# Maxillary Sinus-Floor Elevation with Nanoporous Biphasic Bone Graft Material for Early Implant Placement

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## ABSTRACT

*Background:* Insufficient bone height in the posterior maxilla is caused by bone atrophy after tooth extraction and continued pneumatization of the maxillary sinus. To allow for implant placement in this area, external sinus-floor elevations are performed. For this indication, the application of various bone graft materials can be a reliable alternative to autologous bone.

*Purpose:* The aim of this study was to analyze a nanoporous bone graft material under the condition of early implant treatment in sinus floor elevations.

*Materials and Methods:* Sixty-six patients received 94 individual external sinus-floor elevations as a precondition for implant surgery. As grafting material, a synthetic, nanoporous bone graft material consisting of a mixture of nano-hydroxyapatite and nano-β-tricalciumphosphate crystals, combined with blood from the defect side, was used. Depending on the remaining vertical bone height, implant placement was performed either simultaneously with bone augmentation or consecutively in a delayed approach. After a 4-month healing period, the patients received 218 implants and were followed up clinically, radiographically, and histologically. To quantify the bone situation at implant placement, immuno-histochemical analysis using tenascin-C was performed.

*Results:* We achieved an average vertical bone increase of 8.28 mm (SD, 2.59) for the one-stage approach and 10.99 mm (SD, 1.73) for the two-stage approach after sinus-floor elevation. The augmented areas showed mean resorption rates of 10.32% (one stage) and 10.82% (two stages) of vertical graft during the observation period. Immunohistochemical analysis after 4 months of healing showed high tenascin activity, indicating bone growth. Good primary stability was achieved during implant placement. Mean peri-implant marginal bone loss was 0.45 mm (SD, 0.31).

*Conclusion:* After a mean observation time of 21.45 months, the biomaterial showed good osseointegration and bone stability radiographically. Adding to this the positive histological and immunohistochemical findings, we conclude that, after a relatively short 4-month healing period, the biomaterial showed predictable results.

KEY WORDS: atrophic maxilla, bone augmentation, bone resorption, maxillary sinus-floor elevation, sinus-floor elevation

## INTRODUCTION

Prior to having implant placement, patients with severe bone atrophy usually need jaw reconstruction with autologous bone, considered the gold standard for this procedure. However, the use of various intraoral and extraoral donor sites is the source of additional patient morbidity.

Deficient alveolar ridges in the posterior maxilla, in the form of insufficient bone height, are generally caused by ridge atrophy and continued pneumatization of the maxillary sinus, compounded by poor bone

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quality; these conditions make sinus-floor elevation necessary to allow for implant placement. The technique was initially described with respect to the use of autologous bone.[1] Nowadays, however, this is often successfully performed using bone graft materials with reliable results. Various organic and synthetic[2] bone graft materials have been described in the literature for this procedure. Combinations of different grafting materials, such as bovine xenografts and autologous bone, have been applied as well.[3,4] Concerning the success of different grafting materials, the data have been limited so that implant survival has often been the only comparable outcome criterion.

The aim of this study was to evaluate a nanoporous alloplast as a grafting material with a short healing period of 4 months. Due to the high porosity of the applied nanoporous material, a faster ingrowth of new blood vessels is promoted. The enhanced angiogenesis then leads to an increased initial bone healing,[5,6] which could clinically permit an earlier implant placement due to the earlier bone formation. Additionally, the silica gel matrix of the material has a stimulating effect on the mineralization process.[7,8]

To quantify these effects, clinical, radiographic, histological, and immunohistochemical analyses were performed. Bone core cylinders that were harvested during implant surgery were additionally evaluated by special immunohistochemical analysis. A staining with tenascin-C, an extracellular matrix glycoprotein, which is present in the matrix surrounding osteoblast precursors and osteoblasts during bone development but is absent from mineralized bone matrix and connective tissues adjacent to bone, was selected to evaluate and assess this effect. Abundant tenascin-C matrix is considered as indicator of an active bone tissue formation.[9]

Additionally, vertical dimensional changes of the grafts were measured radiographically at various times. Peri-implant marginal bone stability and implant survival were analyzed as well.

## MATERIALS AND METHODS

### Patients

In this retrospective study, all 66 patients were treated in the Department of Oral and Maxillofacial Surgery, University Hospital Heidelberg between April 2006 and November 2009. Due to different degrees of bone resorption and sinus pneumatization, the patients had insufficient vertical bone in the posterior maxilla to allow for insertion of dental implants. The patients were partially or totally edentulous, and they desired implant-retained rehabilitation.

The study was conducted in accordance with the principles of the Declaration of Helsinki. The Ethics Committee for clinical studies of the Medical Faculty of Heidelberg University reviewed and approved the study protocol.

### Bone Grafting

Prior to surgery, the patients were analyzed radiographically by orthopantographs to determine the amount of residual vertical bone. All patients included in this study received lateral sinus-floor elevations in accordance with the method described by Boyne and James[1] and Tatum[10] under local anesthesia.

After midcrestal incision of the alveolar crest, mesial and distal vertical releasing incisions were performed and a mucoperiosteal flap was elevated, allowing for good visibility and access to the lateral sinus wall. Subsequently, osteotomy of the lateral window was carried out using a round diamond bur under constant irrigation. The size of the window depended upon the defect size and the number of planned implants. After careful elevation of the Schneiderian membrane from the inner bone surface, the sinus membrane was checked for any indication of perforation before inserting the synthetic bone graft material (BONITmatrix, DOT GmbH, Germany) into the newly created space. The material was mixed with blood from the defect side and compacted into the sinus cavity. The bone substitute was not mixed with autologous bone. Depending on the remaining vertical bone height, implant placement (OsseoSpeed, Astra Tech AB, Mölndal, Sweden) was performed either simultaneously with bone augmentation (one-stage approach) or consecutively in a delayed approach (two-stage approach). The decision on which technique to apply depended upon the preoperative radiographic examination of the residual bone height at the floor of the sinus. If a bone height of 3 mm or less was measured, the two-stage procedure was performed, and if the residual bone height was 4 mm or higher, the one-stage procedure was performed.

The implants were placed with the implant neck being at bone level. The defect of the lateral sinus wall was covered with a resorbable collagen membrane (Resodont, Resorba, Nürnberg, Germany). Then, the

mucoperiosteal flap was reflected and finally the wound was sutured.

The patients received postoperative oral antibiotics for 7 days and nasal drops to reduce sinus swelling. Additionally, they were advised to rinse twice per day with chlorhexidine solution. The patients were also instructed not to wear their prostheses until suture removal, which was performed after 10 days.

The chosen augmentation material was a synthetic nanoporous bone graft material based on two calcium phosphates, consisting of nano-hydroxyapatite (nano-HA) and nano-β-tricalciumphosphate (nano-β-TCP) crystals (60:40) embedded in a bioactive silica gel matrix. The material is manufactured in a sol-gel procedure without sintering.

The patients treated with a delayed approach received implants after 4 months of healing. In six of these patients, 10 cylindrical bone biopsy specimens were taken during implant surgery from the grafted posterior maxilla using a trephine bur. The bone cores were then analyzed immunohistolochemically and histomorphometrically. The implants were functionally loaded after an additional 3 months. The abutments were connected with the appropriate insertion torque described by the implant manufacturer.

### Histological and Immunohistochemical Analysis

In this study, biopsies were harvested 4 months after sinus-floor elevation, fixed in 4% buffered paraformaldehyde, ethylene diamine tetra-acetic acid (EDTA) decalcified, dehydrated in graded alcohol (70, 80, 96, and 100%), embedded in paraffin and hematoxylin and eosin stained.

### Immunohistochemistry

The antibody BC-4 was applied to visualize all tenascin-C variants (diluted 1:70).

Immunohistochemical staining was performed with an alkaline phosphatase ChemMate detection kit (DakoCytomation, Glostrup, Denmark) according to the manufacturer's protocol. The primary antibodies were incubated at room temperature (RT) for 30 minutes. After rinsing with Tris buffer, the sections were treated with rabbit antimouse IgG (Z-259, diluted 1:70; DakoCytomation) at RT for 30 minutes. Primary antibodies were replaced by nonimmune serum for negative controls.

Additionally, histomorphometric analysis was performed to quantify the amount of new bone.

### Radiographic Evaluation

During the study, multiple panoramic radiographs were made for each patient at defined times: before surgery, after sinus elevation (T0), at the time of implant placement (T1), and at yearly intervals thereafter. To determine dimensional changes, the panoramic radiographs were analyzed for residual bone height, original graft height after bone augmentation, and graft height at the last follow-up. Implant length was used to correct dimensional distortion and magnification errors (measured implant length divided by actual implant length). Additionally, the tooth closest to the augmentation site in each radiograph was measured for differences in length and thus used as a conversion factor, which was especially necessary for patients with a two-stage approach.

To determine peri-implant marginal bone loss, additional intraoral radiographs were taken and analyzed.

### Statistical Analysis

For descriptive purposes, arithmetic mean values, standard deviations, median and percentile values, and cumulative frequencies were calculated for all clinical and radiographic parameters at the patient and implant level. Results were also presented as box plots. Analyses were performed using SAS Software (Version 9.2; SAS Inc., Cary, NC, USA).

## RESULTS

### Patients

A total of 66 patients (38 female, 28 male) were treated with 94 sinus-floor elevations. The mean age was 55.26 years (range, 27–73). All patients were treated for insufficient vertical dimension of the lateral maxilla.

Twenty-six patients were treated using a one-stage approach with simultaneous bone augmentation and implant placement. Forty patients were treated in a delayed approach with a mean healing period of 5.46 months between bone augmentation and implant surgery.

Thirty-three patients were treated because of partial edentulism, 20 were totally edentulous and 13 were treated because of single-tooth gaps.

## Bone Grafting

All patients were treated under local anesthesia and were successfully grafted. Perforations of the sinus membrane were the only intraoperative complication ($n = 5$). These were treated by further elevation of the respective sinus mucosa; the perforation was then covered with a resorbable collagen membrane, enabling the completion of bone grafting without any further complications. No operation had to be discontinued because of large membrane tears. No intraoperative signs of increased bleeding were found. Postoperative healing was uneventful in all cases but one. In this particular patient, an acute infection occurred during the healing phase, resulting in partial graft loss and making an operative revision of the site necessary. No patient in the study showed any signs of maxillary sinusitis. No signs of postoperative dehiscence occurred.

All implants could be inserted with good primary stability. No implants were lost during the healing period. Throughout the total observation period, only one implant was removed due to severe peri-implantitis after 26 months and was replaced later without further grafting. The patient concerned had received five implants in a delayed approach. The overall implant survival rate of 158 implants placed in the grafted sinuses was 99.4%. According to the success rate of Albrektsson and colleagues,[11] 19 implants failed these criteria.

Bilateral bone grafting was performed in 28 patients, while unilateral grafting was done in 38 patients.

## Immunohistochemical Analysis

In this study, bone core cylinders were obtained from 10 sinuses (six patients) in a delayed approach with 4-mm trephine burs. At the time of implant placement, biopsies were taken from the alveolar crest to the most cranial part of the grafted area. To avoid additional surgery for the one-stage group, these patients had no biopsies taken. The biopsy samples were analyzed histologically and immunohistochemically (Figures 1–3).

Fibroblastic tissue develops between osseous trabecular structures. The fibroblasts have large, round nuclei, indicating fibroblastic cellular activity. Additionally, abundant tenascin-C matrix is demonstrated, typically seen in osseous remodeling processes.

The bone graft material showed good incorporation and bone formation on the surface, indicating ongoing bone growth after 4 months of healing.

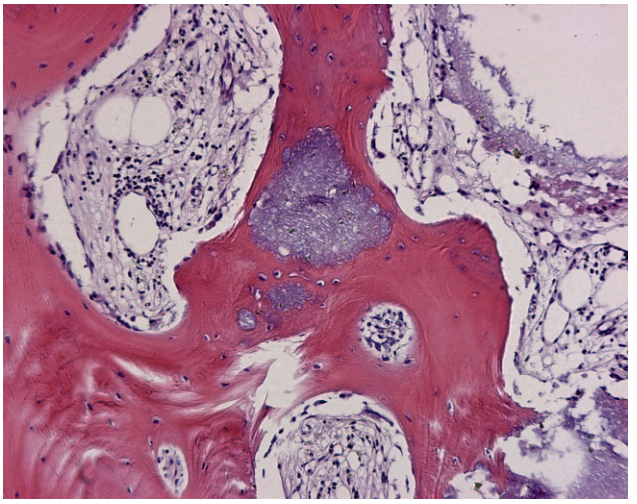

**Figure 1** After 4 months of healing, the newly formed bone incorporates the graft particles (hematoxylin and eosin stain, original magnification ×200).

Histomorphometry revealed that 24.3% of the tissue volume was newly formed bone tissue, 32% residual graft and 43.7% connective tissue. All implants clinically proved high primary stability on insertion.

## Radiographic Evaluation

In the one-stage group, a mean vertical bone gain of 8.28 mm (SD, 2.59; range, 4.14–13.98) was achieved directly after sinus-lift surgery. The two-stage procedure presented a radiographic vertical bone increase of 10.99 mm (SD, 1.73; range, 5.91–14.50). The residual bone height of the maxillary floor prior to bone grafting was 3.42 mm (SD, 1.88). For the one-stage approach, the

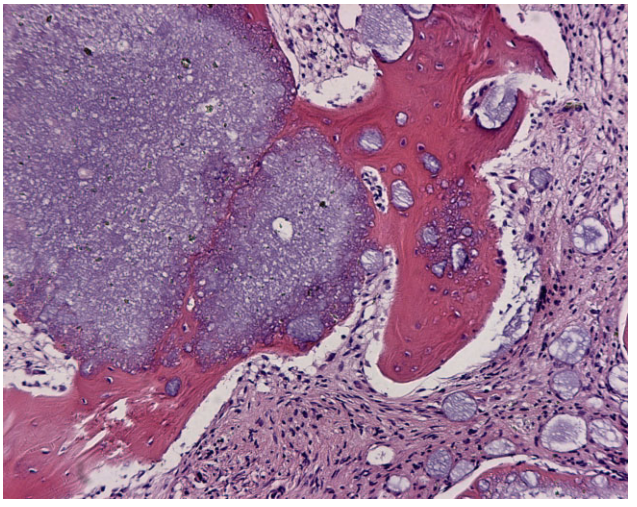

**Figure 2** After 4 months of healing, bone formation on bone graft surface (hematoxylin and eosin stain, original magnification ×200).

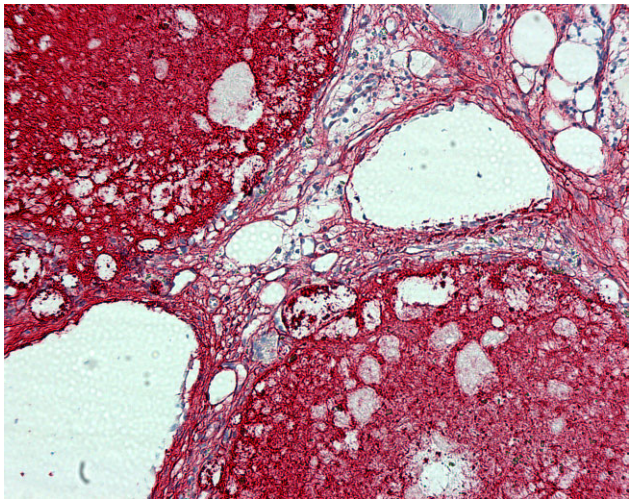

**Figure 3** After 4 months of healing, high tenascin activity indicates ongoing bone formation (tenascin stain, original magnification ×200).

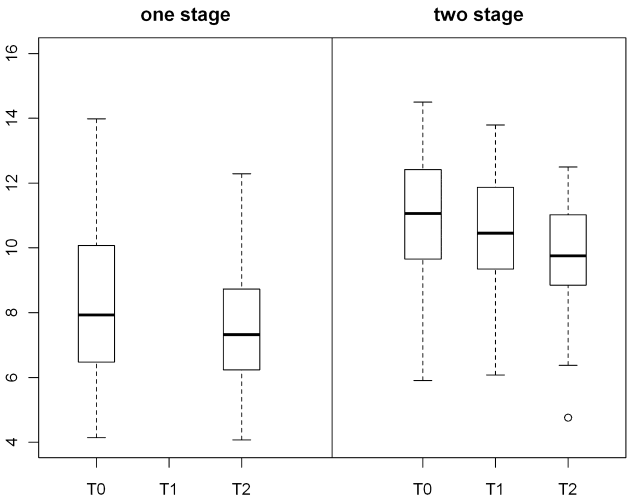


**Figure 4** Box plots analyzing vertical graft height at different points in time of the one- and two-stage approaches; in the one-stage approach, T0 and T1 are identical.

mean remaining bone height was 5.01 mm (SD, 1.1); for the delayed approach, it was 2.38 mm (SD, 1.52).

In the group with the delayed approach, the mean initial vertical postimplantation graft height was 10.52 mm (SD, 1.69) after a mean healing period of 5.46 months (Table 1). After a mean follow-up time of 21.45 months (SD, 7.72), vertical bone height in the one-stage group was 7.40 mm (SD, 2.10; range, 4.07–12.29) and 9.83 mm (SD, 1.72; range, 4.76–12.50) in the two-stage group (Figure 4).

These values resulted in a vertical bone resorption of 10.32% for the one-stage group and 10.82% for the two-stage group at the last follow-up (Figure 5).

Implant diameters, lengths, and distribution are displayed in Table 2. Overall peri-implant marginal bone loss at the implant level achieved a value of 0.46 mm (SD, 0.47). Comparing marginal bone loss of implants placed in grafted and nongrafted sites, we found native bone to have a mean marginal loss of 0.47 mm (SD, 0.47), while grafted sites showed a mean marginal bone loss of 0.46 mm (SD, 0.47) at the last follow-up (Figure 6).

## DISCUSSION

The nanoporous bone graft substitute was analyzed for indication of sinus-floor elevation and was assessed on the basis of clinical, radiographic, and histological parameters.

The nanoporous structure of the used bone graft material with its high porosity leads to a faster angiogenesis, followed by a faster initial bone healing.[5,6] While most materials are fabricated with a high-temperature sintering process, which decreases the porosity and increases the material density, the applied material

**TABLE 1 Vertical Graft Height at Different Time Points for the One- and Two-Stage Approaches; in the One-Stage Approach, T0 and T1 Are Identical**

| | | *n* (Patients/ Elevations) | Mean (mm) | Standard Deviation (mm) | Minimum (mm) | Maximum (mm) | Percentile | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | 25 | 50 (Median) | 75 |
| One stage | Graft height (T0) | 25/32 | 8.28 | 2.59 | 4.14 | 13.98 | 6.48 | 7.94 | 10.08 |
| | Graft height after implant surgery (T1) | | | | | | | | |
| | Graft height follow-up (T2) | 22/29 | 7.40 | 2.10 | 4.07 | 12.29 | 6.24 | 7.32 | 8.73 |
| Two stages | Graft height (T0) | 39/60 | 10.99 | 1.73 | 5.91 | 14.50 | 9.66 | 11.07 | 12.42 |
| | Graft height after implant surgery (T1) | 37/57 | 10.52 | 1.69 | 6.08 | 13.79 | 9.35 | 10.45 | 11.87 |
| | Graft height at follow-up (T2) | 33/51 | 9.83 | 1.72 | 4.76 | 12.50 | 8.84 | 9.76 | 11.05 |

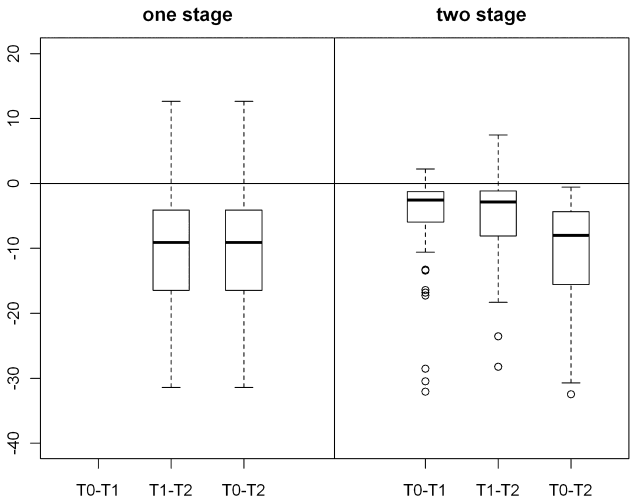


**Figure 5** Vertical bone changes at different time intervals in percent; in the one-stage approach, T0 and T1 are identical.

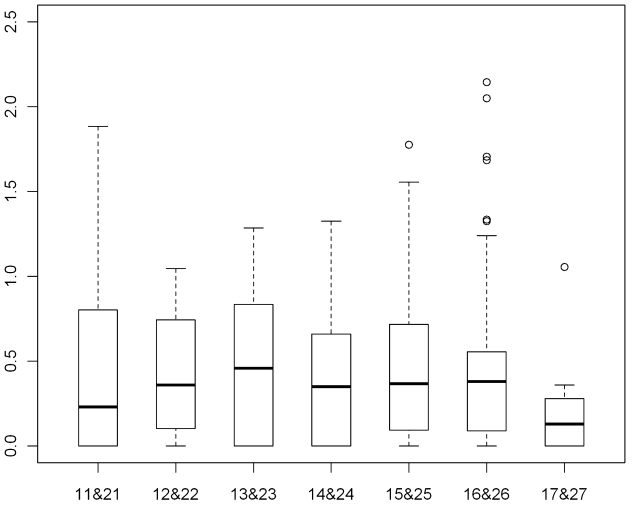


**Figure 6** Peri-implant marginal bone loss according to implant position (on implant level); anterior implants are used as control sites to implants placed in augmented bone.

is fabricated using a low-temperature sintering process leading to a high porosity of almost 80%. The nanoporous structure improves the degradation processes. Additionally, the HA and TCP are embedded in a silica gel matrix that has a stimulating effect on the bone mineralization and calcification processes.[7,8,12]

Thus, a short graft healing period of 4 months was selected to allow for a reduced treatment time as compared with other bone graft substitutes. This healing time is almost comparable with autologous bone grafting, which is portrayed to have a revascularization time of 3 to 4 months.[13] After employing bone graft substitutes, investigators have described healing periods of 6 to 8 months.[14–16]

Bone core cylinders, which were taken before implant placement during the same operation, showed good histological osseointegration of the bone graft substitute. Furthermore, immunohistochemical analysis proved high tenascin-C activity in the tissue samples, indicating that bone remodeling was still in progress. Tenascin-C, an extracellular matrix glycoprotein, exists only during bone development but is absent from mineralized dormant bone matrix and connective tissues adjacent to bone.[9]

The ongoing remodeling process did not seem to have any negative effect on the implant outcome. The high implant survival rate in this study seems to justify the early implant therapy after 4 months of graft healing. In the two-stage approach, clinical results showed high primary implant stability both at the time of implant insertion and at prosthetic loading; no implant showed any lack of osseointegration.

The literature, however, generally describes high implant survival rates for both the one- and two-stage procedures for this indication.

It also has to be discussed, however, that primary stability and subsequent survival of an implant placed in the maxillary sinus are not only influenced by the amount of bone formation of the grafted site and by bone maturity but are also dependent upon the amount of residual bone existing at the implant site prior to augmentation.

**TABLE 2 Implant Diameters, Lengths, and Distribution**

| | | *n* | Percentage |
|---|---|---|---|
| Implant diameter | 3.5 | 96 | 44.0 |
| | 4.0 | 33 | 15.1 |
| | 4.5 | 80 | 36.7 |
| | 5.0 | 9 | 4.1 |
| | Total | 218 | 100.0 |
| Implant length | 9 | 58 | 26.6 |
| | 11 | 134 | 61.5 |
| | 13 | 26 | 11.9 |
| | Total | 218 | 100.0 |
| Implant position | 11 & 21 | 19 | 8.7 |
| | 12 & 22 | 14 | 6.4 |
| | 13 & 23 | 27 | 12.4 |
| | 14 & 24 | 34 | 15.6 |
| | 15 & 25 | 46 | 21.1 |
| | 16 & 26 | 68 | 31.2 |
| | 17 & 27 | 10 | 4.6 |
| | Total | 218 | 100.0 |

Another factor evaluated to determine the success of graft material was vertical dimensional changes of the graft. The presented radiographic data after 21.45 months showed that the remodeling concerned did not seem to result in increased graft resorption, with mean resorption rates of 10.32% (one stage) and 10.82% (two stages). Marginal bone loss of 0.46 mm for implants placed in grafted sites was low as well.

By preventing additional donor site surgery, the use of bone graft substitutes compared with autologous bone grafts can help reduce morbidity and the risk of complications associated with such surgery. Various intraoral and extraoral donor sites have been described for sinus-floor procedures, whose morbidity varies. Although intraoral sites (i.e., mandibular ramus or chin) have limited availability, extraoral donor sites, such as the iliac crest,[1,17] calvarium,[17,18] and tibia,[19,20] often require hospitalization or general anesthesia as well as increased surgical time. Autologous bone, however, has osteogenic, osteoinductive, and osteoconductive properties and a high number of vital cells. Bone graft substitutes can only act as scaffolding for bone formation. Concerning bone stability, on the other hand, autologous bone grafts often undergo uncontrolled resorption.[21]

In a review, Chiapasco and colleagues[22] recommended the use of autologous material for sinus elevation procedures if additional vertical or horizontal block grafting is necessary. In cases of combined defects, autologous bone is the material of choice, allowing not only for an increase of bone volume but also for correcting intermaxillary relationships in terms of simultaneous block grafting. A review by Esposito and colleagues states that some bone substitutes might be a preferable alternative to autologous bone.[23]

Literature, however, also reports on maxillary sinus-floor augmentation performed without adjunctive grafting material, only by elevating the sinus membrane and inserting implants which then keep the membrane elevated. In an animal study, results after 6 months showed no differences between grafted sinuses and nongrafted sinuses, with respect to histologic bone-to-implant contact and implant stability. Oxidized implants showed a more improved osseointegration as compared with turned implants. The osseoinductive potential of the sinus membrane is discussed.[24]

A study by Lundgren and colleagues analyzed the reliability of this technique by performing 12 maxillary sinus-floor elevations on 10 patients with an average residual bone height of 7 mm.[25] Computed tomography clearly demonstrated new bone formation after 6 months of healing. Resonance frequency analysis was additionally performed showing good implant stability. Further studies on the employment of this technique show reliable outcomes.[26,27]

If the residual bone has an adequate remaining height, the osteotome sinus-floor elevation can be an alternative to avoid a lateral window approach. The crestal approach with immediate implant placement is a less invasive procedure for sinus-floor elevation and can even improve initial implant stability by the use of osteotome condensation. This technique is described with and without bone grafts and shows good results with implant survival rates of 95.7 to 96.0%.[28] With this technique, however, implant survival is correlated with the residual bone height. Rosen and colleagues reported on a decreased survival rate of 85.7% when the residual bone height was 4 mm or less. With a minimum bone height of 5 mm, implant survival was described at 96%.[29]

Other surgical approaches described in the literature, such as the use of short, tilted, pterygoid, or zygomatic implants, have been tried in lieu of sinus elevation surgery.

Due to the fact that study design, observation periods, and bone graft material – as well as the success criteria of bone graft and dental implants – often vary, it is difficult to compare the results of different studies analyzing sinus-floor elevation. Moreover, the degree of bone atrophy prior to augmentation has seldom been described.

## CONCLUSION

If applied for the appropriate indication of sinus-floor elevation without requiring simultaneous block grafting, the use of nanoporous bone graft material offers a reliable outcome, permitting predictable and reliable implant placement after a 4-month healing period.

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