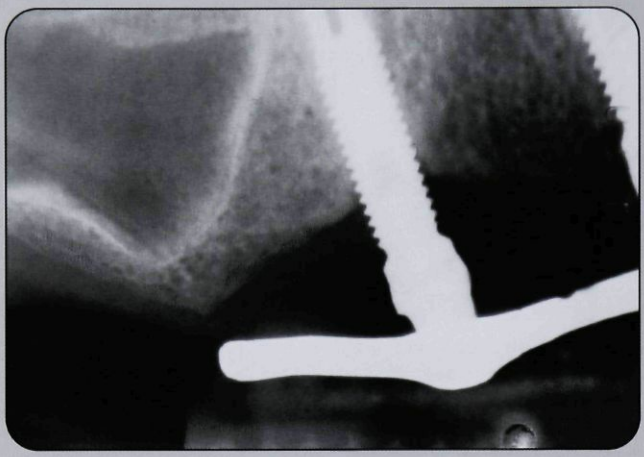
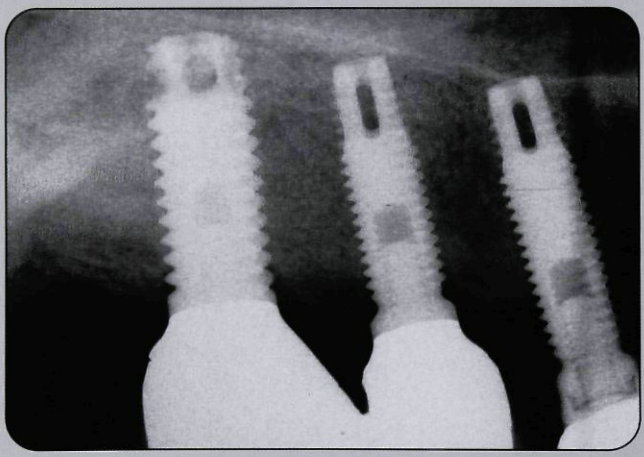
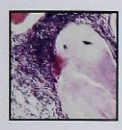




Maxillary Sinus Floor Elevation Using a Combination of DFDBA and Bovine-Derived Porous Hydroxyapatite: A Preliminary Histologic and Histomorphometric Report



Luca Landi, DDS/Robert W. Pretel, Jr, DDS, MSD**/*
*Nicky M. Hakimi, DDS, MSD***/Reza Setayesh, DMD, DMSc*****

The objective of the study was to determine the osteoconductive potential of bovine-derived porous hydroxyapatite (HA) in combination with demineralized freeze-dried bone allograft (DFDBA) as an alternative to autogenous grafting in the maxillary sinus. The study involved 5 patients treated with 2-stage sinus elevation procedures using a combination of DFDBA and Osteograf/N 300 and 700. The healing time before implant placement ranged from 6 to 13 months. At the time of reentry, a bone core was harvested from each patient and processed for histologic and histomorphometric analysis. Woven and lamellar bone formation was evident in all specimens. Mean trabecular bone volume was 27.92%. The amount of newly formed bone was positively correlated with healing time. The range of new bone formation was 5.36% (6 mo) to 43.68% (12 mo). Residual HA graft particles were evident in all specimens, and the amount was inversely correlated with time. HA particles were often surrounded by an intense inflammatory infiltrate. DFDBA particles, largely present in the 6-month biopsy, were not recognizable in the 10-, 12-, and 13-month specimens, suggesting complete replacement. The combination of Osteograf/N and DFDBA appears to be osteoconductive and may be considered a valid alternative to autogenous bone grafts in sinus lift procedures. Histomorphometric and histologic evaluation may also be used to monitor the status of the future implant site. (Int J Periodontics Restorative Dent 2000;20:575–583.)

*Senior Resident, Department of Periodontology and Oral Biology, Boston University School of Dental Medicine, Massachusetts; and Private Practice, Grosseto, Italy.
**Senior Resident, Department of Periodontology and Oral Biology, Boston University School of Dental Medicine, Massachusetts; and Private Practice, Sacramento, California.
***Private Practice, Sacramento, California.
****Associate Professor, Department of Periodontology and Oral Biology, Boston University School of Dental Medicine, Massachusetts.

Reprint requests: Dr Luca Landi, Via Luca Signorelli 10, 58100 Grosseto, Italy. e-mail: lulandi@gol.grosseto.it

Rehabilitation of the atrophied maxillary posterior ridge represents one of the most challenging events in implant dentistry. Reduced bone quantity and quality may severely affect the outcome of implant therapy in the posterior maxilla.[1] Elevation of the sinus membrane with bone grafts, as proposed by Tatum et al[2] and modified by others,[3–5] gives clinicians the opportunity to manipulate and successfully place endosseous implants in previously inadequate posterior ridges. In spite of the absence of long-term prospective clinical trials, clinicians have been successfully using this technique for more than 20 years.[6] Only a few clinical reports are available for analysis of success rate.[6–9] Two limited longitudinal studies analyzed the longevity of implants placed into elevated sinuses, and an excellent success rate (95%) was reported up to 5 years.[10,11] Many important questions regarding the predictability of this procedure remain unanswered. The time of implant placement, the type of graft material, the use of cell-occlusive membranes, and the ability of regen-

erated bone to achieve functional osseointegration with dental implants are all vital questions that require further investigation.

The selection of an appropriate grafting material and the ultimate fate of the material after healing are of special interest. Human histologic reports are available but limited in number.[7,12–19] The use of appropriate graft materials appears to be critical in achieving adequate bone formation. Autogenous bone is unanimously considered the gold standard for regenerative procedures.[14,19] Unfortunately, limitations exist in the procurement of autogenous bone, and the associated morbidity has led to the use of bone substitutes to help complete the filling of the antroplasty. Histologic and histomorphometric analyses of the regenerated tissue in elevated sinuses will provide useful information regarding the nature and amount of the newly formed bone. The application of this information may enhance the predictability of endosseous titanium implants and their ability to maintain osseointegration.

Method and materials

Five systemically healthy nonsmoking women (mean age 51.8 ± 7.50 y) were treated in a private practice setting for posterior maxillary edentulism. Because of resorption of the alveolar crest as shown by computed tomographic (CT) scan evaluation (Fig 1), a sinus elevation procedure was required before implant placement. All patients gave their written consent to have bone cores harvested at the time of implant placement. The healing time between sinus lift and implant placement ranged from 6 to 13 months (mean 10.33 ± 2.36 mo).

Surgical procedure

Sinus elevation

Under local anesthesia (Xylocaine 2% with epinephrine 1:100,000, Astra), a classic surgical approach as described by Tatum[20] and modified by Fugazzotto[21] was followed. Briefly, a full-thickness midcrestal incision was outlined from the tuberosity up to the most mesial tooth present on the arch. A mesial vertical releasing incision on the buccal aspect was used to mobilize the flap and permit adequate access to the lateral wall of the maxilla. The window osteotomy was carried out about 2 mm above the sinus floor by using a round bur mounted on a Striker handpiece with copious cool saline irrigation.

The osteotomy was carefully executed until the bony window could be mobilized to avoid damaging the Schneiderian membrane. At this point, using a blunt instrument and starting from the inferior border of the osteotomy, the Schneiderian membrane was elevated and the bony window reflected inward and up. Sinus membrane integrity was checked by asking the patient to perform the Valsalva maneuver.

A composite graft was used to fill the floor of the sinus. Human demineralized freeze-dried bone (DFDBA) 300 to 500 μm (American Red Cross) was mixed with a bovine-derived porous hydroxyapatite (HA; Osteograf/N 300 and 700, Ceramed) and an antibiotic powder (Cefotaxime, SmithKline Beecham) in a ratio of 2:2:1 by volume. The grafting materials had been previously reconstituted in a mixture of sterile saline solution and blood that was collected from the surgical wound at least 30 minutes before the implantation. The composite graft was then gradually brought into the sinus cavity and tightly packed with moistened gauze. The flap was then released at the base from the periosteum, allowing freedom in an apicocoronal direction, and sutured using expanded polytetrafluoroethylene (e-PTFE) # 4-0 sutures (3i/WL Gore). Antibiotics were prescribed for 7 to 10 days (amoxicillin 500 mg 3 times a day) together with a nonsteroidal antiinflammatory drug (ibuprofen 400 mg 3 times a day) and a generic nasal decongestant. The patients were instructed to rinse twice daily with chlorhexidine (0.2%) and to refrain from any maneuver that had the potential to increase pressure inside the sinus cavity. The suture removal was scheduled at day 14, and the patients were seen every 2 weeks for the first month and then monthly until the second-stage surgery.

Reentry and core harvesting

Before implant placement, the CT scan examination was repeated and compared with the baseline. A similar mucoperiosteal flap was elevated. The first part of the implant osteotomy was performed using a 2-mm trephine bur. A 2 mm × 8 mm bone core was harvested and immediately immersed in a 10% formaldehyde buffered solution for fixation. The osteotomy site was then completed according to the Brånemark protocol, and endosseous root-form titanium implants were placed. The flap was sutured, and the same postoperative instructions were followed by the patients.

Histologic and histomorphometric analysis

After fixation, the harvested bone cores were prepared for light microscopy as follows. After decalcification in HCl for about 2 weeks, the specimens were embedded in paraffin, cut longitudinally in sections 6 to 8 μm thick, and then stained with hematoxylin-eosin and Masson's trichrome. A minimum of 8 sections was obtained from each specimen. The central section was analyzed histomorphometrically using Image Pro+ software (Media Cybernetics). Briefly, the mounted section was positioned under a light microscope (Nikon FXA) that was connected to a video camera interfaced with a computer. The images were transmitted on the computer screen and analyzed. The area of vital bone, marrow spaces, and residual graft particles was calculated and expressed in pixels and relative percentages. Bone formation was expressed as the trabecular bone volume (TBV) according to Parfitt.[22] All histomorphometric analyses were performed by one operator who was unaware of the origin of the specimen.

Results

Clinical observations

No tear or rupture of the membrane was recorded during the first surgery. Healing was uneventful for all patients. The CT scan at the time of implant placement demonstrated apical displacement of the sinus floor and the obliteration of the elevated sinus space by a dense, radiopaque material similar in appearance to bone (Fig 2). In all cases, the distance between the alveolar crest and the new sinus floor was at least 13 mm. At reentry, the osteotomy window, although completely reconstituted, was still recognizable because some residual graft particles were superficially embedded in a bone-like tissue. The resistance of the regenerated tissue to the drill (1,500 rpm) was soft, and the tissue was comparable to Type IV bone for consistency and resistance to cut. The osteotomy sites showed normal bleeding and provided good primary stability for the root-form threaded titanium implants (Figs 3 and 4).

Histologic observations

Residual graft particles with islands of bone formation could be seen in all specimens examined (Fig 5). Bovine porous HA particles were recognizable because of their size and staining properties, which are distinct from both DFDBA particles and surrounding bone. Characteristically, HA particles were surrounded and incapsulated by fibrous tissue that was often enriched by an intense mononuclear inflammatory cell infiltrate. Nodules of early bone formation, arising both at the periphery and inside the particle structure, were visible next to residual HA (Fig 6). In limited areas of the 9- and 12-month specimens, porous HA particles were adjacent to woven and lamellar bone (Fig 7). DFDBA particles appeared to be present only in the 6- and 9-month specimens; no residual allograft could be detected in the 10-, 12-, and 13-month biopsies. In the 6-month specimen, the particles appeared to be virtually unchanged and embedded in a dense matrix made up of fibrous connective tissue. No signs of inflammatory infiltrate were noted, and there was very little new bone formation (Fig 8). In the 9-month specimen, the few particles still visible seemed to be in contact with newly formed bone that appeared woven in nature (Fig 9).

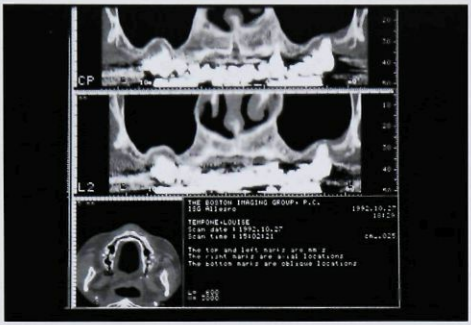


Fig 1 *Preoperative CT scan from patient LT. Note large pneumatization of the right sinus.*

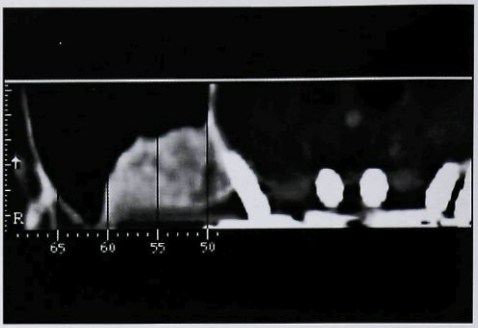


Fig 2 *Postoperative CT scan of the patient shown in Fig 1 at 13 months. Sinus floor is displaced apically. A dense, radiopaque matrix into the sinus suggests bone formation.*

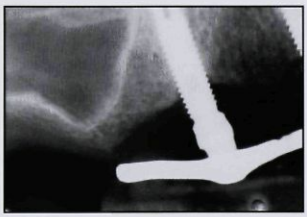
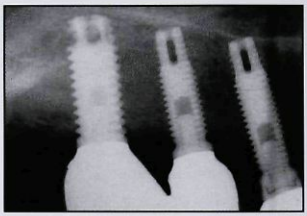


Fig 3 (left) *Periapical radiograph of the maxillary area from patient LT. just before sinus elevation.*

Fig 4 (right) *Periapical radiograph of the area shown in Fig 3 after sinus elevation. Two root-form implants have been placed and loaded. Note the dense trabeculation of the regenerated bone.*



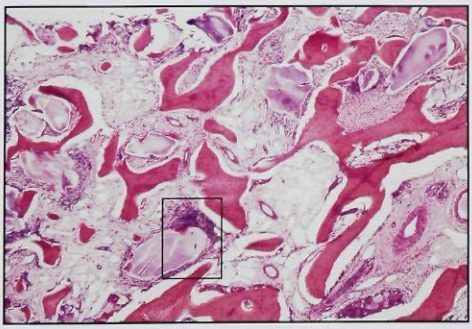


Fig 5 *Photomicrograph of a 9-month biopsy. Large areas of new bone formation are present. Residual Osteograf/N particles are surrounded by fibrous tissue and mononuclear cells. Adipocytes and blood vessels are also evident. (Original magnification × 40; hematoxylin-eosin stain.)*

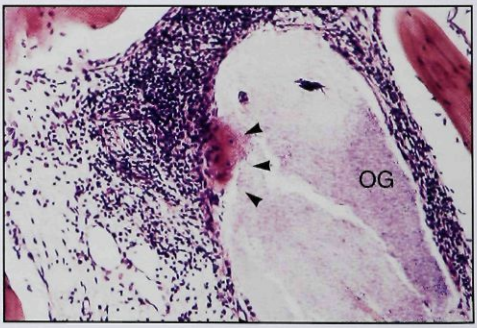


Fig 6 *Higher-power view of framed area in Fig 5, rotated 90 degrees to the left. A large Osteograf/N particle (OG) is almost completely immersed in a dense mononuclear inflammatory cell infiltrate. A nodule of early osteoblastic activity is evident at the periphery (arrowheads). (Original magnification × 200; hematoxylin-eosin stain.)*

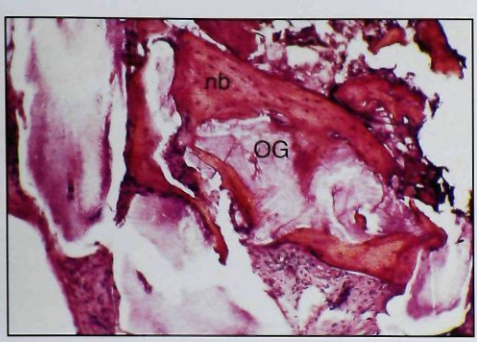


Fig 7 *Photomicrograph illustrates a 12-month specimen. Osteograf/N particle (OG) in close contact with newly formed bone (nb). (Original magnification × 100; hematoxylin-eosin stain.)*

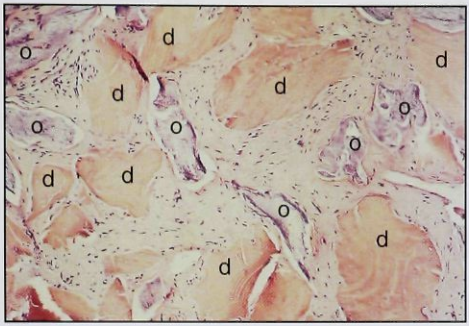
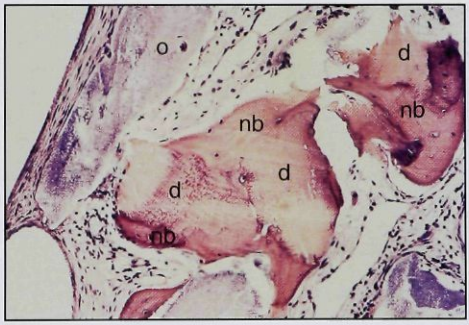


Fig 8 *Photomicrograph taken from a 6-month biopsy. DFDBA (d) and residual Osteograf/N particles (o) are embedded in a dense fibrous matrix with no inflammatory cells. (Original magnification × 100; hematoxylin-eosin stain.)*

Fig 9 *DFDBA particles (d) in contact with newly formed bone (nb) in a 9-month specimen. Cells resembling osteoblasts line the surface of DFDBA particles (arrows). The Osteograf/N particles (o) visible are walled off by a layer of fibrous tissue.*



Histomorphometric analysis

Overall, the mean percent of TBV was 27.92% ± 13.12%, with a wide range among specimens (Table 1). The 6-month specimen contained the least new bone (5.85%) and the highest residual graft material (DFDBA 34.55% and Osteograf/N 15.16%). The most new bone formation was recorded for the 12-month biopsy (43.62%). Overall, the amount of new bone was positively correlated with healing time, and residual graft particles decreased over time (Fig 10).

Table 1 Patients included in the study and histometric data

Patient	Sex	Age (y)	Healing time (mo)	% TBV	% DFDBA	% Osteograf/N
ST	F	48	6	5.85	34.55	15.16
SC	F	55	9	22.26	0.1	13.54
KA	F	42	10	37.27	0	6.09
LR	F	52	12	43.62	0	8.57
LT	F	62	13	30.58	0	8.95
Mean		51.8	10.33	27.92	6.93	10.84
Standard deviation		7.50	2.36	13.12	13.81	3.66

TBV = trabecular bone volume; DFDBA = demineralized freeze-dried bone allograft; Osteograf/N = bovine-derived porous hydroxyapatite.

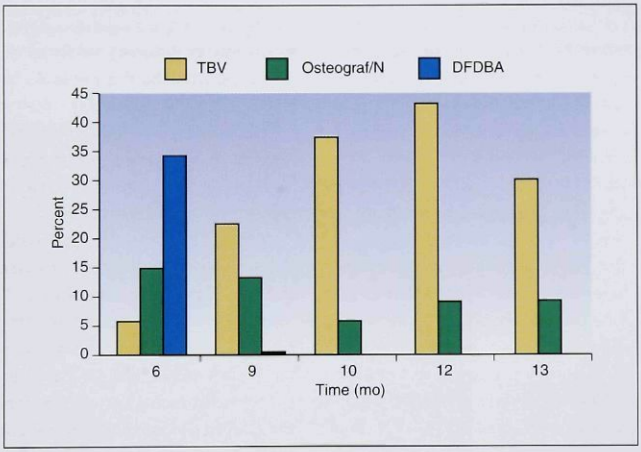


Fig 10 *Relationship between trabecular bone volume* (TBV), *DFDBA, and Osteograf/N and healing time.*

Discussion

Lifting of the sinus membrane has proven to be a successful procedure to overcome the problems related to severe atrophy of maxillary posterior edentulous areas.[17,23] Patient selection, proper surgical technique, and careful follow-up appear to be the keys to reducing the incidence of sinus pathology.[24] All 5 patients selected for this study had no history of sinusitis or allergies and were not smokers. No complications were encountered at the time of surgery or during the healing phase. The procedure resulted in adequate alveolar bone height for the placement of root-form implants at least 13 mm long. All implants placed achieved good primary stability, but the quality of the regenerated bone tissue as assessed during drilling was comparable to Type IV bone. This is to be expected because Type IV bone is physiologic in the most posterior areas of the maxilla.[25] However, this poor quality of bone is thought to contribute to increased implant failure,[1] but other factors, particularly implant length, have also been shown to influence implant success.[26] Apical displacement of the sinus floor increases bone crest height and allows placement of longer implants, thus providing more titanium surface to contact bone. This may contribute to a reduction in the failure rate in posterior areas.

Histologic and histomorphometric data may give significant information regarding the structural features of the regenerated bone tissue. Particularly, the TBV, ie, the ratio of trabecular bone to marrow space, has been suggested to be the best predictor of bone strength.[27] Thus, the greater the TBV, the greater the bone available to achieve osseointegration.

In this study, the mean TBV was 27.92%, but with a wide variability (5.85% to 43.62%). The TBV observed is superior to that reported by Wheeler et al,[17] who were able to obtain a mean of 16.68% bone formation. In their study, they used Interpore-200 HA (Interpore) alone or in combination with autogenous bone harvested from intraoral sources or the iliac crest and in one case a hip bone graft alone. The healing time ranged from 4 to 36 months, with 17 of 19 cases reentered between 4 and 10 months. They noted a positive correlation

between healing time and percent of bone formation. However, there were no significant differences among the different combinations of graft materials used. The overall success rate was 94.5% at 5.5 years.

Likewise, our data suggest a direct positive correlation of new bone formation with time of healing. However, based on our results, waiting beyond 10 to 12 months seems to give no further advantage in terms of bone formation. After that time, a second surgical trauma, as induced by implant placement, may trigger the activation of the regional acceleratory phenomenon (RAP), thus improving the quality of the bone healing. The RAP, described by Frost,[28] suggests that stimulation of bone may improve the rate of healing. Implant loading also appears to produce a significant improvement in the quality and quantity of bone-implant contact.[29] Therefore, the time of reentry should take maximum advantage of bone graft and healing characteristics.

Autogenous endochondral bone grafts, such as from the iliac crest, have been shown to undergo a faster replacement because of the ability of osteoprogenitor cells and vascular elements to readily penetrate cancellous bone; in this case, 4 to 6 months may be sufficient before implant placement. In contrast, intramembranous grafts or composite grafts may require a longer period to be replaced and elicit new bone formation.[30] In this study, we used a composite graft comprised of an allograft (DFDBA) and bovine-derived porous HA. The rationale for using DFDBA in regenerative procedures is based upon its suggested osteopromotive characteristics.[31] While DFDBA is widely accepted as an osteoconductive graft,[31] there is controversy regarding its osteoinductive properties.[32,33] In this report, DFDBA appeared to be completely reabsorbed after 10 months; residual particles were present only in the 6- and 9-month biopsies. It is noteworthy that in the 6-month specimen, DFDBA appeared to be virtually unchanged and only scarce foci of bone formation could be seen. However, in the 9-month biopsy, the residual DFDBA appeared in intimate contact and coalesced with newly formed bone. The fact that no DFDBA particles were present at later time points is contradictory to results reported by other investigators,[15,34] who described residual particles many years after implantation. One possible explanation for these differences may be the large biologic variation that exists between different bone banks and also within the same batch of DFDBA.[33,35,36]

The other graft material involved, Osteograf/N 300 and 700, is comprised of deproteinated, bovine-derived, porous HA that has been shown to be osteoconductive in animal and human models.[16,37,38] Characteristically, the Osteograf/N particles were ubiquitous in all specimens analyzed and were often surrounded by a layer of fibrous tissue that was enriched by an intense inflammatory infiltrate. In contrast to previous reports,[37] we did not identify any giant cells or macrophages around the graft particles. The presence of this inflammatory reaction up to 13 months is in contrast with previous reports[39] in which a local inflammatory reaction occurs and disappears within 6 to 8 weeks of implantation of the HA material. Our findings suggest that ongoing, active replacement of the bovine HA is taking place,[16] or perhaps that there is an immunologic reaction to residual xenogenic proteins.[39] However, areas of osteoblastic activity could be seen within and around the periphery of the particles. Based upon this preliminary information and supported by the available literature,[14–16] we speculate that a longer healing time should be considered when composite grafts such as the one used here are contemplated for sinus lift procedures.

Using this composite graft material, we were not able to reproduce the findings of Lorenzetti et al.[19] They achieved new bone formation of 66% with an iliac crest autogenous graft alone and 44.3% when autogenous bone harvested from the chin was mixed with porous HA granules.

Although autogenous bone grafts seem to be preferable as a grafting material, a meta-analysis by Tong et al[23] reported comparable success rates of implants placed in sinuses grafted with different materials including HA, DFDBA, and autogenous bone. Limitations and side effects related to autogenous grafts should also be considered. A second surgical site, the increase in surgical time, patient morbidity, and the need for hospitalization and general anesthesia should be weighed

against therapeutic alternatives that may be less invasive and expensive. Bone substitutes have the advantage of being readily available, with no limitations in their procurement. Furthermore, they can be considered safe in terms of disease transmission.[40]

Intramembranous grafts should be considered in intraoral regenerative procedures because of their superior ability to maintain architectural and structural characteristics compared to endochondral grafts.[41,42] Endochondral iliac grafts undergo faster reconstitution, but also greater resorption, over time.[19] Unfortunately, grafts harvested from intraoral sources are rarely sufficient to fill the antroplastic cavity. In light of these drawbacks, bone substitutes such as DFDBA and bovine-derived porous HA, used alone or in combination with autogenous bone graft, may be considered a valid therapeutic alternative in sinus lifting procedures. Further investigation is necessary to correlate TBV with implant success rate.

Conclusions

1. Sinus elevation in 5 patients was performed without any complications using a combination of DFDBA and Osteograf/N 300 and 700.
2. After 6 to 13 months of healing, the mean TBV was 27.92%.
3. Osteograf/N was ubiquitous, and the particles were often surrounded by fibrous tissue and inflammatory infiltrate with foci of new bone formation.
4. DFDBA particles could be seen only in 6- and 9-month specimens and appeared to be completely reabsorbed in the other specimens.
5. A minimum of 10 to 12 months should elapse before implant placement when a composite graft is used.
6. This composite graft material was able to promote bone formation and may be a valid alternative to autogenous bone grafts in sinus lift procedures.

Acknowledgments

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