Lateral Sinus Floor Elevation in the Severely Atrophied Maxilla: Concentrated Growth Factors Versus Bone Substitutes. A Controlled Clinical Trial

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The present study clinically and radiographically compares the outcome of implants inserted in maxillary sinuses augmented with concentrated growth factors (CGFs) or demineralized bovine bone matrix (DBBM) in a one-stage lateral approach. In 20 patients with a residual bone height of 1 to 4 mm, lateral sinus floor elevation was performed, using CGFs or DBBM as the sole grafting material, with simultaneous implant placement. Outcome variables were implant and prosthesis failures, complications, subjective satisfaction, and radiographic changes in marginal bone level (MBL) 12 months after surgery. The patients were consecutively recruited: 10 to the CGF group and 10 to the DBBM group. No implant failed in either group at 12 months postsurgery, and there were no complications. There was no statistically significant difference in MBL change between the CGF and DBBM groups (difference of –0.3 mm, favoring the CGF group; 95% confidence interval [CI]: –0.8 to 0.2; P = .18). There was no statistically significant difference in satisfaction (difference of 0.2, favoring the CGF group; 95% CI: –0.2 to 0.6; P = .29).

Within the limitations of the present study, the lateral sinus floor elevation performed with the use of CGFs as the sole grafting material showed implant survival rates and marginal bone level changes comparable to DBBM grafting. Int J Periodontics Restorative Dent 2022;42:65–72. doi:10.11607/prd.5509

Insufficient bone volume is a frequent issue in the treatment of the maxillary posterior sextants with the placement of implants.1 In particular, a residual bone height of 1 to 4 mm represents a great challenge, as it reduces the alternative solutions to bone reconstruction, such as short implants. To gain vertical bone height, either sinus floor elevation, guided bone regeneration, or onlay grafting can be performed.2 A minimally invasive technique for lateral maxillary sinus elevation that can be used with autogenous bone or with a bone substitute of bovine origin was recently described.3,4

Implants inserted in augmented sinuses with autogenous bone graft have shown high survival rates.1,5 However, because the use of autogenous bone grafts could be associated with donor site morbidity and complications, other graft techniques have been proposed.6–15 In order to reduce morbidity due to the harvesting procedures, to accelerate and promote the healing process, and to reduce costs, research has focused on the development of concentrated growth factors (CGFs).16–19 Compared with platelet-rich fibrin (PRF) and platelet-rich plasma (PRP), the fibrin matrix of CGF is larger, denser, and equally rich in growth factors. Unlike PRP, CGF does not dissolve rapidly following application.20,21 Therefore,
CGFs could be expected to have better properties for clinical manipulation and regenerative potential. A case report examined the use of CGF for sinus augmentation without bone substitute. A comparison between demineralized bovine bone matrix (DBBM) and CGF that studies the effectiveness of these grafting materials on implant survival rate, promotion of the healing process, and effective volume increase when used in a lateral sinus floor augmentation procedure has not yet been performed. The present study aimed to determine whether the use of the CGF as the sole grafting material had results comparable to using DBBM as the only graft substitute when both were used in a lateral sinus lift procedure in patients with residual bone height of 1 to 4 mm. Specifically, implant and prosthesis failures, complications, subjective satisfaction, and bone marginal level changes were compared.

Materials and Methods

Study Design and Setting

This single-center, examiner-blinded, parallel, controlled nonrandomized clinical study was conducted in a private clinic in Rimini, Italy, that specialized in advanced oral surgery and implant rehabilitation. The study was conducted between January 2017 and April 2019. The published data refer to the 12 months of follow-up after the sinus floor augmentation and simultaneous implant placement.

Participants

Patient in need of sinus bone augmentation for an implant-supported rehabilitation were consecutively recruited, informed, and screened for inclusion.

Eligible participants were 18 years or older and partially dentate, characterized by 1 to 4 mm of residual bone thickness in which sinus floor augmentation is desired for placement of single or multiple implants for prosthetic reasons. Periodontitis patients had to be treated before inclusion in the trial. Patients had to have carried out recent complete blood chemistry tests (not exceeding 3 months).

Exclusion criteria were as follows: (1) general contraindications to implant surgery; (2) patients irradiated in the head and neck area; (3) patients with poor oral hygiene (full-mouth plaque score and full-mouth bleeding score ≥ 20%) and lack of motivation; (4) uncontrolled diabetes (reported levels of glycaemia over the threshold of 130 mg/dl and/or HbA1c ≥ 6.5%); (5) metabolic disease and drugs affecting bone remodeling; (6) pregnancy and lactating period; (7) substance abusers; (8) heavy smokers (> 10 cigarettes/day); (9) inadequate marginal bone width; (10) sinus cyst and active sinusitis; (11) severe anemia; (12) thrombocytopenia and coagulation disorders; and (13) therapy with antiplatelet agents or anticoagulants.

Before surgery, the following patient-related variables were recorded: age, gender, and smoking habit. In addition, the height of the residual bone (HRB) in correspondence with implant insertion was measured based on periapical radiographs.

The study was conducted in accordance with the Declaration of Helsinki, and each participant provided written informed consent according to the above-mentioned principles.

Clinical Procedure

Screening

Patients were scheduled for a screening visit. At this time, clinical and radiographic examinations were completed, and blood test results were analyzed.

CGFs preparation

CGFs were prepared as described by Bozkurt Doğan et al. Before surgery, 20 to 60 mL (2 to 6 tubes) of whole blood were drawn into 10-mL glass-coated plastic tubes without anticoagulant reagent and were processed with a centrifuge (Medifuge, Silfradent) using the following pre-set program: 30-second acceleration, 2,700 rpm for 2 minutes, 2,400 rpm for 4 minutes, 2,700 rpm for 4 minutes, 3,000 rpm for 3 minutes, and 33-second deceleration and stop. The total spin time was approximately 14 minutes. The tubes now consisted of three layers: (1) the bottom red blood cell (RBC) layer; (2) the growth factor and stem cell layer (CGFs); and (3) the platelet-poor plasma layer. The CGF layer was separated using sterile scissors. CGF clots were compressed and turned into
membranes with a constant thickness of 1 mm.

Lateral sinus floor elevation surgery
One surgeon (Mauro Merli) with more than 30 years of experience in implant therapy performed all of the operations. All patients underwent conscious sedation with continuous monitoring of the vital signs throughout the entire surgical procedure. The patients received the same pharmacologic protocol composed of a fractioned administration of midazolam (0.5 to 1 mg) and atropine (0.5 mg), ceftriaxone (1 g), tramadol (100 mg), ketorolac (30 mg), and betamethasone sodium phosphate (4 mg).

After local anesthesia (articaine with epinephrine, 1:100,000), a midcrestal incision followed by one or two vertical mesial and distal incisions were performed. Then, a full-thickness flap was raised to expose the bone wall prior to piezo-electric lateral window antrostomy and sinus membrane elevation. The antrostomy was made with a piezo-electric device (Piezosurgery, Mectron). The lateral wall was eroded with a specific insert (OP3, Mectron; erosion technique), and the sinus membrane was gently elevated using manual and ultrasonic tools: Stoma (Sinus Lift sinus membrane elevators specifically designed by the surgeon) and Piezosurgery ultrasonic tools (Sinus Lift Kit, Mectron) to generate a compartment for the grafting material. In the CGF group, two or three CGF membranes were placed against the medial sinus wall and below the sinus membrane to protect it during implant insertion. In the DBBM group, the graft (Bio-Oss, Geistlich; particle sizes 0.25 to 1 mm) was previously moistened with patient’s blood and compressed into the created space. The lateral window was covered with two layers of CGF membranes in the CGF group, while in the DBBM group, a collagen membrane was applied and fixed with miniscrew.

Element (Thommen Medical) or NobelParallel CC (Nobel Biocare) implants were used. The surgeon chose the type, diameter, and length of the implants.

Double-layer suturing technique with horizontal mattress (5-0) and single (6-0) sutures were used.

Ice packs were used for the first 2 to 3 hours after surgery, and antibiotics and analgesics were administered: amoxicillin-clavulanate (1 g) twice a day for 6 days and ibuprofen (600 mg) twice a day for 3 to 4 days. Patients were instructed to gently use chlorhexidine mouthrinse (0.12%) twice a day beginning the first day after surgery and to apply chlorhexidine gel on the wound area twice a day for 15 days. Six months postsurgery, a screw-retained provisional prosthesis was delivered. Representative cases from the CGF and DBBM groups are shown in Figs 1 and 2, respectively.

Outcomes
Twelve months after surgery, the outcome measures were:

(1) Implant failure: the presence of any mobility of the individual implant and/or any situation dictating implant removal;

(2) Any biologic complications (hemorrhaging during and after implant placement, sinus membrane perforation, fistulae, sinusitis, sensory loss and peri-implantitis) or prosthetic complications (implant fracture, prosthesis fracture, and chipping) defined as unexpected deviations from the normal treatment outcome;

(3) Subjective evaluation of the patient satisfaction with a visual analogue scale (VAS) was recorded: In the 10-cm VAS, a score of 0 indicated “no functional or esthetic satisfaction”, and a score of 10 indicated “very high satisfaction”; and

(4) Peri-implant marginal bone level (MBL) and the amount of bone in the vertical direction (total bone height [TBH]): Periapical intraoral radiographs were taken with the parallel technique at implant insertion and 12 months postsurgery. An individual stent was not used. Using commercially available software, the digitized radiographs were evaluated by an examiner (Marco Merli) who was blinded to the group assignment. The examiner was previously calibrated and subjected to an intrarater agreement test on 21 implants. The intraclass correlation coefficient for radiographic intrarater agreement analysis was 0.98, which is considered excellent. For MBL, the radiographic measurement was taken from the implant–abutment junction to the most coronal point of the bone-to-implant contact. For TBH, the measurement was taken from the most coronal point of the bone-to-implant contact to the sinus floor. The measurements were made parallel to the long axis of the implant, along the mesial and distal surface.
of the implants. In all cases, the radiographic measurements were adjusted to correlate to the length of the implants used, based on the following formula: \( \text{Rx length} \times \frac{\text{Real implant length}}{\text{Rx implant length}} \).

The mesial and distal sites were averaged for each implant.

**Sample size**

Sample size calculation was performed to detect a difference of 1 mm in MBL. Based on this data, with \( \alpha = .05 \) (type I error), a standard deviation (root mean square error) of 0.67 mm,\(^4\) and considering a 20% dropout rate, 20 patients (10 in each group) needed to be enrolled to
achieve 80% power (type II error of 0.20).

Statistical Methods

Descriptive statistics were performed using mean and standard deviation for quantitative data, and frequency and percentage for qualitative data. The patient was the statistical unit.

A patient was considered a failure if at least one implant failed, and the patient was considered with complications if at least one complication occurred. Qualitative data were summarized using the relative risk and tested using Fisher exact test. For changes in MBL and TBH from baseline (immediately postsurgery) to the 12-month follow-up, analysis of covariance was performed using the baseline value as a covariate. For patient satisfaction, unpaired t test was used.

Results

Twenty patients were consecutively enrolled in the present controlled clinical study: 10 patients (11 implants) in the CGF group (test group) and 10 patients (14 implants) in the DBBM group (control group).

Patients were recruited and operated on from January 2017 to April 2019. Radiographs were taken before surgery, at baseline, and 12 months after surgery (at the delivery of the definitive prosthesis).

The main baseline patient characteristics are shown in Table 1. There were no apparent baseline imbalances between the two groups except for HRB before surgery, which was greater in the CGF group. In all cases, torque value was equal or superior at the 20 N/cm cut-off level.

No implant failed in either group at 12 months postsurgery, and there were no surgical or prosthetic complications. All planned prostheses could be delivered, and there was no loss of the prostheses secondary to implant failures.

MBL at 12 months, change in MBL between baseline and 12 months, TBH at 12 months, change in TBH between baseline and 12 months, and VAS for satisfaction are shown in Table 2.

There was no statistically significant difference in the change in MBL between the CGF and DBBM groups (difference of −0.3, favoring the CGF group; 95% CI: −0.8 to 0.2; \( P = .18 \)). There was no statistically significant difference in the change in TBH (difference of −0.2, favoring the DBBM group; 95% CI: −1.3 to 0.8; \( P = .61 \)). There was no statistically significant difference in satisfaction (difference of 0.2, favoring the CGF group; 95% CI: −0.2 to 0.6; \( P = .29 \)).

Discussion

The objective of the present controlled clinical study was to com-

<table>
<thead>
<tr>
<th>Table 1 Baseline Values</th>
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<tr>
<td>Parameter</td>
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<td>Age, y</td>
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<tr>
<td>Mean (SD)</td>
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<tr>
<td>Range</td>
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<tr>
<td>Female patients, n (%)</td>
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<tr>
<td>Smokers, n (%)</td>
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<tr>
<td>Total sinuses treated, n</td>
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<td>Total implants, n</td>
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<tr>
<td>Implant type received, n (no. of patients)</td>
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<tr>
<td>Thommen</td>
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<tr>
<td>Nobel</td>
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<tr>
<td>Implant dimensions (SD), mm</td>
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<tr>
<td>Diameter</td>
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<tr>
<td>Length</td>
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<tr>
<td>HRB (SD), mm</td>
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<td>MBL (SD), mm</td>
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<td>TBH (SD), mm</td>
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DBBM = demineralized bovine bone matrix group; CGF = concentrated growth factor group; HRB = height of the residual bone; MBL = marginal bone level; TBH = total bone height.
pare implant failure, complications, radiographic bone augmentation, and VAS satisfaction between CGF membranes and DBBM used as a filler biomaterial for lateral maxillary sinus floor elevation with simultaneous implant placement in patients treated for a severely atrophied maxilla. A minimal invasive technique for lateral maxillary sinus elevation was performed.3

No differences between treatments were found for implant failure, complications, radiographic bone augmentation, or VAS satisfaction.

Numerous experimental and clinical studies showing bone regeneration in the sinus without bone graft materials have been reported.9,10 Patients’ venous blood, absorbable collagen sponge, or fibrin-rich blocks were grafted alone to accelerate new bone formation in the widely accepted new paradigm.15,23,27 To the present authors’ knowledge, a comparison between DBBM alone and CGF alone in lateral sinus augmentation has not yet been performed.

Growth factors are bioactive proteins that control the process of wound healing. Growth factors have a critical role in cell migration, cell proliferation, and angiogenesis for tissue regeneration.20 These growth factors are present in blood, within platelets, and in plasma. Platelet concentrates such as PRP, PRF, and CGF have been used for reconstruction of bony defects.20 CGFs have been reported to increase implant stability and accelerate osseointegration.28 Similar to PRF, the use of CGF membranes presents an easy and successful method to cover the sinus membrane and the antrostomy window.27 PRF and CGFs both have the ability to stimulate a continuous and constant release of growth factors for a period of 14 days.29

A previous uncontrolled, short-term study in 10 patients performed sinus augmentation using a flapless transcrestal approach and the hydrodynamic piezoelectric internal sinus elevation technique with autologous CGF alone.23 Like the present study, no complications were reported.23

A recent controlled study compared CGF with a graftless approach in sinus augmentation and simultaneous implant placement.30 Surprisingly, the group with no graft obtained a greater bone gain, but the CGF group obtained a greater density of bone formation.30 Another controlled study compared use of a xenograft with use of a mixture of CGF (70%) with xenograft (30%) in a sinus augmentation procedure, and the use of CGF showed less postoperative morbidity.31 In the present study, no differences were observed comparing the DBBM and CGF groups. Moreover, with the use of blood products, the treatment cost is reduced.32

Limitations of this clinical study were the low number of recruited patients and the short-term follow-up. Another limitation was the non-use of an individual stent for radiographs. This study was carried out in a private clinic, and an expert surgeon with 30 years of experience in implant surgery performed the interventions. This should be taken into consideration when extrapolating the results from this trial to other settings.

### Conclusions

The use of CGF compared to DBBM resulted in similar clinical outcomes. The use of the autogenous material

<table>
<thead>
<tr>
<th>Parameter</th>
<th>DBBM (n = 10 patients)</th>
<th>CGF (n = 10 patients)</th>
<th>Difference</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>MBL (SD), mm</td>
<td>0.7 (0.6)</td>
<td>0.5 (0.3)</td>
<td>−0.3</td>
<td>−0.8 to 0.2</td>
<td>.18</td>
</tr>
<tr>
<td>Change in MBL (SD), mm</td>
<td>0.7 (0.6)</td>
<td>0.3 (0.2)</td>
<td>−0.3</td>
<td>−0.8 to 0.2</td>
<td>.18</td>
</tr>
<tr>
<td>TBH (SD), mm</td>
<td>8.9 (1.9)</td>
<td>9.0 (2.1)</td>
<td>−0.2</td>
<td>−1.3 to 0.8</td>
<td>.61</td>
</tr>
<tr>
<td>Change in TBH (SD), mm</td>
<td>−0.5 (1.0)</td>
<td>−0.7 (1.1)</td>
<td>−0.2</td>
<td>−1.3 to 0.8</td>
<td>.61</td>
</tr>
<tr>
<td>VAS satisfaction score (SD)</td>
<td>9.7 (0.4)</td>
<td>9.9 (0.3)</td>
<td>0.2</td>
<td>−0.2 to 0.6</td>
<td>.29</td>
</tr>
</tbody>
</table>

DBBM = demineralized bovine bone matrix group; CGF = concentrated growth factor group; CI = confidence interval; MBL = marginal bone level; TBH = total bone height; VAS = visual analogue scale.
could decrease the treatment cost for patients. Long-term randomized clinical trials are needed to support these findings.

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References


