

# The Sinus Bone Graft

Second edition

Chapter 17

Edited by

**Ole T. Jensen, DDS, MS**

Private Practice

Oral and Maxillofacial Surgery

Denver, Colorado



**Quintessence Publishing Co, Inc**

Chicago, Berlin, Tokyo, London, Paris, Milan, Barcelona, Istanbul,  
São Paulo, New Delhi, Moscow, Prague, and Warsaw

The sinus bone graft / edited by Ole T. Jensen. -- 2nd ed.

p. ; cm.

Includes bibliographical references and index.

ISBN 0-86715-455-1 (hardcover)

1. Maxillary sinus. 2. Maxillary sinus--Surgery. 3. Bone-grafting.

I. Jensen, Ole T.

[DNLM: 1. Maxillary Sinus--surgery. 2. Bone Transplantation

--methods. 3. Reconstructive Surgical Procedures. WV 345

S618 2006]

RF421.S55 2006

617.5'2--dc22

2005032653



© 2006 Quintessence Publishing Co, Inc

All rights reserved. This book or any part thereof may not be reproduced, stored in a retrieval system, or transmitted in any form or by any means, electronic, mechanical, photocopying, or otherwise, without prior written permission of the publisher.

Quintessence Publishing Co, Inc

4350 Chandler Drive

Hanover Park, Illinois 60133

[www.quintpub.com](http://www.quintpub.com)

Editor: Lisa C. Bywaters

Production: Sue Robinson

Cover and internal design: Dawn Hartman

Printed in China

# chapter 17 Use of Xenografts for Sinus Augmentation

*Stuart J. Froum, DDS*

*Stephen S. Wallace, DDS*

*Sang-Choon Cho, DDS, BDS, MS*

*Dennis P. Tarnow, DDS*

The use of xenografts has been demonstrated to be effective for increasing bone height and bone volume in the deficient posterior maxilla.<sup>1</sup> Anorganic bovine bone matrix alone and in combination with autogenous bone is the graft material of choice for many practitioners who perform sinus augmentation procedures. In fact, a survey of the literature on bone replacement grafts (BRGs) showed that studies of the use of xenografts are the most complete and well documented.<sup>2,3</sup> This chapter presents the clinical and scientific reasons for the gradual shift from using autogenous bone alone to substituting xenografts for part or all of the graft, as shown in two recently published evidence-based reviews<sup>2,3</sup> and other recent literature.

## Criteria for Evaluation and Comparison

The success of the sinus elevation procedure is best evaluated by considering therapeutic goals and patient outcomes. The goals of sinus augmentation include formation of vital bone where no bone existed and the long-term survival and success of functionally loaded implants placed in graft bone. From a clinical perspective, the latter is determined by prospective long-term studies of implant survival. The problem with this approach is that while the

comparison of efficacy of different graft materials is multifactorial, it is most often measured indirectly by a single variable: implant longevity.

Variations in technique and materials combined with timing of implant placement, differences in sinus anatomy, residual alveolar height, and host factors such as smoking and compliance make it impossible to compare disparate results from the myriad array of bone graft regimens.<sup>3</sup>

This is why no definitive data have established the minimal amount of vital bone that is necessary for implant integration (see chapter 5). Addressing this question, histologic measurements of vital bone formation in sinuses filled with either a xenograft (BRG) or a composite graft were compared to define the grafts' capacity for healing as well as osseointegration.

Data from evidence-based reviews correlated with histologic studies formed the basis of this review, focusing on the percentage of vital bone formed after grafting with xenograft alone, with xenograft combined with autogenous bone, and with autogenous bone alone.

Implant survival rates in sinuses grafted with these different materials were also compared. Given the paucity of randomized controlled clinical trials, the review also considered noncontrolled human trials, case series, retrospective studies, and selected case reports that included human histologic data. However, this review relies most heavily on evidence-based reviews.<sup>2,3</sup>

## Evolution of Graft Material

In 1996, the Sinus Consensus Conference evaluated 2,997 implants placed in 1,007 augmented sinuses. Five-year data revealed that 229 implants failed, resulting in a 92.4% implant survival rate.<sup>1</sup>

A consensus statement from the conference concluded that "autogenous bone is appropriate for sinus grafting." The majority opinion concerning allografts, alloplasts, and xenografts, alone or in combination with each other, stated that "these materials may be effective as a graft material in selected clinical situations" but that "there are limited published data to make a statement about their use in severely atrophic situations."<sup>1</sup>

A literature review by Tolman<sup>4</sup> covered 58 articles, 591 patients, 733 grafts, and 2,315 implants. Another review by Tong et al<sup>5</sup> analyzed 10 articles (those that met their inclusion criteria), including 484 implants in 130 patients followed for 6 to 60 months. Implant survival was reported as follows: 90% for autogenous bone, 94% for hydroxyapatite (HA) combined with autogenous bone, 98% for demineralized freeze-dried bone combined with HA, and 87% for HA alone.<sup>5</sup> Neither of these review articles included xenograft as a grafting material, instead focusing primarily on success rates with autogenous bone.

Since these reviews were published, a large body of research on xenografts as bone replacement material for sinus augmentation has been documented and analyzed.

The use of 100% autogenous bone harvested extra-orally from the ilium, tibia, and cranium or intraorally from the ramus, symphysis, or maxillary tuberosity has been deemed the gold standard of sinus grafting materials, for good reason. Autogenous bone contains all of the elements necessary to promote vital bone formation, including mineral, collagen matrix, growth factors, and, depending on the source and time of delivery, vital cells. Moreover, autograft is osteoinductive as well as osteoconductive. However, the use of 100% autogenous bone as a graft has certain disadvantages. For example, the need for a second surgical site increases postsurgical morbidity and surgical risks. Further, depending on the size of the sinus and the selected donor site, the postsurgical pain from the donor site may be significant. Use of autogenous bone also increases the surgical time, costs, and logistics of the surgical intervention.

A recent evidence-based review of the sinus augmentation by Wallace and Froum<sup>2</sup> included a total of 5,267 im-

plants followed for a minimum period of 1 year after loading. The studies included 34 lateral window approaches of which 11 used xenograft alone or in combination with autogenous bone (composite) or mixed with platelet-rich plasma (PRP). The survival rate of the implants placed in xenografts was statistically the same as for implants placed in particulate autogenous bone grafts. This comparison is significant because implants placed into sinuses augmented with particulate grafts show a higher rate of survival than those placed in sinuses augmented with block grafts.<sup>2</sup> Del Fabbro et al<sup>3</sup> conducted a systematic review of survival rates in 39 articles that met their inclusion criteria, which consisted of 6,913 implants in 2,046 subjects with follow-up times ranging from 12 to 75 months. They reported an average survival rate of 87.7% for implants placed in 100% autogenous grafts of all categories, including block grafts, block plus particulate grafts, and particulate grafts alone. This was significantly lower than the 94.9% survival rate of implants placed in composite grafts of xenograft and autogenous bone and the 96% survival rate of implants placed in 100% xenograft.

Comparative studies by Hising et al,<sup>6</sup> Hallman et al, and Valentini and Abensur<sup>8</sup> report higher survival rates for implants placed in sinuses augmented with 100% xenograft than for those augmented with 100% autogenous bone or composite grafts of xenograft and autogenous bone.

Hising et al<sup>6</sup> studied 231 implants placed in 92 augmented sinuses. The implant survival rate in sinuses grafted with 100% xenograft (Bio-Oss, Osteohealth) was 92.2% compared to a 77.2% survival rate of implants placed in sinuses augmented with a composite of Bio-Oss and autogenous bone.

Hallman et al<sup>7</sup> reported an overall survival rate of 91.0% for 111 implants placed in 36 sinuses and loaded for at least 1 year. The survival rate in sinuses augmented with 100% autogenous bone in this limited study was 82.4%. With a 20:80 composite of autogenous bone and bovine bone, the survival rate was 94.4%, and in sinuses grafted with 100% xenograft (Bio-Oss), the survival rate was 96.0%.

A recent retrospective study by Valentini and Abensur evaluated the survival rate of titanium plasma spray coated cylindrical and machined screw-type implants placed in sinus grafts in 59 consecutively treated patients. A total of 187 implants were placed in 78 grafted sinuses. The overall implant survival rate was 94.5% after a mean period of  $6.5 \pm 1.9$  years of function. The implant survival

**BOX 17-1 Technical considerations for the use of xenografts in sinus augmentation**

1. Elevate the sinus membrane from the floor and medial sinus walls to the height of the lateral window osteotomy.
2. Use a 1:1 mixture of small (0.25–1.00 mg) and large (1.00–2.00 mg) particles. This results in optimal interparticle spacing. Using only small particles under compression may impede vascular ingrowth, while using only large particles may delay resorption and new bone formation.
3. Hydrate the xenograft particles with sterile saline.
4. After hydration, remove any excess saline. Placing the xenograft material in a relatively dry state makes it easier to control the placement and allows the material to hydrate with blood.
5. Fill the anterior compartment first to reduce the possibility of leaving empty voids.
6. Visualizing the medial wall, compress the xenograft particles against the floor and medial wall but not superiorly against the sinus membrane.
7. Place the membrane barrier over the window and extend approximately 3 mm over remaining bone.
8. Achieve tension-free suturing of the flap, including vertical and periosteal releasing incisions where necessary.

rate was 96.8% in sinuses grafted with xenograft alone versus 90% in sinuses grafted with a composite of xenograft and demineralized freeze-dried bone allograft.

A histologic report by Froum et al<sup>9</sup> showed that the addition of PRP resulted in only a 2% increase in vital bone formation when the same graft material was used in bilateral sinuses. A recent animal study by Roldan et al<sup>10</sup> similarly showed that the addition of PRP to xenograft was less effective in improving bone-implant contact in sinus graft procedures than was recombinant human bone morphogenetic protein-7 (rhBMP-7) and xenograft. Based on all of the data analyzed, a recent evidence-based review concludes that insufficient evidence exists to recommend the use of PRP in sinus graft surgery.<sup>2</sup>

When sinus grafting is followed by bone augmentation using autografts or demineralized allografts, a tendency for volumetric resorption on the order of 25% has been noted, along with a change in the density of the grafted sinus similar to that found in native bone. The result is an implant site that features type 3 or 4 bone. Histologic studies by Ulm et al,<sup>11</sup> Moy et al,<sup>12</sup> and Hanisch et al<sup>13</sup> report average posterior maxillary bone density of 17.1% to 23.4%, 45%, and 32.6%, respectively. Ulm et al reported that the mean trabecular bone counts may be as low as 6.73% in the maxillary molar area.<sup>11</sup> In addition, significant graft resorption has been reported with iliac autografts.<sup>12,14</sup> Recent studies in animals<sup>15</sup> and humans<sup>16</sup> showed significant reduction in bone height when either autogenous bone alone or a 2:1 mixture of autogenous bone and xenograft

was used. In contrast, the cases submitted to the 1996 Sinus Consensus Conference showed minimal evidence of re-pneumatization in 3-year postoperative panoramic radiographs when sinuses were augmented with xenograft compared to allograft.<sup>1</sup>

Unpublished data from sinus studies conducted at New York University also show no significant change in the height of sinuses grafted with xenograft over a 3-year period. Such stability may perhaps be explained by the fact that the grafts do not completely resorb, but persist even as new vital bone is forming.

To study the performance of a material in human histomorphometric studies, bilateral sinuses of similar size should be used, and only one variable (graft type) should be altered. This is the principle applied in ongoing sinus augmentation studies at the New York University Department of Implant Dentistry. The sinus augmentation procedure utilizes a lateral window technique with adherence to certain clinical considerations (Box 17-1; Figs 17-1a to 17-1h). At the time of implant placement, new bone formation in the sinus is evaluated based on cores taken with a trephine from the healed lateral window (to avoid the possibility of including native bone) (Figs 17-1i to 17-1k). The cores are sent to an independent laboratory for non-decalcified sectioning, and the percentages of vital bone, connective tissue, and residual xenograft are reported for each specimen.<sup>17–19</sup>

The osteoconductive properties of xenograft in human sinus grafts<sup>17,19,20</sup> derive from its chemical composition as

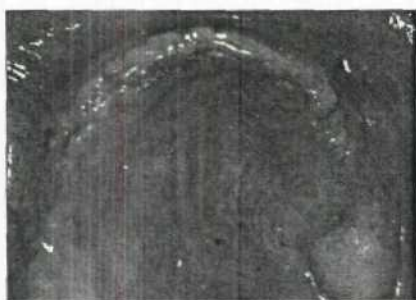


Fig 17-1a Presurgical site.



Fig 17-1b Crestal incision.

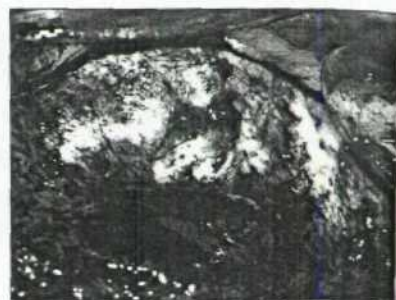


Fig 17-1c Presurgical outline of osteotomy in lateral sinus wall.

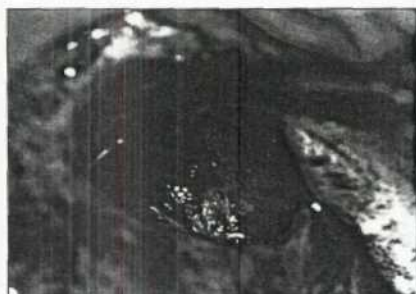


Fig 17-1d Sinus membrane elevated prior to graft placement.

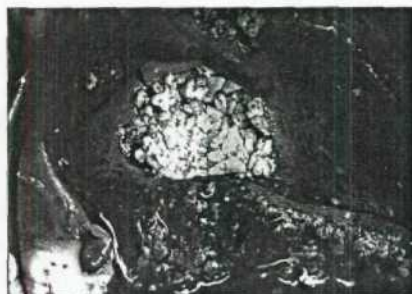


Fig 17-1e Sinus filled with xenograft.



Fig 17-1f Barrier membrane placed over the lateral window.

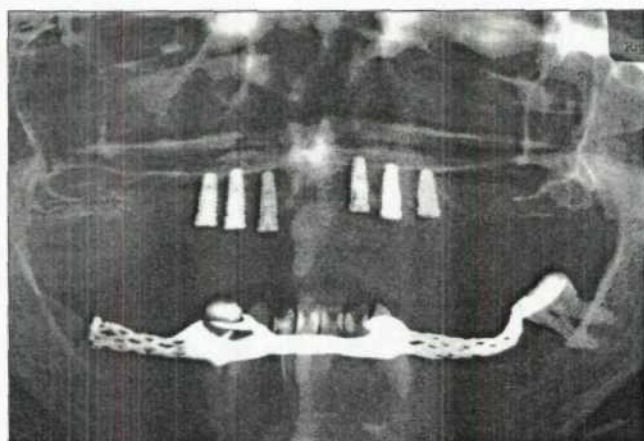


Fig 17-1g Panoramic radiograph prior to bilateral sinus graft surgery.

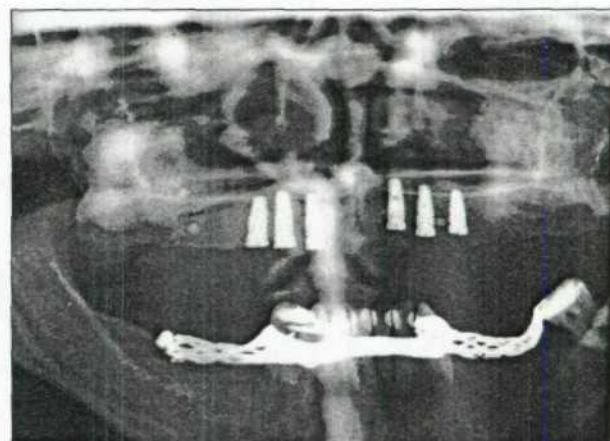


Fig 17-1h Panoramic radiograph following bilateral sinus graft surgery, demonstrating the fill of the sinus cavities with xenograft particles on one side and xenograft with autogenous bone on the other side.



Fig 17-1i Re-entry at 12 months to harvest bone core for histologic study.



Fig 17-1j Donor site following core harvesting.

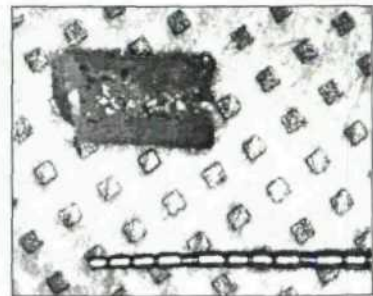
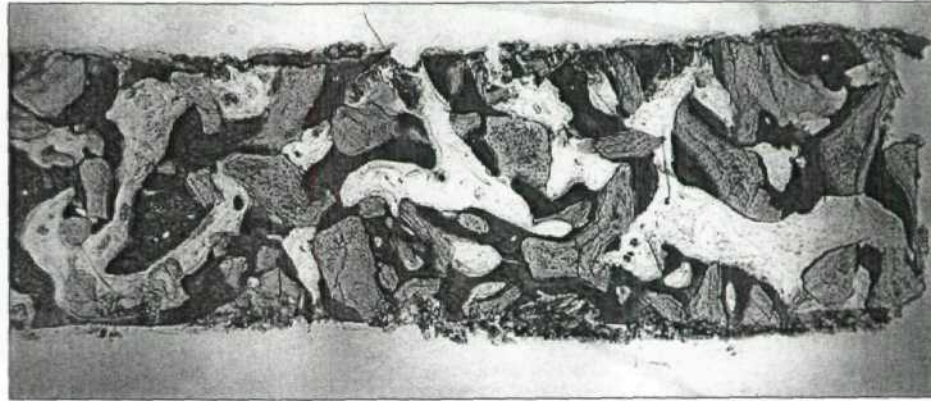
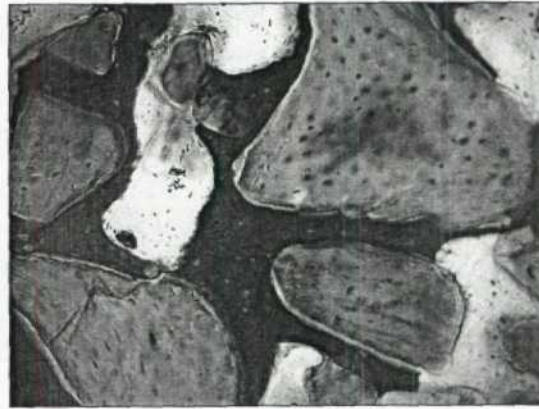


Fig 17-1k Core prior to histologic processing.

**Fig 17-2a** Low-power histologic view of sinus core specimen demonstrating bone growth (*red*) surrounding xenograft particles (*yellow*) at 6 months. (Stevenel blue and picric acid fuchsin; original magnification  $\times 4$ .)



**Fig 17-2b** High-power histologic view of sinus core specimen demonstrating bone deposition (*red*) directly on Bio-Oss particles (*yellow*). Note that "bridging" bone growth connects the particles (green = osteoid). (Stevenel blue and picric acid fuchsin; original magnification  $\times 20$ .)



**Fig 17-2c** Higher-power view (original magnification  $\times 40$ ) of the histology shown in Fig 17-2b.

well as its macro- and micromorphology. Histologic sections of sinus cores (Fig 17-2) in studies by Froum et al<sup>17</sup> and Wallace et al<sup>19</sup> reveal the presence of osteoblasts and osteoid, as well as bone apposition directly on the surface of the xenograft particles. Vital bone is observed to "bridge" the gaps between xenograft particles and has been shown histologically to increase over time.<sup>21</sup> Moreover, while the formation of vital bone occurs more rapidly in sinuses grafted with 100% autogenous bone<sup>22,23</sup> and to a greater extent<sup>17</sup> initially than it does when bone replacement grafts are used, these studies also show that bone formation with xenografts equalize over time. As previously noted, xenografts have been shown to resorb slowly and incompletely (Table 17-1). For example, Piatelli et al<sup>24</sup> retrieved 20 biopsy specimens at time intervals ranging

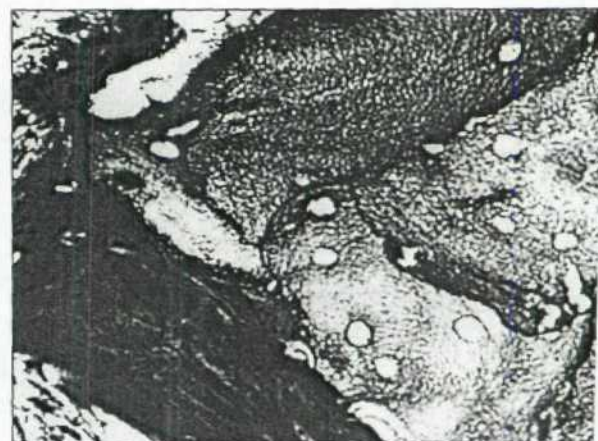
from 6 months to 4 years from sinuses augmented with 100% Bio-Oss. Findings at 6 to 9 months showed them to be composed of about 40% marrow space, about 30% newly formed bone, and about 30% residual Bio-Oss particles. Four-year specimens showed that Bio-Oss particles were still easily recognizable. Also present were osteoclasts in the process of resorbing Bio-Oss particles adjacent to newly formed bone<sup>24</sup> (Fig 17-3). In no way does this inhibit osseointegration of the implant<sup>28-30</sup>; in fact, the resorption of xenograft is accompanied by an increase in vital bone. Valentini et al,<sup>20</sup> for example, published a 6-month histology showing that proportions of bone and Bio-Oss were 21% and 39%, respectively; at 12 months, the proportion of bone had increased to 28% while the relative proportion of Bio-Oss decreased to 27%.

**TABLE 17-1** Histologic composition of sinuses grafted with anorganic bovine bone (Bio-Oss) alone and with autogenous bone

Author	Graft material	Time (mos)	Bone (%)	Residual Bio-Oss (%)	Connective tissue (%)
Piatelli et al, 1999 <sup>24</sup>	Bio-Oss alone	6–12	30	30	40
Valentini et al, 2000 <sup>20</sup>	Bio-Oss alone	6	21	39	40
Valentini et al, 2000 <sup>20</sup>	Bio-Oss alone	12	28	27	45
Yilderman et al, 2001 <sup>25</sup>	Bio-Oss + autog	7.1	18.9	29.6	51.5
Yilderman et al, 2000 <sup>26</sup>	Bio-Oss + blood	6.8	14.7	29.7	55.6
John and Wenz, 2004 <sup>27</sup>	Bio-Oss alone	3–8	29.5	14.9	55.6
John and Wenz, 2004 <sup>27</sup>	Bio-Oss + autog	3–8	32.2	17.8	50
NYU (unpub), 2005	Bio-Oss alone	6–12	18.5	28	53.5
NYU (unpub), 2005	Bio-Oss + autog	6–12	15.7	29.6	54.7



**Fig 17-3a** High-power histologic view of direct contact of new vital bone to xenograft (Bio-Oss) and osteoclasts adjacent to the xenograft. Bone cores harvested from augmented sinus at New York University Department of Implant Dentistry. (Hematoxylin and eosin; original magnification  $\times 20$ .)



**Fig 17-3b** Higher-power view (original magnification  $\times$  histology shown in Fig 17-3a).

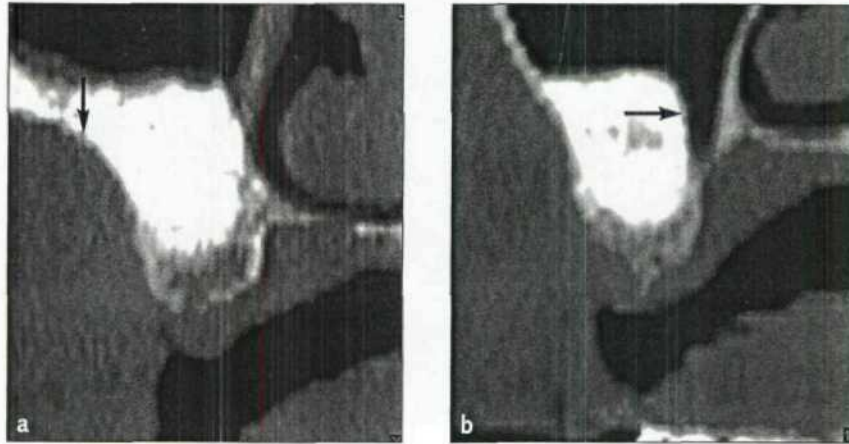
Histomorphometric studies<sup>17,19,20,25,26</sup> at 6 to 12 months after grafting consistently report findings of relative proportions of vital bone, connective tissue, and residual xenograft to be approximately 25%, 50%, and 25%, respectively. Due to this residual volume of xenograft, the *matured graft functions as type 2 bone*. This contrasts with demineralized allograft material, which cannot mechanically support implants under function.

## Disease Transmission Risk

Questions have been raised about whether xenografts increase the risk of transmitting bovine spongiform encephalopathy (BSE) to humans. While there has never been a case of disease transmission associated with the use of a xenograft, clinicians should review the processing

**Fig 17-4a** Reflection of the sinus membrane from the medial wall of the sinus, indicating complete fill of the sinus with xenograft particles (*arrow*).

**Fig 17-4b** Inadequate reflection of sinus membrane, indicating the presence of a void and an unfilled area (*arrow*).



sterilization procedures for these materials to be confident of their safety and to address any patient concerns about them. Rigorous, thorough, and extensive testing and regulation of xenograft materials are performed by the companies that manufacture them. Raw material consisting of long bones is obtained only from US cattle, and not from European sources. No case of BSE traced to long bones from bovine sources has ever been reported anywhere in the world. The material is processed either by high heat alone or by both high heat and chemicals to ensure that it is prion-free. Proof of anorganification is obtained through BioRad assay, SDS-PAGE testing, and SDS-PAGE and Western blotting.<sup>31,32</sup> Sogal and Tofe<sup>33</sup> calculated the risk of disease transmission based upon the testing model of the German Ministry of Health as 1 infection per  $1.3 \times 10^{19}$  1-g doses, an infinitesimal rate.

## Conductive Efficacy

Based on the preceding factors, Del Fabbro et al concluded that "Grafts utilizing bone substitute materials are as effective as autogenous bone, either when used alone or when used in combination with autogenous bone."<sup>3</sup> However, the clinician must remain aware that xenografts are osteoconductive, not osteoinductive, and thus the bony walls of the sinus must provide the vascularity, cells, and growth factors responsible for bone formation. To obtain the best results, the sinus membrane should be elevated medially as well as from the floor of the sinus so that the entire graft

can be vascularized and a maximum number of graft particles are in contact with bony walls (Fig 17-4). Autogenous bone also provides growth factors that stimulate new bone formation during bone turnover. Because it lacks such growth factors, xenograft requires a longer period of graft healing to achieve new vital bone.<sup>2,20,21</sup> This essential difference was emphasized by Merckx et al,<sup>34</sup> who reported that autogenous grafts had produced a higher percentage of vital bone than anorganic bone replacement grafts at 4 to 6 months. However, at 3 to 8 months, John and Wenz<sup>27</sup> showed only a small difference in vital bone sections of sinuses grafted with Bio-Oss plus autogenous bone (vital bone = 32.2%) compared to those grafted with Bio-Oss alone (vital bone = 29.5%). A recent histomorphometric study by Degidi et al<sup>35</sup> compared new bone formation following sinus grafting in 7 patients at an average of 7 months. Autogenous bone (50%) harvested from intraoral sources was combined with two different xenografts (50%); new bone formation was similar in both groups. However, in a large sinus, graft maturation may be 1.5 to 2 times longer for delayed implant placement with 100% xenograft than with 100% autogenous bone (ie, 8 to 12 months compared to 4 to 6 months).

Looking toward the future, a recent study by Fuerst et al<sup>36</sup> in minipigs showed that cultured bone cells derived from the iliac crest, then combined with bovine bone mineral significantly increased the amount of new bone formed in sinus augmentations compared with bovine bone alone. This may have implications in humans for earlier and more rapid bone formation when cultured bone-derived cells are used with xenograft in sinus augmentation procedures.

## Conclusion

Xenograft is the unheralded success story of sinus graft augmentation. When used by the prescribed methods elucidated here, xenograft is better than autograft or allograft at maintaining load-bearing bone volume, with a high percentage of vitality, safety, and lack of complication. Though xenograft is not the material of choice for bone graft reconstruction in general, for the sinus floor graft site and for the sole purpose of dental implant osseointegration, it may be the graft material of choice.

## References

- 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.
- 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.
- Del Fabbro M, Testori T, Francetti L, Weinstein R. Systematic review of survival rates for implants placed in the grafted maxillary sinus. *Int J Periodontics Restorative Dent* 2004;24:565-578.
- Tolman DE. Reconstructive procedures with endosseous implants in grafted bone: A review of the literature. *Int J Oral Maxillofac Implants* 1995;10:275-294.
- Tong DC, Rioux K, Drangsholt M, Beirne OR. A review of the survival rates for implants placed in grafted maxillary sinuses using meta-analysis. *Int J Oral Maxillofac Implants* 1998;13:175-182.
- Hising P, Bolin A, Branting C. Reconstruction of severely resorbed alveolar crests with dental implants using a bovine mineral for augmentation. *Int J Oral Maxillofac Implants* 2001;16:90-97.
- 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.
- 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.
- Froum SJ, Wallace SS, Tarnow DP, Cho S-C. Effect of platelet-rich plasma on bone growth and osseointegration in human maxillary sinus grafts: Three bilateral case reports. *Int J Periodontics Restorative Dent* 2002;22:45-53.
- Roldan JC, Jepsen S, Schmidt C, et al. Sinus floor augmentation with simultaneous placement of dental implants in the presence of platelet-rich plasma or recombinant human bone morphogenetic protein-7. *Clin Oral Implants Res* 2004;15:716-723.
- Ulm C, Kneissel M, Schedle A, et al. Characteristic features of trabecular bone in edentulous maxillae. *Clin Oral Implants Res* 1999;10:459-467.
- Moy PK, Lundgren S, Holmes RE. Maxillary sinus augmentation: Histomorphometric analysis of graft materials for sinus floor augmentation. *J Oral Maxillofac Surg* 1993;51:857-862.
- Hanisch O, Lozada JL, Holmes RE, Calhoun CJ, Kan JYK, Spiekermann H. Maxillary sinus augmentation prior to placement of endosseous implants: A histomorphometric analysis. *Int J Oral Maxillofac Implants* 1999;14:329-336.
- Garg AK. Current concepts in augmentation grafting of the maxillary sinus for the placement of dental implants. *Dent Implantol Update* 2001;12:17-22.
- Schlegel KA, Fichtner G, Schultze-Mosgau S, Wiltfang J. Histologic findings in sinus augmentation with autogenous bone chips versus a bovine bone substitute. *Int J Oral Maxillofac Implants* 2003;18:53-58.
- Hatano N, Shimizu Y, Ooya K. A clinical long-term radiographic evaluation of graft height changes after maxillary sinus floor augmentation with a 2:1 autogenous bone/xenograft mixture and simultaneous placement of dental implants. *Clin Oral Implants Res* 2004;15:339-345.
- Froum SJ, Tarnow DP, Wallace SS, Rohrer MD, Cho S-C. Sinus floor elevation using anorganic bovine bone matrix (Osteo Graf/N) with and without autogenous bone: A clinical, histologic, radiographic, and histomorphometric analysis—Part 2: an ongoing prospective study. *Int J Periodontics Restorative Dent* 1998;18:529-543.
- Tarnow DP, Wallace SS, Froum SJ, Rohrer MD, Cho S-C. Histologic and clinical comparison of bilateral sinus floor elevation with and without barrier membrane placement in 12 patients: Part 3 of an ongoing prospective study. *Int J Periodontics Restorative Dent* 2000;20:116-125.
- Wallace SS, Froum SJ, Tarnow DP, Cho S-C. Sinus augmentation utilizing ABBM (Bio-Oss) with and without osteotomy site coverage with various membranes. *Int J Periodontics Restorative Dent* 2005;25:551-559.
- Valentini P, Abensur D, Wenz B, Peetz M, Schenk R. Sinus grafting with porous bone mineral (Bio-Oss) for implant placement: A 5-year study on 15 patients. *Int J Periodontics Restorative Dent* 2000;20:245-253.
- Wallace SS, Froum SJ, Tarnow DP. Histologic evaluation of sinus elevation procedure. A clinical report. *Int J Periodontics Restorative Dent* 1996;16:47-51.
- Tadjoedin ES, DeLange GL, Holzmann PJ, Kuiper L, Burger E. Histologic 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.
- Tadjoedin ES, DeLange GL, Lyaruu DM, Kuiper L, Burger E. High concentrations of bioactive glass material (BioGran) + autogenous bone for sinus floor elevation. *Clin Oral Implants Res* 2002;13:428-436.
- Piatelli M, Favero G, Scarano A, Orsini G, Piatelli A. Bone reactions to anorganic bovine bone (Bio-Oss) used in sinus augmentation procedures: A histologic long-term report of 20 cases in humans. *Int J Oral Maxillofac Implants* 1999;14:835-840.

25. Yilderman M, Spiekermann H, Handt S, Edelhoft 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.
26. Yilderman M, Spiekermann H, Biesterfeld S, Edelhof D. Maxillary sinus augmentation using xenogenic bone substitute material (Bio-Oss) in combination with venous blood: A histologic and histomorphometric study in humans. *Clin Oral Implants Res* 2000;11:217-229.
27. John H-D, Wenz B. Histomorphometric analysis of natural mineral for maxillary sinus augmentation. *Int J Oral Maxillofac Implants* 2004;19:199-207.
28. Valentini P, Abensur D, Densari D, Graziani JN, Hammerle C. Histological evaluation of Bio-Oss in a sinus floor elevation and implantation procedure: A human case report. *Clin Oral Implants Res* 1998;9:59-64.
29. Rosenlicht J, Tarnow DP. Human histologic evidence of functionally loaded hydroxyapatite-coated implants placed simultaneously with sinus augmentation: A case report 2½ years post-placement. *Int J Oral Implantol* 1999;25:7-10.
30. Scarano A, Pecora G, Piattelli M, Piattelli A. Osseointegration in a sinus augmented with bovine porous bone mineral: Histological results in an implant retrieved 4 years after insertion. A case report. *J Periodontol* 2004;75:1161-1166.
31. Benke D, Olah A, Möhler H. Protein-chemical analysis of Bio-Oss bone substitute and evidence on its carbonate content. *Biomaterials* 2001;22:1005-1012.
32. 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.
33. Sogal A, Tofe AJ. Risk assessment of bovine spongiform encephalopathy transmission through bone graft material derived from bovine bone used for dental applications. *J Periodontol* 1999;70:1053-1063.
34. Merx MAW, Maltha JC, Stoelinga PJW. Assessment of the value of anorganic bone additives in sinus floor augmentation: A review of clinical reports. *Int J Oral Maxillofac Surg* 2003;32:1-6.
35. Degidi M, Piattelli M, Scarano A, Iezzi G, Piattelli A. Maxillary sinus augmentation with a synthetic cell-binding peptide: Histological and histomorphometrical results in humans. *J Oral Implantol* 2004;30:376-383.
36. Fuerst G, Tangl S, Gruber R, Gahleitner A, Sanroman F, Watzek G. Bone formation following sinus grafting with autogenous bone-derived cells and bovine bone mineral in minipigs: Preliminary findings. *Clin Oral Implants Res* 2004;15:733-740.