline (Reverin, Hoechst; 25 mg/kg body weight) subcutaneously 4 weeks postoperatively, calcein green (CGr, Merck, Darmstadt, Germany; 20 mg/kg body weight) 2 weeks prior to sacrifice, and alizarin complexon (AC, Merck; 30 mg/kg body weight) halfway through the follow-up time (Fig 3).

Specimen Preparation

The animals were sacrificed with an overdose of thiopental and ebutramide (T61, Hoechst). The facial part of the skull was removed, and a block section with 1 implant of each sinus was randomly selected for histologic analysis. The other implant was subjected to pull-out tests to evaluate its mechanical strength. The implants were sectioned along the frontal longitudinal axis immediately after retrieval and stored in buffered formalin. Following dehydration in ascending grades of alcohol, the specimens were embedded in light-curing resin



Fig 2b The Schneiderian membrane is carefully elevated.



Fig 2d The drill holes for the 2 implants are created distal to the osteotomy. Note the grafting material in the implant drill holes.



Fig 3 Outline of the experimental design. OP = operation; T = tetracycline; A = alizarin complexon; C = calcein green; S = sacrifice; number of weeks is shown in parentheses.

(Technovit 7200 VCL + BPO, Kulzer, Wehrheim, Germany) and cut with saws and grinding machines (Exakt Cutting and Grinding Equipment, Exakt Apparatebau, Norderstedt, Germany) into 10- to 20-µm sections.¹³ These were stained with toluidine



Fig 4 Schematic indicating areas of interest distant from implant in histologic sections. a = apical; b = crestal.

blue. Three to 5 sections of each implant were used for histologic studies.

Histomorphometric Analysis

Five digital photographs (Kodak Professional DCS 420, Kodak, Rochester, NY) of 1 representative section per implant at a magnification $\times 10$ (Nikon Microphot-FXA, Leitz, Wetzlar, Germany) were recorded. Photographs were arranged so that the entire implant surface could be evaluated. They were then transferred into black-and-white mode and evaluated histomorphometrically (Artma software program, Acuity Imaging, Nashua, NH).

At each sampling time (12, 16, and 26 weeks) the following data were recorded:

- 1. Absolute length of the implant surface in mm
- 2. Absolute length of the contact between the implant and bone in mm
- 3. Relative length of the implant surface in direct contact with the bone, in %

Other variables evaluated were the percent distribution of bone, grafting material, and soft tissue at a distance of 1 mm from the implant. For this purpose, 3 rectangular templates 3×1 mm in size were grouped around the implant tips in a U-shape, with the upper borders of the 2 perpendicular rectangles 2 mm below the implant tip (Fig 4). In these rectangular templates the bone and the HA were highlighted

in different colors (Adobe Photoshop 4.0.1, Adobe, San Jose, CA) and the areas occupied by them were computed (Openlab, version 1.7.5, Improvision, Conventry, United Kingdom).

Statistical Data Analysis

The differences in the length of the bone-implant contact between the groups were assessed by weighted analysis of covariance with due consideration to implant length, bone-implant contact, and implant retention time. A distinction was made between the crestal and apical portions of the implants, with data computed both jointly and separately for these 2 sites. Correlations between individual portions were evaluated with Spearman's coefficient of correlation.

To evaluate the amount of bone and HA at a distance from the implant, means and standard deviations of the area occupied by them in percent were calculated. Weighted analysis of covariance was used for assessing the percent bone volume as a function of group affiliation and retention time. Pvalues less than .05 were considered significant.

RESULTS

Histology

All implants were osseointegrated in the local host bone. Newly formed bone had grown onto the surface of all implants from the local buccal antral wall and the elevated periosteum.

Control Group. All implants showed a thin bony layer that originated from the local cortical bone and covered about half the length of the implants (Figs 5a and 5b). The gap between the implant and the drill hole was bridged by newly formed bone, most of which was in direct contact with the implant surface. Initially, only woven bone was present, but by week 26 this had largely been replaced by lamellar bone with regular osteons. On the side facing the implant, the newly formed bone still contained osteoid with an osteoblast seam and secondary osteons at 26 weeks. This suggested that bone apposition was still in progress. On the sites without bony growth onto the implant surface, numerous uni- or multinucleated macrophages and collagen fiber bundles, arranged mostly alongside the implant surface, were present.

Autogenous Cancellous Bone-Grafted Group. While the implants were largely covered by bone on their crestal portion, the apical portions of the implant were surrounded predominantly by loosely structured connective tissue, suggesting that the cancellous bone graft had been resorbed (Figs 6a







Fig 6a Frontal section through left sinus at 26 weeks after grafting with autogenous cancellous bone from the iliac crest and simultaneous implant placement.

and 6b). If present at all, bone around the implant tips was cancellous in nature, with bone marrow–like hollow spaces. In most cases this bone had contact with Schneiderian membrane overlying it. Otherwise, the implant tips were surrounded by no more than a thin layer of fibrous connective tissue and respiratory epithelium. The bone deposited around the crestal part of the implants was mainly compact in nature, while that along the mid-third of the implant and at the apical portion was mostly cancellous. **Fig 5a** (*Left*) Frontal section through a left ungrafted control sinus at 16 weeks postoperatively.

Fig 5b (Below) Longitudinal section through implant of control group, 16 weeks postoperatively (magnification \times 4). (Inset) Histiocytes on the implant surface (magnification \times 250).





Fig 6b Frontal section through implant 26 weeks after grafting with autogenous cancellous bone from the iliac crest. Note resorption of the cancellous graft around the implant tip (magnification \times 2).

Bone-implant contacts around the crestal implant portion were fairly well distributed. In the mid-third of the implants, the trabecular cancellous bone had distinctly less extensive contact with the implants. Implant portions not surrounded by bone were colonized by macrophages.

On fluorescence microscopy, bone remodeling and apposition of new bone were seen to continue throughout the follow-up time and were still in progress at 26 weeks.



Fig 7a (*Above*) Frontal section through left sinus at 16 weeks after grafting with porous HA.

Fig 7b (*Top right*) Longitudinal section through implant at 16 weeks after grafting with HA. Note abundant bone formation (magnification \times 5).

Fig 7c (*Right*) Longitudinal section through implant at 16 weeks after grafting with HA. Note sparse bone formation (magnification $\times 5$).





HA-Grafted Group. The crestal third of the implants was embedded in local cortical bone throughout (Figs 7a to 7c). From this a thin layer of woven bone was seen to push up along the implant surface. This was replaced by lamellar bone during the follow-up period.

Throughout the follow-up time, the implants were completely surrounded by grafting material. At 12 weeks the HA particles were interspersed with connective tissue containing abundant collagen fibers. HA particles in the immediate vicinity of the crestal cortical bone were surrounded by osteoid and woven bone at this time. On their surfaces, Howship's lacunae were present, reflecting incipient resorption of the grafting material. Signs of resorption were seen mainly in areas without bone. At 16 weeks most of the HA particles, particularly those near the local bone, had been incorporated in the bone. Signs of resorption were most prominent at those sites where the particles were surrounded by soft tissue. Secondary transformation of HA particles by osteons was not seen in any case. The periimplant bone remained fairly constant quantitatively, but increasingly assumed a lamellar appearance. By week 26 most of the particulate material was replaced by a wallpaper-like bony layer and had thus made contact with the peri-implant bone.

On fluorescence labeling, bone remodeling and apposition were seen to progress throughout the follow-up period. As soon as the HA particles became ensheathed by newly formed bone, bone remodeling was clearly reduced. HA particles completely surrounded by bone no longer showed any signs of resorption.

In some cases HA particles had penetrated the Schneiderian membrane. At these sites inflammatory cells were clearly more abundant.

Histomorphometry

Control Group. The mean bone-implant contact length was 3.9 ± 0.3 mm. It increased from 20% to 25.1% during the follow-up time. A separate evaluation of the crestal and apical implant portions showed gains from 53% to 55.7% crestally and from 6.4% to 7.9% apically (Table 1).

Autogenous Bone Group. The mean boneimplant contact length was 5.7 ± 0.3 mm. It increased from 30.4% to 35.5% between weeks 12

		12 w	eeks			16 we	eks			26 week	S	
	l-length (mm)	Contacts	C-length (mm)	%	l-length (mm)	Contacts	C-length (mm)	%	I-length (mm)	Contacts	C-length (mm)	%
Control group												
Crestal	6.5 ± 0.9	30.5 (10; 90)	2.9 ± 0.8	44.6	6.7 ± 0.9	41 (14; 52)	3.6 ± 0.6	53.7	6.0 ± 1.0	39 (32; 82)	2.7 ± 0.9	45.0
Apical	11.0 ± 1.3	2 (0; 35)	0.7 ± 0.9	6.4	11.2 ± 1.3	16 (0; 56)	0.9 ± 1.0	8.0	11.4 ± 0.9	28 (13; 42)	0.9 ± 0.6	7.9
Total	17.5 ± 1.2	36.5 (10; 119) 3.5 ± 1.6	20.0	17.9 ± 1.5	52 (30; 88)	4.5 ± 1.2	25.1	17.4 ± 0.8	67 (46; 124)	3.6 ± 1.1	20.7
Cancellous bone												
Crestal	6.8 ± 0.6	35 (22; 48)	3.6 ± 1.0	53.0	6.4 ± 0.5	28.5 (6; 60)	3.9 ± 0.9^{d}	60.9	6.1 ± 0.1	34 (14; 42)	3.4 ± 0.9	55.7
Apical	11.3 ± 0.9	29 (0; 43)	1.9 ± 1.3	16.8	11.1 ± 1.5	24 (4; 42)	1.7 ± 0.6	15.3	10.4 ± 0.9	38 (16; 86)	2.5 ± 0.9	24.0
Total	18.1 ± 1.0	58 (48; 86)	$5.5 \pm 0.8^{a,c}$	30.4	17.5 ± 1.7	56 (29; 71)	5.6 ± 1.3 ^{a,c}	32.0	16.6 ± 0.9	70 (30; 124)	5.9 ± 0.6 ^{a,c}	35.5
Hydroxyapatite												
Crestal	6.0 ± 0.1	24.5 (14; 47)	2.6 ± 0.9	43.3	6.1 ± 0.1	28 (19; 33)	2.5 ± 0.5	41.0	6.0 ± 0.2	30.5 (24; 36)	3.5 ± 0.3	58.3
Apical	11.8 ± 0.5	28 (6; 44)	2.7 ± 1.0	22.9	12.6 ± 0.5	18 (9; 35)	2.2 ± 1.3^{e}	17.5	12.7 ± 1.8	35 (24; 60)	4.4 ± 1.6 ^{a,b,c,f,g}	34.6
Total	17.8 ± 0.6	58 (22; 83)	5.3 ± 1.0 ^d	29.8	18.7 ± 0.5	46 (28; 68)	4.7 ± 1.5^{e}	25.1	18.7 ± 1.8	68.5 (48; 87)	$7.8 \pm 1.4^{a,b,c}$	41.7

r < .05 versus control at 12 weeks, r < .05 versus control at 16 weeks, r < .05 versus control at 27 r < .05 versus control at 28 weeks; P < .05 bone at 16 weeks versus HA at 26 weeks; P < .05 bone at 16 weeks versus HA at 26 weeks; P < .05 bone at 16 weeks versus HA at 26 weeks; P < .05 bone at 16 weeks versus HA at 26 weeks; P < .05 bone at 16 weeks versus HA at 26 weeks; P < .05 bone at 16 weeks versus HA at 26 weeks; P < .05 bone at 16 weeks versus HA at 26 weeks; P < .05 bone at 16 weeks versus HA at 26 weeks; P < .05 bone at 16 weeks versus HA at 26 weeks; P < .05 bone at 16 weeks versus HA at 26 weeks; P < .05 bone at 16 weeks versus HA at 26 weeks; P < .05 bone at 16 weeks versus HA at 26 weeks; P < .05 bone at 16 weeks versus HA at 26 weeks; P < .05 bone at 16 weeks versus HA at 26 weeks; P < .05 bone at 16 weeks; P < .05 bone at 16 weeks versus HA at 26 weeks; P < .05 bone at 16 weeks; P000

Hydroxyapat	ite at a Dista	nce of 1	mm from the	e Implant	us-IIIt Procedure	s in St	ep Augmen		n Autogenous		ous bone or Po	orous
		12 \	veeks			16 w	eeks			26 we	eks	
	Bone volume (%)	(%)	HA volume (%)	SD (%)	Bone volume (%)	(%)	HA volume (%)	SD (%)	Bone volume (%)	SD (%)	HA volume (%)	(%)
Cancellous bone												
Crestal	19.48	22.17	I	I	40.96ª	21.44	I	I	55.69	13.89	Ι	
Apical	8.82	12.61	I	I	13.46	19.92	I	Ι	12.18a,b,c,d	27.23	I	
Total	16.01	14.39	I	I	31.84 ^{a,b}	13.77	I	Ι	41.34 ^{a,b,d}	7.58	I	
Hydroxyapatite												
Crestal	8.19	15.77	34.02	9.62	5.12	8.37	31.23	6.26	19.70	15.96	32.66	8.11
Apical	5.9	11.37	27.51	16.29	10.30	12.92	26.04	10.41	19.02	11.0	26.1	10.03
Total	7.44	14.26	32.01	3.15	6.79	9.8	29.65	3.91	19.45	13.16	30.52	6.85

 ${}^{_{B}P}$ < .05 versus HA at 12 weeks; ${}^{_{b}P}$ < .05 versus HA at 16 weeks; ${}^{_{o}P}$ < .05 versus HA at 26 weeks; ${}^{_{d}P}$ < .05 versus bone at 12 weeks.

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and 26. While contact changed little crestally (from 44.6% to 45%), it clearly increased at the apical part (from 16.8% to 24.0%).

At a distance of 1 mm from the implant, the mean bone volume was $29.7 \pm 15.7\%$ (38.7% laterally and 11.5% apically) (Table 2). While the amount of bone present laterally clearly increased from 19% to 56% between weeks 12 and 26, it remained relatively constant around the crestal portion of the implant (9% versus 12.2%).

HA Group. The mean bone-implant contact length was 5.9 ± 0.3 mm. It increased from 29.8% to 41.7% during the follow-up time. This increase occurred mainly toward the end of the follow-up time, since very little change in contact length was seen up to week 16. A major gain in contact length was observed at both the crestal (from 43.3% to 58.3%) and at the apical implant portions (from 22.9% to 34.6%).

At a distance of 1 mm, the mean amount of bone was $11.2 \pm 13.0\%$. It increased markedly both laterally (from 8% to 20%) and apically (from 5.9% to 19%). The mean amount of HA present was $30.7 \pm 4.7\%$; this remained relatively constant throughout the follow-up time (31% to 34% laterally and 26% to 27% apically) (Table 2).

Comparison of Groups. Statistical analysis showed both the group type (P = .0001) and the retention time (P = .04) to have a significant effect on bone-implant contacts. This effect was significantly more pronounced in the HA group (P = .0002) and the autogenous bone group (P = .0005) than in the control group. Grafting with HA or autogenous bone did not produce significant differences (P = .89) (Table 1).

Statistical analysis of the bone volume at a distance from the implants was confined to the autogenous bone and the HA group (Table 2). Again, both group type (P = .0004) and retention time (P = .0094) played a significant role. Thus, significantly more peri-implant bone was present in the autogenous bone group than in the HA group. In both groups, bone volume increased substantially during the follow-up period.

DISCUSSION

The purpose of this study was to establish the role of porous HA in providing bony support for dental implants in a single-stage sinus elevation. Moreover, other interindividual factors influencing the measuring results were eliminated by avoiding exposure of the implants to the oral environment and to masticatory functional forces. It may well be that functional implant loading would have increased the contact area, as mechanically loaded implants have been shown to have more extensive contact with the bone than sleeping implants, at least in beagle dogs.^{1,8}

Another point to be considered is that the metabolic activity in sheep is higher than that in humans. For example, fracture healing in sheep was reported to take 6 to 8 weeks less in sheep than in humans.¹⁴ This would mean that the healing time in humans should be expected to be about 2 months longer than in sheep and that when porous HA is used clinically for elevating the maxillary sinus, substantially longer healing times may be needed.

The maxillary sinus seems to be ideally suited for the use of various bone substitutes, because it has a high osteoregenerative potential. This was reflected by minor new bone formation in the non-grafted control group. Whether the formation of new bone was attributable to the osteogenetic potential of the Schneiderian membrane is questionable. While sporadic islands of bone were present along the Schneiderian membrane, their origin was unclear. A relation to the local bone may perhaps have been detectable on 3-dimensional reconstructions of ground sections. However, Hürzeler² found no evidence of osteoneogenesis from the Schneiderian membrane in monkeys.

Autogenous bone is currently regarded as the "gold standard" among grafting materials. This was supported by the results reported, as the sites grafted with autogenous bone showed significantly more peri-implant bone than those grafted with HA.

Histologically, the grafted material was found to have accumulated mainly along the sides of the implants. In contrast, at the implant tips, the Schneiderian membrane was seen mostly to be closely related to the implant surface. This suggests that the grafted material was largely resorbed, so a larger amount of bone graft should perhaps have been used. Fluorescence microscopy revealed that bone remodeling and apposition were still in progress at 26 weeks.

Unlike the implants in the autogenous bone group, most of the implants in the HA group were completely surrounded by graft material. Histologically, 2 distinct mechanisms were found to underlie new bone formation. By more than 12 weeks, a thin bone layer was seen to push up from the implant base along the rough titanium surface. By that time the HA particles near the local cortical bone had been surrounded by newly formed bone; it took 26 weeks until a compound effect occurred between the 2 mechanisms and until peripheral bone and peri-implant bone increasingly coalesced. The histologic appearance of the HA-grafted samples mimicked that of a chronic inflammatory reaction characterized by a reduction of macrophages on the particle surface and an increasing apposition of bone.^{15,16} In an experimental study designed to examine the response of HA in the dog femur for 1 year, resorption was absent.¹⁷ This was partly confirmed by the present study, insofar as signs of resorption were no longer detectable as soon as the HA particles had been incorporated into the bone. Resorption occurred mainly along the particle surfaces not in contact with bone, although major regional differences were seen in the same animal.

The immaturity of the bone growing onto the implant surface would appear to suggest that bone remodeling and new bone formation were still in progress at the end of the 26-week follow-up time and that more bone volume may have been gained if the study had been prolonged.

In both grafted groups, mineralized boneimplant contacts were significantly more extensive than in the non-grafted control group (P = .0002 for HA and P = .0005 for bone). Retention time had a significant effect in both grafted groups. In the HA group, the contact length increased from 29.1% to 41.7%. This roughly agrees with what Quinones found in beagles.^{1,8} Using titanium plasma–flamesprayed implants and porous HA, he achieved boneimplant contact of 45.8% at 8 months.

Major differences were seen between the implant tips and the implant bases. In all 3 groups there was clearly less contact apically than at the base. This difference is because of the fact that the examination of the crestal part of the implant also included the bone-implant contact with the local host bone. In the non-grafted controls and in the autogenous bone group, the crestal bone-implant contact remained virtually constant, while it clearly increased in the HA group. This may be the result of the predominantly osteoconductive properties of porous HA.^{1,17}

In the HA-grafted samples, the bone volume at a distance from the implants was significantly lower at 16 weeks than in the samples grafted with autogenous bone. The HA content remained relatively constant. This implies that, despite clearly detectable signs of resorption, HA was resorbed very slowly and entered into a sort of dormant complex because of the surrounding bone. Further studies are needed to shed light on the response of this complex to inflammatory processes, which determines the clinical usefulness of HA.

Both bone contact and bone volume showed major variations in the animals in the HA group. New bone formation and resorption of HA particles also varied extensively in the same animal. These results suggest that, in sinuses grafted with HA, new bone formation is unpredictable and varies widely. Therefore, HA alone should be used with critical discretion in sinus-lift procedures.

CONCLUSIONS

In this study the role of HA as a grafting material for single-stage sinus elevation to provide a bony support for dental implants was investigated in sheep. HA was found to produce the same boneimplant contact as autogenous bone. With both HA and autogenous bone, the results were superior to those seen in the non-grafted controls. However, as the results varied widely, the use of HA alone for sinus grafting should be investigated critically despite satisfactory statistical data.

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REFERENCES

- Quinones C. Maxillary sinus augmentation using different grafting materials and dental implants in monkeys. Part II. Evaluation of porous hydroxyapatite as grafting material. Clin Oral Implants Res 1997;8(6):487–496.
- Hürzeler M. Maxillary sinus augmentation using different grafting materials and dental implants in monkeys. Part III. Evaluation of autogenous bone combined with porous hydroxyapatite. Clin Oral Implants Res 1997;8(5):401–411.
- White E, Shors E. Biomaterial aspect of Interpore-200 porous hydroxyapatite. Dent Clin North Am 1986;30(1): 49–67.
- Tidwell J, Blijdorp P, Stoelinga P, Brouns J, Hinderks F. Composite grafting of the maxillary sinus for placement of endosteal implants. Int J Oral Maxillofac Surg 1992;21: 204–209.
- Wheeler S, Holmes R, Calhoun C. Six-year clinical and histologic study of sinus-lift grafts. Int J Oral Maxillofac Implants 1996;11(1):26–34.
- Krekeler G, Schilli W, ten Bruggenkate C, Schen R, Gahlert G. Sinusbodenaugmentation—Eine zuverlüssige Methode zur Verbesserung der Implantatintegration? Z Zahnärztl Implantol 1998;14:198–207.
- Small S, Zinner I, Panno F, Shapiro H, Stein J. Augmenting the maxillary sinus for implants: Report of 27 patients. Int J Oral Maxillofac Implants 1993;8(5):523–528.
- Quinones C. Maxillary sinus augmentation using different grafting materials and dental implants in monkeys. Part IV. Evaluation of hydroxyapatite-coated implants. Clin Oral Implants Res 1997;8(6):497–505.

- Wetzel A, Stich H, Caffesse R. Bone apposition onto oral implants in the sinus area filled with different grafting materials. Clin Oral Implants Res 1995;6:155–163.
- Haas R, Donath K, Fodinger M, Watzek G. Bovine hydroxyapatite for maxillary sinus grafting: Comparative histomorphometric findings in sheep. Clin Oral Implants Res 1998; 9(2):107–116.
- Haas R, Haidvogl D, Donath K, Watzek G. Allogeneic and xenogenic freeze-dried bone for sinus augmentation. Comparative histomorphometric findings in the sheep. Clin Oral Implants Res 2002;13(6).
- Plenk HJ. Knochengewebe und Zähne. In: Böck P, Romeis B (eds). Mikroskopische Technik, ed 17. Munich: Urban und Schwarzenberg, 1989:527–566.

- Donath K. Die Trenn-Dünnschliff-Technik zur Herstellung histologischer Präparate von nicht schneidbaren Geweben und Materialien. Der Präparator 1988;34:197–206.
- Szyszkowitz R, Weiss H, Muhr G. Nekrosecallus nach stabiler Osteosynthese. Arch Orthop Unfallchir 1974;79: 281–295.
- Sennerby L, Ericson LE, Thomsen P, Lekholm U, Åstrand P. Structure of the bone-titanium interface in retrieved clinical oral implants. Clin Oral Implants Res 1991;2:103–111.
- Donath K, Laass M, Günzl H-J. The histopathology of different foreign-body reactions in oral soft tissue and bone tissue. Virchows Archiv A Pathol Anat Histopathol 1992;420: 131–137.
- Chang R, Kao A. Biomechanical and histologial studies of particulate hydroxyapatite implanted in femur bone defects of adult dogs. Int J Oral Maxillofac Surg 2000;29:54–61.