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Graftless sinus augmentation with simultaneous dental implant placement: clinical results and biological perspectives

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Abstract. After a sinus lifting procedure, the compartment around the implants under the sinus mucosal lining in the sinus floor is filled with a blood clot from surrounding bleeding. The aim of this study was to evaluate the feasibility of bone formation following graftless sinus lifting with the simultaneous placement of dental implants. Thirty graftless sinus lifting procedures were performed and 72 dental implants placed in 18 consecutive patients, using the lateral window approach. Clinical and radiological follow-up was conducted throughout the 6-month healing period. Biopsies of 30 cases were collected at 6 months post-treatment: 15 biopsies were taken from the newly formed bone near the basal floor and 15 from the newly formed bone near the elevated membrane. New bone consolidation in the maxillary sinus was apparent radiologically and histologically at 6 months after sinus augmentation, providing an average 6.14 ± 1.34 mm of bone-gain. Based on histological analysis and histomorphometric data, the consolidated bone in the augmented sinus comprised 56.7 ± 11.9% to 59.9 ± 13.4% vital bone tissue. Out of the 72 implants placed, only four failed, indicating a 94% overall implant survival rate. Based on this case series, blood clot can be considered autologous osteogenic graft material, to which osteoprogenitors can migrate, differentiate, and regenerate bone.

Key words: sinus lifting; maxillary sinus; Schneiderian membrane; fibrin clot.

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Sinus lifting procedures are performed routinely to provide the required height of proper and stable bone tissue around inserted dental implants.[1,2] The surgical technique of maxillary sinus Schneiderian membrane (MSSM) lifting with immediate/simultaneous installation of dental implants, generally results in significant bone formation.[1,3–8] The recently reported graftless MSSM elevation procedure and the subsequent augmentation of bone have greatly changed our perspective of bone

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neoformation potential.[8–10] The blood clot formed under the lifted MSSM appears to be of critical importance in bone neoformation potential, precluding the need for exogenous graft materials.[11–13] Computed tomography (CT) data have demonstrated no difference in bone density following the use of allogeneic filling materials versus following a graftless sinus procedure.[12] The compartment made in-between the MSSM and the maxillary bone floor, including the blood clot formed, bears very high osteogenic potential, and as such, is assumed to be one of the most important factors dictating the success of graftless sinus procedures.[11–13] Review papers have recently concluded that ungrafted sinus lifting is a reliable and established technique; however, the exact mechanism of bone augmentation is still not well understood.[8,9]

Recent studies have provided some insight into the mechanism and source of osteoprogenitor cells leading to bone formation following graftless sinus lifting.[14,15] The osteogenic potential of the MSSM and the bone-forming cells beneath the membrane has been demonstrated in both in vitro and in vivo assays, and osteoprogenitor cells originating from the sinus membrane have been shown to drive bone formation.[14,15] Subcutaneous bone formation after transplantation of a MSSM folded around a fibrin clot has also been demonstrated.[14] These studies strongly indicate the importance of the MSSM and its component cells, as well as the fibrin clot, to a certain extent, in the bone formation processes.

On the other hand, Cicconetti et al.[16] and Bianco and Robey[17] have proposed that the osteogenic potential is inherent to the sinus maxillary bone floor or, more accurately, to the maxillary tuberosity and the maxillary/mandibular periosteum. These bone sites have been shown to be the sources of osteoprogenitor cells, as sample explants of the maxillary tuberosity and mandibular periosteum have been found to contain cells with early expressed osteogenic markers that could form bone structures upon ectopic transplantation.[16]

In the present clinical study, 18 patients underwent 30 graftless maxillary sinus lifting procedures followed by the immediate insertion of 72 dental implants without exogenous graft material filler. Only blood clots occurring from bleeding due to the surgical procedure filled the compartment beneath the tented MSSM. The aim of this study was to assess new bone formation within and over the compartment created and around implants under the sinus mucosal lining in the sinus floor. Moreover, it was aimed to assess the biological contribution of either or both the MSSM and the maxillary floor to the new bone formation, as well as to analyze the new bone tissue formed near the basal floor and the elevated membrane at 6 months after the procedure.

Materials and methods

Patient selection

The study patients (n = 18) were partially or completely edentulous in the posterior maxilla and required unilateral or bilateral maxillary sinus augmentation.

Study design

All participants were informed about the surgical treatment procedure and provided their written consent to participate in the study. The study was approved by the necessary ethics committee and was conducted between 2011 and 2013. Patients were only eligible if they were physically healthy, with no medical history of systemic or local diseases, such as certain bone metabolism disorders that could contraindicate sinus or implant surgery. A ridge bone height of at least 4 mm, required for primary stabilization of the implants, was a key inclusion criterion. The complexities of implant rehabilitation were described and the patients were provided with necessary information about the procedure, including the prognosis, complications, and any potential hazard. Smoking was not considered a contraindication, but patients were informed that it can reduce success rates of the procedure and compromise the sinus lift.

The surgical protocol and the criteria described by Buser et al.[18] were used to evaluate the osseointegration of implants. In accordance with the criteria, implant mobility was considered a failure and required implant removal. The implant survival rate was calculated by measuring the time elapsed from implant placement to the last follow-up visit or implant removal. For radiographic analysis, preoperative panoramic view examinations (OC200D; Instrumentarium Dental, Tuusula, Finland) and dental cone beam computed tomography (CBCT) scans (i-CAT; Imaging Sciences, Hatfield, PA, USA) were performed to evaluate the available maxillary alveolar bone height, as well as any possible existing sinus pathology. Software programs were used to calculate the existing preoperative residual bone height in millimetres. The measurement of the elevated membrane was performed using the apical point of the implant as a standard reference point after the surgery.

Surgery

All participants received dexamethasone (6 mg) 1 h before surgery and oral prophylactic antibiotics 45 min before surgery. Patients routinely received 2 g amoxicillin–clavulanate before surgery. In the case of a penicillin allergy, 600 mg clindamycin was administered. Antibiotics were administered postoperatively for 10 days: 875 mg amoxicillin–clavulanate twice a day, or 300 mg clindamycin three times daily for those with a penicillin allergy. The surgery was performed under local anaesthesia (2% lidocaine and 1:100,000 epinephrine).

After exposing the posterior maxillary edentulous area and the lateral maxillary sinus wall using a crestal incision, a buccal mucoperiosteal flap was raised and an osteotomy made in the anterior wall of the sinus using a 5-mm-radius round drill in an oval or rectangular fashion, 5–6 mm cranial to the intended implant site (Fig. 1). After exposing the sinus membrane, it was dissected carefully from the

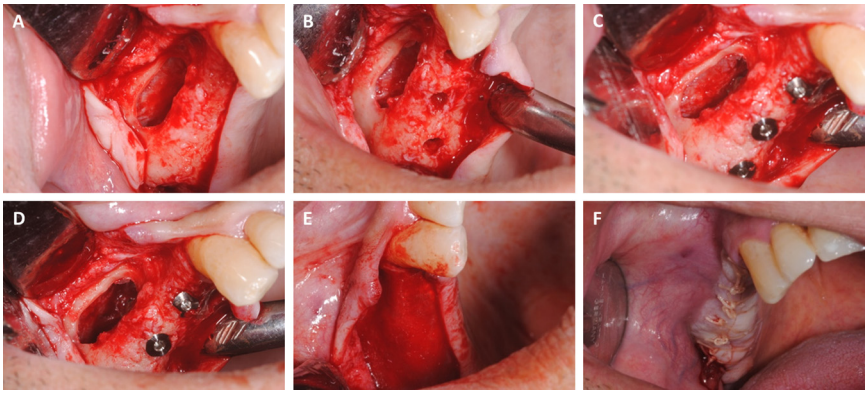

Fig. 1. Sinus lifting procedure. (A) The maxillary sinus lateral wall is exposed and a bone window is cut out. (B) Sinus elevation. (C) and (D) 'Tenting' of the sinus mucosal lining membrane by simultaneous installation of implants in the residual sub-antral bone. (E) and (F) The dental membrane is placed over the lateral window and the incision is then closed with resorbable sutures.

sinus floor walls with a flat, blunt-edged instrument. In the case of small perforations of the sinus membrane, the mucosal lining was treated by further dissection of the mucosal lining and folding of the perforated site.

After sinus membrane elevation, all implants (MIS Implants Technologies Ltd, Carmel, Israel) were inserted simultaneously in the residual sub-antral bone. The remaining bone height was measured with a depth gauge probe during surgery, and recorded.

In the case of minimal residual alveolar bone height (4 mm), primary implant stability was secured by preparing a hole smaller than that described in the original dental implant installation protocol.[1] The compartment around the implants under the sinus mucosal lining in the sinus floor was allowed to fill with blood from surrounding bleeding, and a dental membrane (MIS Implants Technologies Ltd) was placed over the open window before the incision was closed with resorbable sutures (Vicryl 3-0; Ethicon Inc. Somerville, NJ, USA) (Fig. 1).

Postoperative instructions

Patients were instructed not to blow their nose for 2 weeks after the surgery. Postoperative panoramic radiographs and CT scans were performed during and after the 6-month healing period, after which the implant was assumed to have integrated. Dental CBCT scans were taken before the second-stage procedure. During the uncovering procedure (Fig. 2), 30 cylindrical bone biopsies were taken from two levels with a 3-mm-wide trephine bur: 15 biopsies were taken from the newly formed bone near the basal bone and 15 biopsies were taken from the newly formed bone near the elevated membrane (points 1 and 2, illustrated in Fig. 3). The site of each biopsy was determined after measurements were obtained from the 6-month postoperative CT scan.

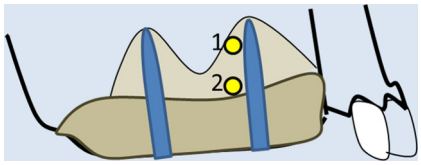

Fig. 3. Locations of the installed implants and 'tenting' of the sinus mucosal lining membrane. Points 1 and 2 indicate the biopsy sites in the newly formed bone; biopsies were taken 6 months after surgery.

Bone gain height evaluation

For the radiographic analysis, panoramic view (OC200D; Instrumentarium Dental) and dental CBCT scan (i-CAT; Imaging Sciences) examinations were performed to measure and evaluate the existing maxillary alveolar bone height before and at 6 months after surgery. The gain in bone height was measured by comparing the preoperative and final dental CT scans using special software programs. Bone height is presented in millimetres.

Histomorphometric evaluation

The histomorphometric evaluation was conducted according to the protocol of Moon et al.[19] Histomorphometric data were obtained from the bone biopsies retrieved from both sites in the lateral window (i.e., points 1 and 2 in Fig. 3). Biopsy specimens were immediately fixed in 4% formaldehyde (24 h, 4 °C) and decalcified in 10% ethylenediaminetetraacetic acid solution for 10 days. Thereafter, specimens were dehydrated in an ascending alcohol series, then embedded in paraffin, and sliced into 5-μm-thick sections parallel to the longitudinal axis. Sections were stained with Mayer's haematoxylin and eosin as well as trichrome stain, and visualized by light microscopy. Using a computerized technique, the sections were evaluated histomorphometrically and photomicrographs were taken using an Olympus BH2 microscope equipped with an Olympus DP50 digital camera (Olympus Optical Company, Tokyo, Japan). After digitization of the picture, histomorphometric data were collected by a picture analysis program (iMT Image Analysis Software; iMTechnology, Daejeon, Korea).[19] The ratio of mineralized bone tissue to the total tissue volume was used to calculate the total bone volume.[20]

Statistical analysis

Comparison of the mineralized bone volume pre- and post-surgery was performed using the paired Student *t*-test. Two-tailed *P*-values of ≤ 0.05 were considered statistically significant. Data are expressed as mean values of bone height (mm) or percentage (%) $\pm$ standard deviation (SD).

Results

The study population comprised eight men and 10 women, of ages ranging from 38 to 60 years (mean 52 years). Thirty sinus lift procedures (12 bilateral and six unilateral) were performed, followed by the placement of 72 implants. During the healing period, the patients had no significant complications or any other signs or symptoms of infection or diseases in the maxillary sinus, except for minor postoperative physiological swelling. Three small sinus membrane perforations (2 mm) occurred during membrane elevation and these were managed with further dissection of the mucosal lining and folding of the perforation site, which enabled formation of a blood clot around the implants. Out of the 72 implants placed, only four failed, indicating a 94% overall implant survival rate. Of the failed implants, only one fixture was clinically mobile at the time of second-stage surgery at 6 months, and this implant was removed; the other implant failures arose due to insufficient primary stability in the residual bone height. All other implants were stable. Patients were followed for 1 year after prosthesis placement; no complications were observed.

In all cases, the new bone formation was notable, with good continuity with the native sinus floor (Fig. 4). The newly formed bone on the maxillary sinus floor was clearly discernible around and on the apical side of the dental implants (Fig. 4). In parallel, apparent radiographic differences between non-perforated and perforated sites, as well as cases of ongoing marginal bone loss around the implants, were not noted. The preoperative residual bone height varied from 4 mm to 7 mm and the average bone thickness of the sub-antral bone was 5.61 $\pm$ 1.2 mm (Fig. 5). At 6 months after surgery, no signs of infection in the maxillary sinus were observed. An

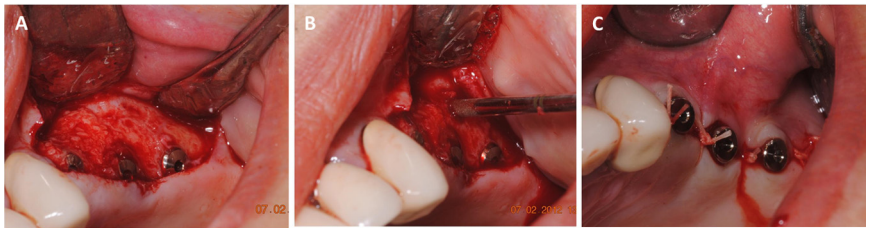

Fig. 2. Exposure of the implants at 6 months post-surgery and the collection of bone biopsy specimens. (A) Exposure of the healed window and successful dental implant. (B) Biopsy collection from the lateral wall, as indicated in Fig. 3. (C) Installation of healing cups and closure of the incision with resorbable sutures.

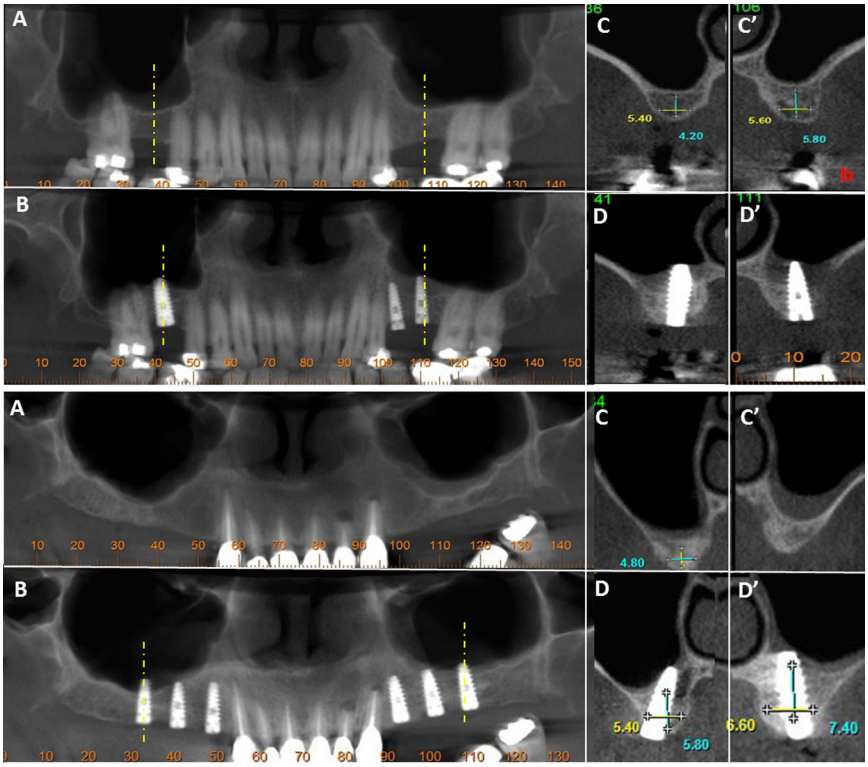

Fig. 4. Radiographic evaluation of new bone consolidation on the maxillary sinus floor. Preoperative and postoperative panoramic CT scan views of two cases are presented. (A) Preoperative bilateral partially edentulous maxillary posterior sites. (B) Postoperative CT scan panoramic view at 6 months after maxillary sinus lifting and implant insertion. (C, C′) Preoperative coronal or sagittal sections of the respective CT scan of the right and left maxillary sinus. (D, D′) Postoperative coronal or sagittal sections of the respective CT scan of the right and left maxillary sinus after 6 months.

apparent increase in alveolar bone height was observed radiographically (Fig. 4), and was shown quantitatively, with an average bone height of 11.76 ± 1.2 mm at 6 months post-surgery, a net bone gain of 6.14 ± 1.34 mm (Fig. 5).

Bone biopsies were collected from two different sites in the newly formed bone: 15 biopsies were taken from point 1 (near the apical side of the dental implant) and 15 from point 2 (near the baseline alveolar bone) (Fig. 3). Relatively well-arranged trabeculae were observed, without evidence of inflammation or foreign body reaction. The blood-filled area contained arranged woven bone tissue. The deposition of new bone was apparent from the proximity of the repositioned bony window (Fig. 2). The percentage of vital bone volume in the blood clot-filled area ranged from 56.7 ± 11.9% to 59.9 ± 13.4%, as determined histomorphometrically (Fig. 6).

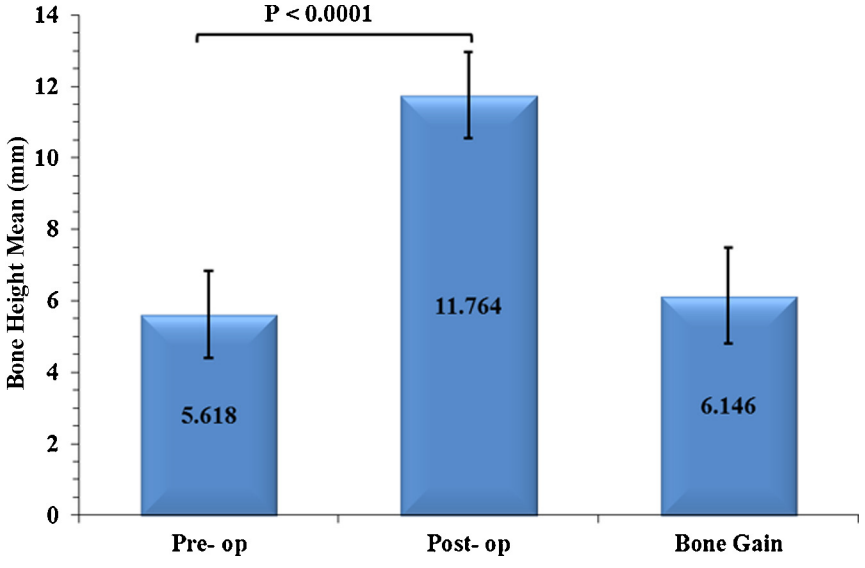

Fig. 5. Preoperative and postoperative alveolar bone height on the side of dental implant insertion, as determined from radiographic images. The graph presents bone height at the maxillary floor ($P < 0.0001$), as well as bone gain.

Discussion

Bone graft material is considered a prerequisite for the clinical success of dental implants inserted into the augmented maxillary sinus. In the current clinical study, it was found that new bone can form directly on and around inserted dental implants without the use of bony substitutes. Thus, the cost-effectiveness and time-saving benefits are obvious, as instead of using autogenous bone or allografts, which involve a remodelling period of 6 months or 9–12 months, respectively, implants can be placed at the time of sinus lifting and left to osseointegrate without bone substitutes.[1,21] While the rate of failure with this technique is similar to those of conventional procedures, there is less contamination associated with this procedure, as no external grafts and/or additional surgeries are involved.

With this line of reasoning, a broad and firm consensus has been established regarding the importance of blood clot formation, which serves as autogenous graft filler material for bone regeneration during graftless maxillary sinus lifting.[8–10] Numerous materials, including the blood clot, have been tested and compared as graft fillers. The blood clot bears excellent growth factor activity, which initiates and promotes bone formation.[22] The osteoinductive properties of the blood clot alone have also been stressed in various studies.[10,23] The authors of the present study believe that because implant placement was immediate with this surgical technique and sinus membrane tenting was maintained by the implants, clot formation throughout the entire sinus compartment was feasible.

The current study demonstrated graftless bone neoformation beneath the MSSM, which was tented by direct placement of implants, maintaining a cavity for blood clot formation. As the only graft filler of this space between the sinus

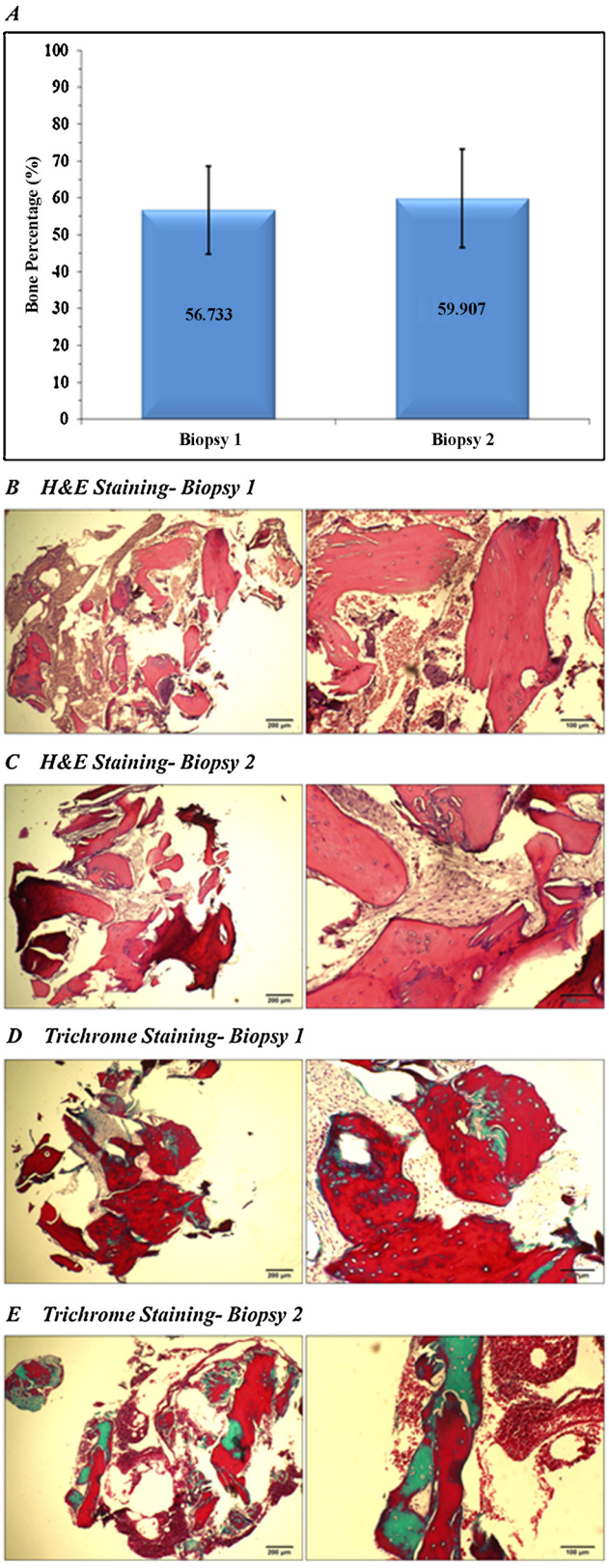

Fig. 6. Evaluation of newly formed bone in the maxillary floor via biopsies retrieved from two sites in the lateral wall ($n = 15$ per site). (A) Histomorphometric data obtained from the newly formed bone (% of bone volume ± SD). (B) and (C) Representative histological haematoxylin and eosin-stained biopsy sections. (D) and (E) Representative histological trichrome-stained biopsy sections. For all histology sections: magnification 4× for the left panel and magnification 10× for the right panel.

membrane and basal bone, the blood clot was later entirely replaced by newly formed bone (Fig. 4). The mean bone height gain of the newly formed bone within the first 6 months of surgery was 6.14 ± 1.34 mm (Fig. 5). The percentage of newly formed bone determined near the basal floor and near the elevated membrane was fairly similar, and the histological analysis confirmed perfect vital bone formation (Fig. 6). Based on these results, it is postulated that the bone formation was initiated from within the fibrin scaffold or clot, giving rise to arranged woven bone tissue, as seen in the histological sections (Fig. 6). These results strongly suggest that the MSSM and maxillary bone floor are most likely the source and origin of osteoprogenitor cells. A recent study in the canine model indicated that the surrounding bony walls and the MSSM of the maxillary sinus bear the osteogenic capability, with the MSSM appearing to demonstrate lesser osteogenic potential.[24] Since the graftless procedure approach is well documented in the literature, the present study was directed towards the important investigation of the mechanism and elements responsible for graftless sinus augmentation. Although the number of patients and biopsies on which the study relied was restricted to a certain extent, the experimental design and the results have provided a significant indication that the MSSM and the maxillary sinus floor contribute to bone formation within the sinus.

According to previous studies by this study group, the inherent osteogenic potential of the MSSM arises from its resident osteoprogenitor cells, which migrate to the fibrin clot and differentiate, leading to bone formation on and around the inserted implants.[14,15] The fibrin clot, which acts as a space retainer and provides an advantageous microenvironment or natural scaffold, also has a potentially beneficial effect on triggering the osteogenic potential of the cells residing within the MSSM.[25] These results are in agreement with those of another study, which showed that the injection of peripheral venous blood appeared to be beneficial for new bone formation in a graft-free maxillary sinus augmentation procedure.[4]

The traumatic sinus lifting procedure and subsequent bleeding, ending with the formation of fibrin or a blood clot, may stimulate cells with osteogenic and probably angiogenic potential to migrate to the surgical site. Through the healing process, these cells can differentiate to osteoblasts and vascular cells and the clot can serve as a scaffold, creating a natural construct or a centre for the initiation of

new bone formation. As indicated, mesenchymal stem cells (MSCs) derived from peripheral blood may contribute to the bone formation in the sinus compartment.[26] These cells, although present in the peripheral circulating blood in low numbers, can be mobilized in large numbers from bone marrow to tissues undergoing traumatic or damaging events.[26] MSCs have been found in the blood of trauma patients with multiple bone fractures,[27] suggesting that the disruption of bone marrow leads to the release of MSCs into the bloodstream. The cells then migrate or are recruited to the injury site to aid in tissue repair.[28,29] A similar mechanism may underlie the graftless sinus lifting procedure, which involves controlled trauma to the bone tissue and to the sinus membrane.[14] In sinus lifting procedures, where tissue damage occurs, the peripheral blood haemorrhage fills the compartment between the MSSM and the maxillary sinus floor. This blood is most likely very rich in MSCs and endothelial progenitor cells (EPCs), which are attracted by the stimulating factors of the traumatic event of the procedure. When this blood coagulates and forms a fibrin clot, it locks or forms an anchorage mesh for MSCs and EPCs. Cells can thereafter differentiate to osteoprogenitors and endothelial cells within the fibrin. These cells, which are evenly distributed throughout the fibrin scaffold or clot, may simultaneously initiate the formation of new bone tissue within the sinus compartment created.

To this effect, it is hypothesized that these osteoprogenitor cells migrate from outside and from within the fibrin clot, and serve as the main players in bone formation. The current clinical study confirms and further proves the authors' own assumptions and those of other authors that new bone formation arises from the MSSM and floor upon graftless sinus lifting immediately followed by dental implant insertion. Based on the size of the present case series, blood clots beneath the MSSM tented by direct placement of implants can be considered an autologous osteogenic graft material filler onto which osteoprogenitors can migrate, proliferate, differentiate to osteoblasts, and regenerate new bone through the healing process. The similarities observed between bone biopsies taken from sites near the basal bone and those from the elevated membrane have only hinted to the possible role of such cells.

In conclusion, this study described a maxillary sinus lift technique followed by immediate implant placement without the use of graft materials. The procedure was associated with a high success rate and reduced the surgical morbidity associated with autogenous grafts, as well as some of the limitations of other osteoconductive grafting materials. To further directly and effectively distinguish between the roles of the MSSM and bony walls in bone formation, we may suggest graftless procedure similar to the study conducted previously in canine model.[24] Further studies must also be conducted to explore the possibility that cells are recruited from the circulation to the formed clot and to assess their role in bone formation.

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Competing interests

No conflict of interest. None of the authors has any financial or personal relationships with other people or organizations that may inappropriately have influenced their actions.

Ethical approval

This study was approved by the Local Helsinki Committee at the Carmel Medical Center, Haifa, Israel.

Patient consent

Not required.

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