

Manuscript 1111

---

Subject Area:

**Comparison between Injectable Platelet Rich Fibrin with Collagen Carrier and  $\beta$ -Tricalcium Phosphate in Lateral Maxillary Sinus Lift with Simultaneous Implant Placement**

Ahmed Adel Refaat

Noha Ahmed Mansour

Sally Awad

Follow this and additional works at: <https://www.mansjdent.com/home>



Part of the [Dentistry Commons](#), and the [Medical Sciences Commons](#)

---

# Comparison Between Injectable Platelet-rich Fibrin with Collagen Carrier and $\beta$ -tricalcium Phosphate in Lateral Maxillary Sinus Lift with Simultaneous Implant Placement

Ahmed A. Refaat\*, Noha Ahmed Mansour, Sally Awad

Department of Oral & Maxillofacial Surgery, Faculty of Dentistry, Mansoura University, Mansoura, Egypt

## Abstract

**Objective:** This study aimed to compare injectable platelet-rich fibrin (I-PRF) with a collagen carrier and  $\beta$ -tricalcium phosphate ( $\beta$ -TCP) for maxillary sinus floor augmentation (MSFA) with simultaneous implant placement.

**Patients and methods:** Fourteen patients with missed maxillary posterior teeth and 3–5 mm residual bone height were selected to perform lateral MSFA with simultaneous implant placement. A total of 18 sites (implants) in 13 patients were qualified for analysis, 10 sites with I-PRF and collagen carrier (group I) and eight sites with  $\beta$ -TCP (group II). Six months later, implant stability was recorded, and all sites were analyzed using cone-beam computed tomography for measuring apical bone height, vertical bone gain, and final bone height.

**Results:** After 6 months 100 % implant success was observed, the mean of implant stability quotient was  $75.90 \pm 2.56$  and  $76.13 \pm 2.23$  for group I and II, respectively ( $P = 0.300$ ), the median of apical bone height was 0 (0–4.5) for group I and 4.33 (0.5–9.6) for group II ( $P = 0.004$ ), the mean of vertical bone gain for group I was  $6.52 \pm 1.71$  mm and  $9.81 \pm 2.47$  mm for group II ( $P = 0.004$ ), the mean of final bone height for group I was  $10.96 \pm 1.50$  mm, while group II was  $14.08 \pm 2.32$  mm ( $P = 0.003$ ).

**Conclusions:** I-PRF with collagen carrier is an economical biomaterial that preserves the created subantral space with adequate new bone formation congruous to implant apices. So, lateral MSFA using I-PRF and collagen carrier with simultaneous implant placement could be a simple, reliable, and predictable surgery with a high success rate that could be comparable to using  $\beta$ -TCP.

**Keywords:** Collagen, Injectable platelet-rich fibrin, Maxillary sinus floor augmentation, Simultaneous implant, Sinus elevation,  $\beta$ -tricalcium phosphate

## 1. Introduction

Oral and maxillofacial surgery has become more and more reliant on dental implants. They provide patients with the most comfortable and convenient way to replace missing teeth and restore aesthetics and function.<sup>1</sup>

The maxillary double-direction reabsorption, caused by centripetal loss of alveolar bone and sinus pneumatization, together with thin cortex and low trabecular density, presents a challenge for oral

rehabilitation with dental implants.<sup>2</sup> Since Bråne-mark discovered osseointegration in the 1950s, several surgical approaches for rehabilitating atrophic maxillae with dental implants have been proposed.<sup>3</sup> This includes maxillary sinus floor augmentation (MSFA), short implants, angled implants, zygomatic implants, and pterygoid implants.<sup>4</sup>

MSFA is a reconstructive surgery that includes the crestal and the lateral approaches with simultaneous or delayed implant insertion.<sup>5</sup> The major criteria for selecting the appropriate approach, is the residual

bone height (RBH).<sup>6</sup> When the RBH less than 4–6 mm, maxillary sinus elevation via lateral approach is the preferred treatment. This method involved elevating the sinus mucosa after access through the lateral wall and placement of biomaterial,<sup>7</sup> devices,<sup>8,9</sup> implants alone,<sup>10,11</sup> or in combination with biomaterial,<sup>12</sup> to maintain the elevated space and allow bone formation within the subantral space.<sup>13</sup> It is essential to be aware of various anatomic and pathologic abnormalities in the sinus to reduce the risk of complications of sinus lifting and other procedures in this region.<sup>14,15</sup>

Several graft types (e.g. autogenous grafts, allografts, xenografts, synthetic grafts, and platelet concentrates) have been used for augmentation.<sup>16</sup>  $\beta$ -tricalcium phosphate ( $\beta$ -TCP) is a synthetic biomaterial commonly used as a bone substitute through many years, has shown proven efficacy in bone regeneration due to its good biocompatibility and osteointegration properties.<sup>17</sup> It has been used in several studies as a graft material for MSFA alone or mixed with other graft materials.<sup>18,19</sup>

Collagen is widely used in the oral and maxillofacial field as a hemostatic agent, a scaffold, and a drug carrier.<sup>20</sup> In tissue engineering, it is considered a good scaffold regarding biocompatibility and biodegradability.<sup>21</sup> Collagen could remain for weeks allowing time for the provisional matrix to develop into new bone tissue.<sup>22</sup> Furthermore it is an economical biomaterial and simplifies surgical procedures.<sup>23</sup>

One of the most challenges facing researchers today is developing a biomaterial that can be used to improve tissue regeneration with the greatest degree of predictability.<sup>24</sup> Platelet-rich fibrin (PRF) is a second-generation platelet concentrate produced from a patient's blood without the addition of biochemicals or anticoagulants.<sup>25</sup> PRF is widely applied in various surgical procedures as it can be considered a natural fibrin-based biomaterial with a high concentration of platelets and a great release of growth factors (GFs),<sup>26</sup> which enhance healing and tissue regeneration by promoting angiogenesis, cellular proliferation, and differentiation.<sup>27</sup> Some researchers have hypothesized that PRF could be an advantageous substitute for applying in a sinus lift surgeries.<sup>28,29</sup>

Injectable platelet-rich fibrin (I-PRF) is a flowable form of platelet concentrate produced by centrifuging blood in nonglass centrifugation tubes at a low centrifugation speed.<sup>30</sup> This would allow a higher number of cells to remain in the top layer where I-PRF can be produced, making it rich with leukocytes and platelets with a greater concentration of GFs when compared with other formulations

of PRF with higher centrifugation speeds. This advanced form could enhance wound healing and subsequently hard and soft tissue regeneration.<sup>30–32</sup> Furthermore I-PRF has a three-dimensional fibrin network with uniform distribution of the cellular components within the mesh,<sup>33</sup> offering the advantage of a controlled release system with slow release of GFs, which could preserve proper bioactivity over the healing period.<sup>34</sup>

To our knowledge, there are not enough reports in the literature about the use of I-PRF with collagen carriers in MSFA procedures. Therefore, the current study aimed to compare I-PRF with collagen carrier and  $\beta$ -TCP in lateral maxillary sinus lift procedure with simultaneous implant placement.

## 2. Patients and methods

Fourteen patients seeking replacement of missed maxillary posterior teeth and having pneumatized maxillary sinus at the planned implant sites were selected to perform lateral MSFA with simultaneous implant placement. All patients were selected from the outpatient clinic of Oral and Maxillofacial Surgery Department, Faculty of Dentistry, Mansoura University. The following were the inclusion criteria: age range from 18 to 50 years, RBH between the alveolar ridge crest and the floor of the maxillary sinus at the planned implant site from 3 to 5 mm, with adequate bone width that can accommodate implant fixture and adequate space that can accommodate the implant abutment and the future restoration. The general exclusion criteria<sup>35</sup> included medical conditions that would compromise surgical procedures or affect bone healing as recent myocardial infarction and cerebrovascular accident, valvular prosthesis surgery, immunosuppression, bleeding disorders, as well as treatment with intravenous bisphosphonate, uncontrolled diabetes (glycated hemoglobin >7.5 %), radiation therapy in the head and neck area or ongoing chemotherapy. Also, patients with parafunctional habits, untreated periodontal disease, pregnancy, heavy smokers, drug and alcohol addicts, patients with psychiatric problems, and patients not fully able to comply with the study protocol were excluded. The local exclusion criteria were related to the surgery site as any maxillary sinus conditions (anatomical or pathological) contraindicating sinus floor elevation and implant placement,<sup>36</sup> previous bone augmentation procedures in the same maxillary region, and poor oral hygiene.

According to the ethical committee guidelines, every patient was informed about possible expected

risks and benefits of the planned surgery, and written informed consent was obtained from all included individuals before the surgical procedure. This study was approved by the ethical committee Faculty of Dentistry, Mansoura University (No. M12160321).

Sample size calculation was based on mean RBH after 6-month postoperative with I-PRF-soaked collagen plug retrieved from previous research by Gülsen and Dereci.<sup>37</sup> Using G power program, version 3.1.9.4, to calculate sample size based on effect size of 0.97, using two-tailed test,  $\alpha$  error = 0.05 and power = 90.0 %, the total calculated sample size would be 14 at least.

The patients were assigned randomly to two equal groups to perform lateral MSFA with simultaneous implant placement: group I using I-PRF and collagen carrier and group II using  $\beta$ -TCP as a filling material in the subantral space.

### 2.1. Preoperative evaluation

Clinical examination: extraoral and intraoral examination, complete blood count, and bleeding profile were done for each patient, study casts were made as presurgical records, and preoperative intraoral photographs were taken (Figs. 1a,2a).

Radiographs: orthopantomogram was performed as a screening method, then cone-beam computed tomography (CBCT)<sup>38</sup> was performed when the patient was considered as a candidate for lateral MSFA for measuring RBH, bucco-lingual and mesio-distal width of edentulous space, detecting prominent alveolar antral artery or any abnormal maxillary sinus conditions (anatomical or pathological), assessing the thickness of sinus membrane and lateral sinus wall, determination of the lateral window osteotomy site and dimensions before operation, and detecting ostium condition.

Presurgical phase: all patients received professional dental scaling 1 week before surgery and were prescribed 0.2 % chlorhexidine digluconate mouthwash (Orovex; Macro Pharmaceuticals, Cairo, Egypt) twice a day. A 7-day course of twice-daily amoxicillin/clavulanic acid 875/125 mg (Augmentin 1 g tablet; GSK, UK), or clindamycin 300 mg (Dalacin c 300 mg capsule, New York; Pfizer, USA) three times a day (for patients allergic to penicillin) as antibiotic prophylaxis, was administered to all patients starting 24 h before surgery.

Surgical procedure: mouth rinse with 0.2 % chlorhexidine digluconate was used before surgery. Surgeries were done under local anesthesia using articaine 4 % with epinephrine 1 : 100 000 (Artinibsa 4 % 1 : 100 000; Inibsa, Spain).

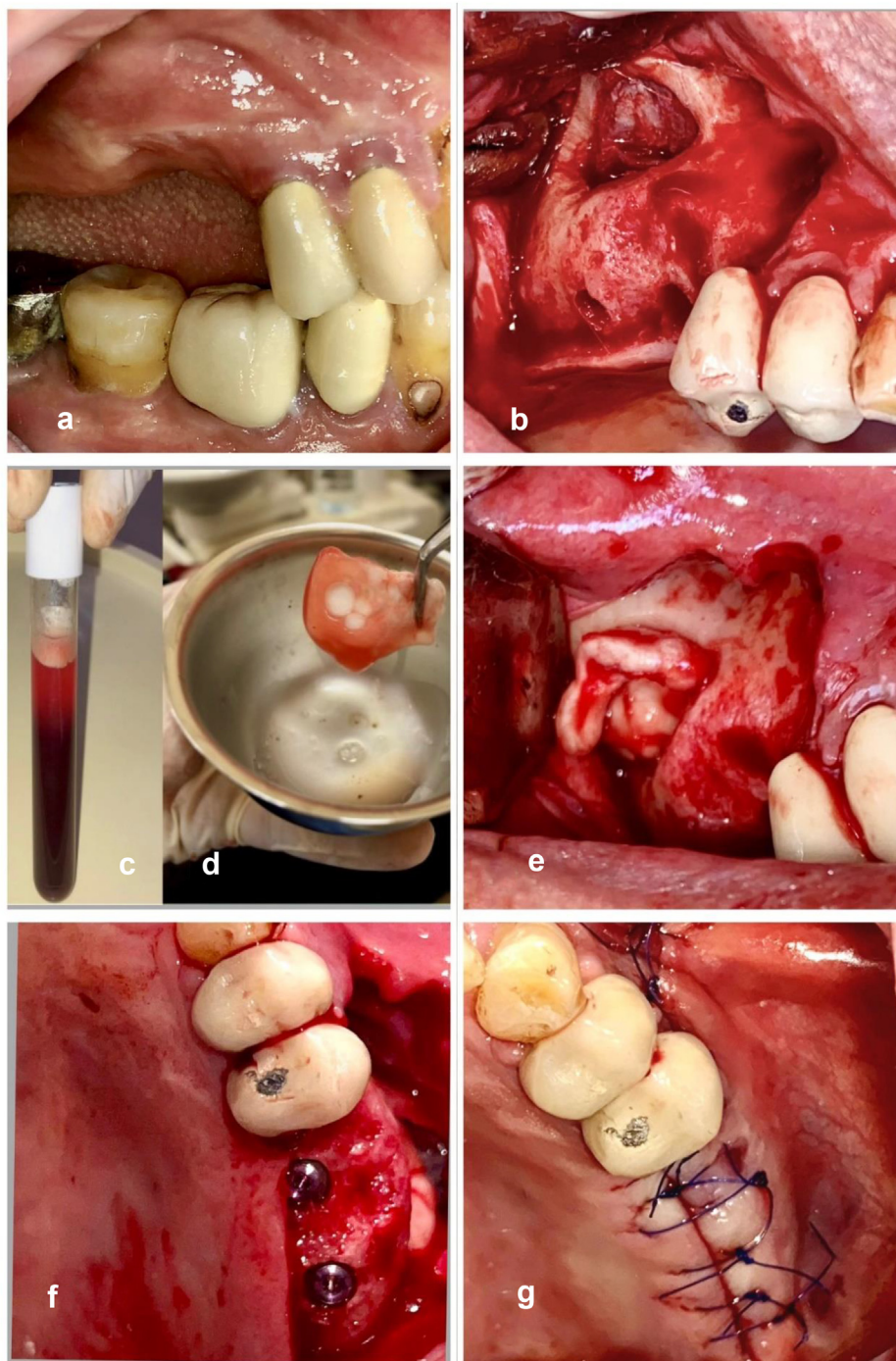
A full-thickness buccal mucoperiosteal flap was reflected following crestal incision with vertical releasing incisions to provide adequate access and visualization. Using Dentium Advanced Sinus Kit (Dentium, South Korea), an osteotomy was made in the lateral wall of the maxillary sinus, the lateral wall was thinned out with Dentium Advanced Sinus Kit Drill #4 or #5 at a speed of 800–1200 rpm (30–45 Ncm] using light pressure and rotating strokes at a 45° angle, using a series of sinus elevation curettes the membrane gently detached from the bony window's edge, elevated, and separated from the sinus walls to create adequate space for the graft material. The implant osteotomy site was prepared with underdrilling at least 0.5 mm narrower in diameter than the diameter of the implant fixture to be inserted to achieve good primary stability (Figs. 1b,2b).

Group I (I-PRF with collagen carrier): two white cap tubes (Vacutest Kima s.r.l Arzergrande, Italy) were filled with 9 ml blood collected from the patient, tubes were balanced in the centrifuge, centrifugation launched at 700 rpm/3 min protocol for females and 4 min protocol for males.<sup>30,39</sup> At the end of the spin, an orange supernatant formed on the surface was collected with a 21 G needle mounted on a syringe and applied to the collagen (Parasorb; Fleece HD) (RESORBA Medical GmbH, Germany), and then waited until I-PRF transformed to a viscous fibrin network sticking to the collagen fleece. The collagen carrier with coagulated I-PRF was packed into the sinus cavity below the elevated sinus membrane (Fig. 1c–e).

Group II ( $\beta$ -TCP): the subantral space was filled with adbone TCP (Medbone; Biomaterials, Portugal) mixed with normal saline. The collagen membrane was prepared from Parasorb Fleece HD by compressing with an instrument's cylindrical handle and was placed to cover the lateral osteotomy window (Fig. 2d, e).

For both groups: implant fixtures (T6 Nucleoss, Turkey) of 10 mm length were guided into their places, 1 mm below the alveolar crest bone, implant stability was recorded using Osstell implant stability quotient (ISQ) (Integrate Diagnostic AB, Gothenburg, Sweden), cover screws were attached to implant fixtures. The flap was repositioned and sutured by interrupted sutures using 4/0 polypropylene (GMS, Egypt) (Fig. 1f, g and 2e, f).

Postoperative management: patients were instructed to maintain good oral hygiene, avoid hard food and apply ice packs postoperatively externally 20 min/h for 24 h. Specific postoperative instructions for sinus surgery were given to the patients as follows: sneeze with mouth open, avoid



*Fig. 1. Surgical procedure for a patient from group I: (a) Preoperative intraoral lateral view of the planned implant site. (b) Prepared lateral window osteotomy site and implant osteotomy site. (c) I-PRF obtained after centrifugation. (d) Coagulated I-PRF sticking to collagen fleece. (e) Subantral space filled with collagen soaked with I-PRF. (f) Implants placed in alveolar ridge with cover screws. (g) Primary closure of the flap with interrupted polypropylene sutures. I-PRF, injectable platelet-rich fibrin.*

nose blowing, and avoid using straws for drinking. Patients were instructed to continue with the prescribed antibiotic, in addition to NSAIDs as ibuprofen 600 mg (Brufen 600 mg; Abbott, USA), 0.2 % chlorhexidine digluconate mouthwash twice a

day for 1 week, and nasal decongestant as Xylometazoline (Otrivin 1 %; Novartis, Germany) two drops into each nostril up to three times a day for 3–5 days. Sutures were removed after 10 days; patients were recalled at 1, 3, and 6 months postsurgical to

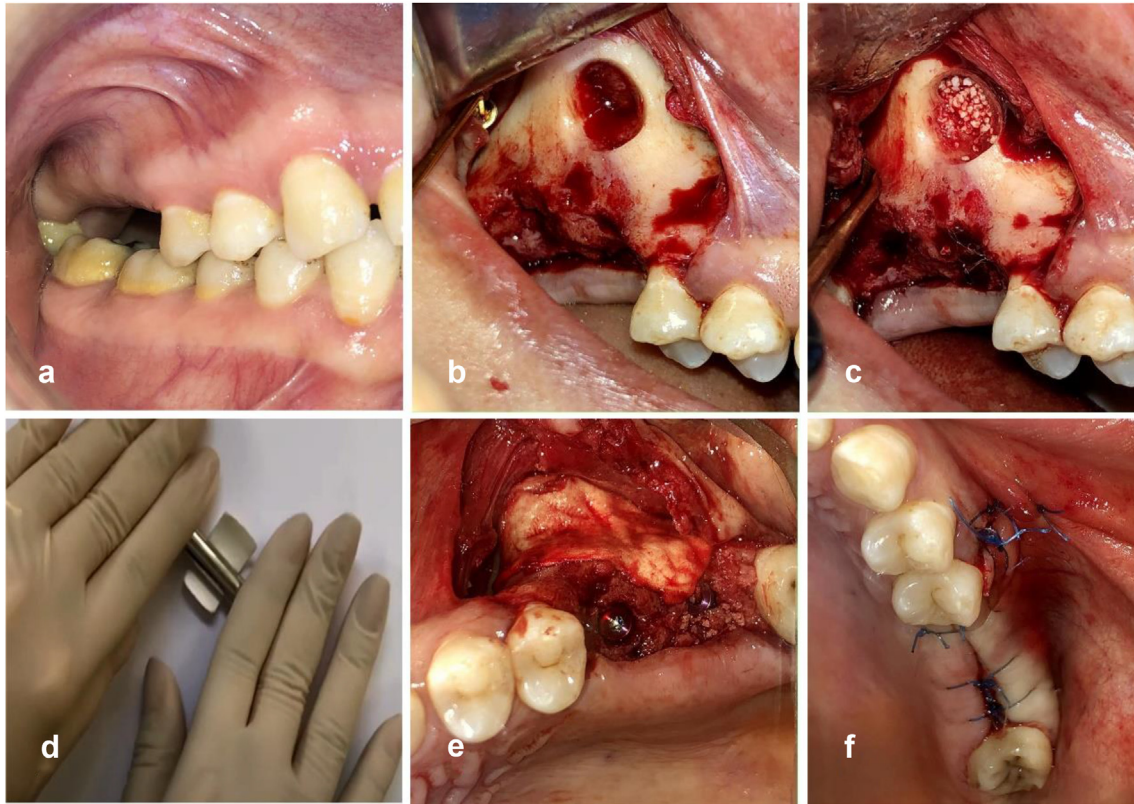


Fig. 2. Surgical procedure for a patient from group II. (a) Preoperative intraoral lateral view of the planned implant site. (b) Prepared lateral window osteotomy site. (c) Subantral space filled with  $\beta$ -TCP. (d) Collagen membrane preparation from PARASORB Fleece HD. (e) Implants in place with cover screws and collagen membrane covering the lateral window osteotomy site. (f) Primary closure of the flap with interrupted polypropylene suture.  $\beta$ -TCP,  $\beta$ -tricalcium phosphate.

check the course of healing. Six months post-surgical, healing abutments were fixed for 10–14 days, then the final prosthesis was cemented.

**Patient's evaluation:** all patients were evaluated clinically and radiographically 6 months after the operation.

**Clinical evaluation:** all surgical sites were evaluated for any complications, including infection, hemorrhage, wound dehiscence, and any kind of sinus complications or implant failure.

**Implant stability** was re-assessed for all implants 6 months after surgery by recording the ISQ values with Osstell ISQ device.

**Radiographic evaluation:** CBCT was performed for all patients; preoperatively ( $T_x$ ), immediately after surgery 'within 1 week' ( $T_0$ ), and 6 months after surgery ( $T_6$ ) for measuring the following parameters (Figs. 3–5). **RBH:** RBH was measured at  $T_x$  as the shortest distance from the alveolar ridge crest to the floor of the maxillary sinus at the intended implant placement site. **Implant protrusion length (IPL):** IPL inside the maxillary sinus was measured as the distance from the sinus floor to the implant apex at  $T_0$ . ( $IPL = \text{implant length} - \text{RBH}$ ). **Apical bone height (ABH):** ABH represented the bone above the

implant. It was calculated as the distance from the apical implant apex level to the most apical level of the radiopaque area at  $T_0$  and  $T_6$ . **Vertical bone gain (VBG):** the VBG at  $T_0$  or  $T_6$  ( $VBG = IPL + ABH$ ). **Final bone height (FBH):** it was the new bone height of the maxillary sinus floor after augmentation ( $FBH = \text{RBH} + \text{VBG}_{T_6}$ ).

All collected data were statistically analyzed using IBM SPSS Statistics (Version 27). The level of significance was set at 5 %. Number and percent were used to describe qualitative data. The normality of distribution was confirmed using the Kolmogorov–Smirnov test. To describe the quantitative data, range, mean, median, and SD were used. Analysis of variance with repeated measures and paired  $t$  test were used for the normally distributed quantitative data and to compare between more than two periods. Wilcoxon signed-ranks test was used for abnormally distributed quantitative variables and to compare between two periods.

### 3. Results

A total of 14 patients with single or multiple missed maxillary posterior teeth were selected to

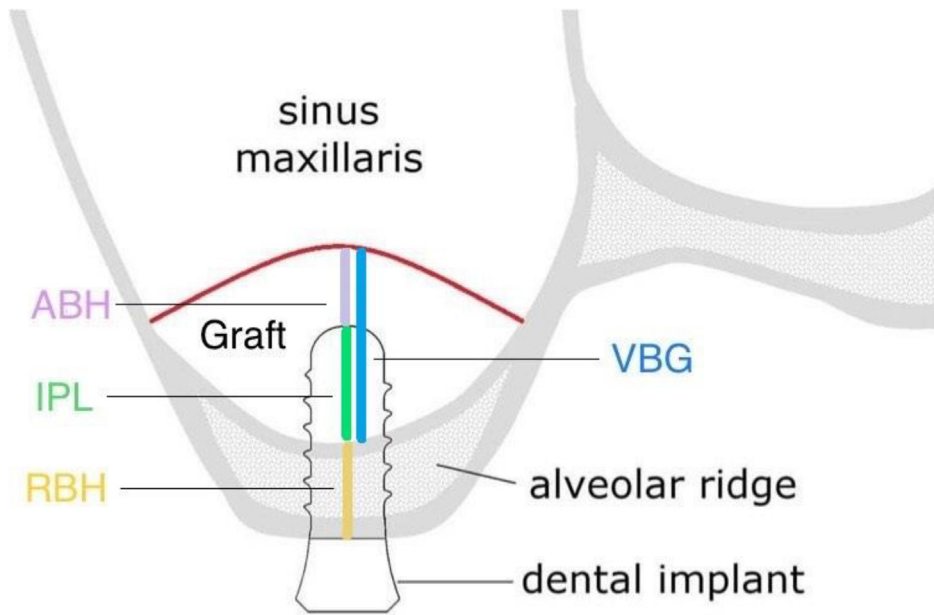


Fig. 3. Schematic representation for linear measurements.

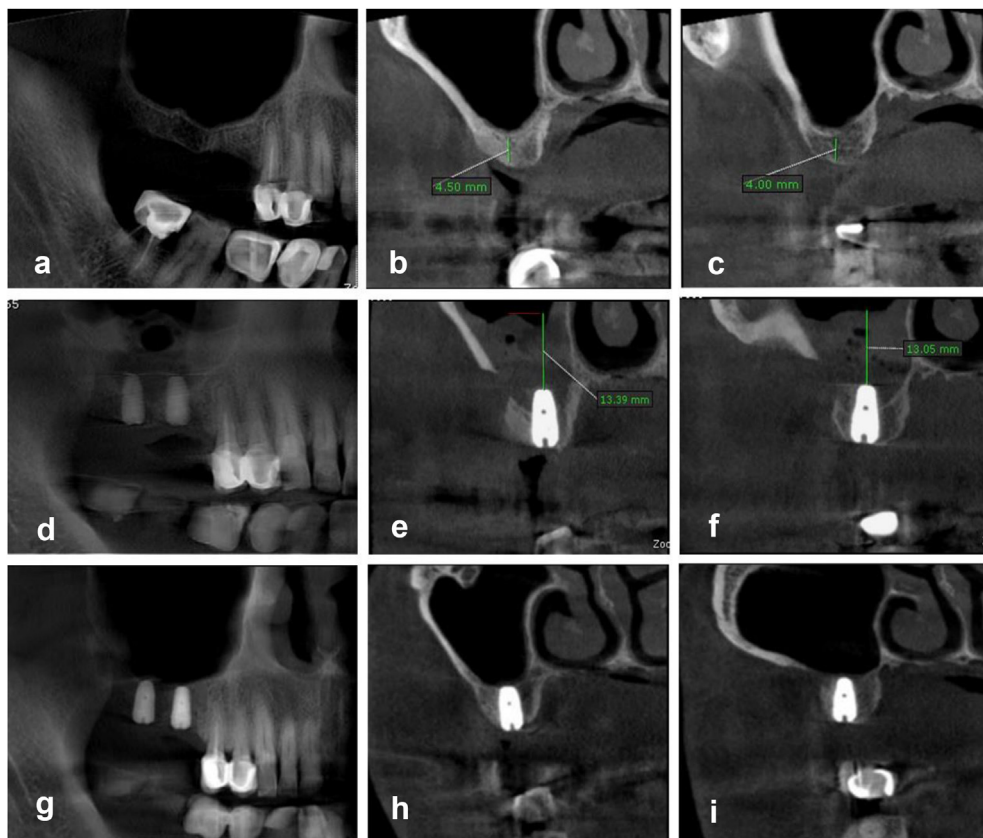


Fig. 4. CBCT of patient I. (a) Panoramic view at  $T_x$ . (b, c) Cross-sectional views at  $T_x$  showing RBH of intended implants sites. (d) Panoramic view at  $T_0$ . (e, f) Cross-sectional views at  $T_0$  showing ABH of both sites. (g) Panoramic view at  $T_6$ . (h, i) Cross-sectional views at  $T_6$  for both sites. ABH, apical bone height; CBCT, cone-beam computed tomography; RBH, residual bone height.

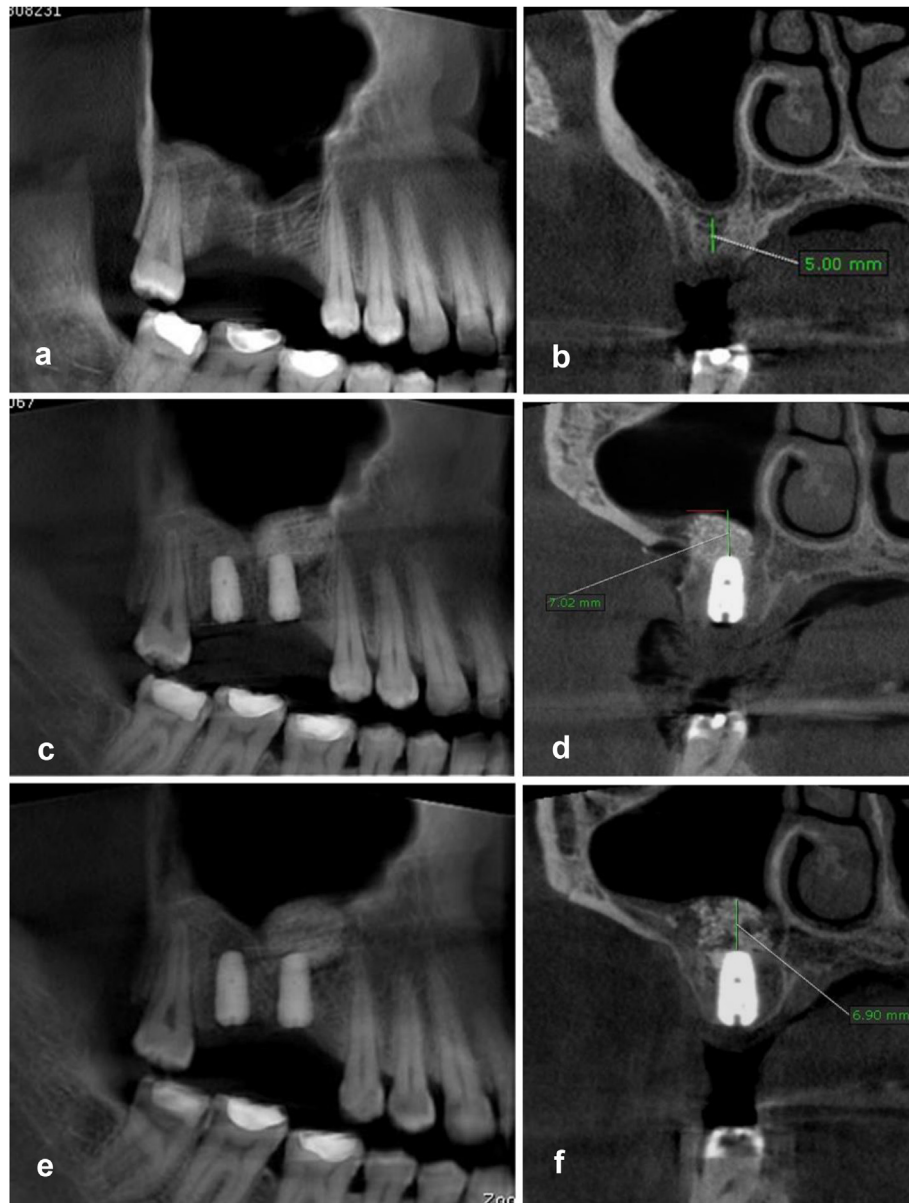


Fig. 5. CBCT of patient II. (a) Panoramic view at  $T_x$ . (b) Cross-sectional view at  $T_x$  showing RBH of intended implant site. (c) Panoramic view at  $T_0$ . (d) Cross-sectional view at  $T_0$  showing ABH. (e) Panoramic view at  $T_6$ . (f) Cross-sectional view at  $T_6$  showing ABH. ABH, apical bone height; CBCT, cone-beam computed tomography; RBH, residual bone height.

perform lateral MSFA with simultaneous implant placement, 13 patients were included in the study and one patient was excluded due to sinus membrane perforation during elevation, collagen membrane used for treatment of this complication, and implant placement postponed. A total of 18 sites (implants) were qualified for analysis, 10 sites in seven patients were in the I-PRF group, and eight sites in six patients were in the  $\beta$ -TCP group. All fixtures used were 10 mm in length.

The mean age of patients was  $38.43 \pm 15.71$  and  $42.33 \pm 11.39$  in groups I and II, respectively, with no

statistically significant difference between both groups ( $P = 0.624$ ). Group I included four (57.1 %) males and three (42.9 %) females, while group II included three (50 %) males and three (50 %) females with no statistically significant difference between the two groups ( $P = 1.0$ ).

The mean RBH for group I was  $4.45 \pm 0.89$  mm and for group II was  $4.28 \pm 0.94$  mm with no statistically significant difference between the two groups ( $P = 0.700$ ).

As regards implant stability; the mean of implant stability increased from  $68.3 \pm 4.32$  at  $T_0$  to



$75.90 \pm 2.56$  at  $T_6$  with 11.1 % change in group I, while in group II; it increased from  $66.38 \pm 2.97$  at  $T_0$  to  $76.13 \pm 2.23$  at  $T_6$  with 14.7 % change. Within each group, there was a statistically significant difference comparing stability over time from  $T_0$  to  $T_6$  ( $P < 0.001$ ), yet there was no statistically significant difference between groups I and II at  $T_0$  and  $T_6$  ( $P = 0.300$ ) (Fig. 6).

For both groups I and II the mean IPL was  $5.56 \pm 0.89$  and  $5.73 \pm 0.94$  mm accordingly with no statistically significant difference between the two groups ( $P = 0.700$ ).

In group I; the median of ABH was 13.2 with a range 5.5–20 at  $T_0$  and it decreased to 0 with a range 0–4.5 at  $T_6$  with 92.5 % change and a statistically significant difference ( $P = 0.005$ ), while in group II; the median of ABH was 4.5 with a range 0.75–11.2 at  $T_0$  and it decreased to 4.33 with a range 0.5–9.6 at  $T_6$  with 15.7 % change and a statistically significant difference ( $P = 0.012$ ). By comparing ABH between both groups, there was a statistically significant difference at  $T_0$  ( $P = 0.003$ ) and  $T_6$  ( $P = 0.004$ ) (Table 1).

The mean of VBG for group I was  $18.29 \pm 5.35$  at  $T_0$  and it decreased to  $6.52 \pm 1.71$  at  $T_6$  with a 64.4 % change and a statistically significant difference ( $P < 0.001$ ). For group II, the mean of VBG was  $10.57 \pm 3.36$  at  $T_0$  and it decreased to  $9.81 \pm 2.47$  at  $T_6$  with a 7.2 % change and no statistically significant difference ( $P = 0.188$ ). Between both groups, there was a statistically significant difference at  $T_0$  ( $P = 0.003$ ) and  $T_6$  ( $P = 0.004$ ) (Table 2).

The mean of FBH for group I was  $10.96 \pm 1.50$ , while the mean FBH for group II was  $14.08 \pm 2.32$  with a statistically significant difference between the two groups ( $P = 0.003$ ).

#### 4. Discussion

The rehabilitation of an atrophic maxilla represents a challenge for oral and maxillofacial surgeons. Conventional implant treatments cannot be performed due to alveolar bone resorption and pneumatization of the maxillary sinus. MSFA is a predictable technique for obtaining the volumetric amount of ‘vertical height’ of bone required to place the implants.<sup>4,40</sup> The use of graft biomaterials to assist bone formation after sinus membrane elevation is highly controversial; the grafting materials currently used in MSFA appear to have a more mechanical function that is not purely biological.<sup>22</sup> Unfortunately, artificial bone substitutes only have osteoconductive properties.<sup>41</sup>

The goal of this study was to apply materials in which the body could exhibit the maximum healing capacity with the minimum possible residual graft material and maximum new bone formation. The study aimed to compare I-PRF with collagen carrier and  $\beta$ -TCP in lateral MSFA with simultaneous implant placement. I-PRF is readily available, inexpensive, and could increase the concentration of GFs and leukocytes in the surgical area, which control the inflammatory process with an antimicrobial effect, enhance healing, cell proliferation, and differentiation, promote angiogenesis, and encourage remodeling.<sup>42–44</sup>

In this study, I-PRF was prepared according to the newer PRF protocols introduced by Choukroun, which are known as the low-speed centrifugation concept, which has proven considerable advantages in many studies.<sup>30,39</sup> The low relative centrifugation forces (700 rpm) inhibit the displacement of cells

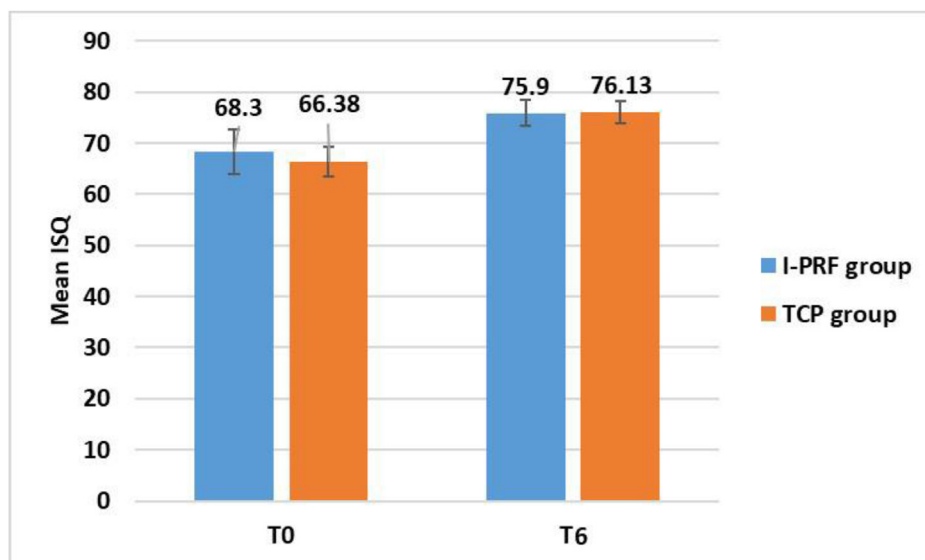


Fig. 6. Mean implant stability quotient (ISQ) among studied groups.

Table 1. Comparison of median of apical bone height between studied groups.

ABH	I-PRF group (N = 10)	$\beta$ -TCP group (N = 8)	Test of significance (Mann–Whitney U test)
T <sub>0</sub>	13.2 (5.5–20)	4.5 (0.75–11.2)	Z = 3.02 P = 0.003*
T <sub>6</sub>	0 (0–4.5)	4.33 (0.5–9.6)	Z = 2.89 P = 0.004*
Wilcoxon signed-rank test	z = 2.80 P = 0.005*	Z = 2.52 P = 0.012*	
% of change	92.5	15.7	

$\beta$ -TCP,  $\beta$ -tricalcium phosphate; ABH, apical bone height; I-PRF, injectable platelet-rich fibrin; T<sub>0</sub>, immediately after surgery; T<sub>6</sub>, 6 months after surgery; Z, Mann–Whitney; z, Wilcoxon.

P: level of significance (significant  $\leq 0.05$ ).

\* Statistically significant.

Table 2. Comparison of vertical bone gain (mean  $\pm$  SD) between studied groups.

VBG	I-PRF group (N = 10)	$\beta$ -TCP group (N = 8)	Test of significance (Student t test)
T <sub>0</sub>	18.29 $\pm$ 5.35	10.57 $\pm$ 3.36	t = 3.54 P = 0.003*
T <sub>6</sub>	6.52 $\pm$ 1.71	9.81 $\pm$ 2.47	t = 3.34 P = 0.004*
Paired t test	t = 8.96 P < 0.001* 64.4 %	t = 1.46 P = 0.188 7.2 %	

$\beta$ -TCP,  $\beta$ -tricalcium phosphate; I-PRF, injectable platelet-rich fibrin; T<sub>0</sub>, immediately after surgery; T<sub>6</sub>, 6 months after surgery; t, Student t test; VBG, vertical bone gain.

P: level of significance (significant  $\leq 0.05$ ).

\* Statistically significant.

from the upper third layer to the lower layers before the fibrin clot formation,<sup>45</sup> offering greater quantities of basic inflammatory cells of platelets and leukocytes with considerably greater release of GFs in PRF matrices than the higher relative centrifugal forces (2800 rpm).<sup>30–32</sup> Miron et al.<sup>46</sup> demonstrated that I-PRF kept releasing GFs creating a small clot even 10 days after implantation, while PRP dissolved in 10 days with no further release of GFs.

I-PRF is flowable and requires a carrier material to preserve the space under the elevated sinus membrane. Collagen type I was used in this study; it acts as a scaffold with controlled time-release delivery of GFs to keep their bioactivity throughout the therapeutic window and reduce unfavorable inflammatory responses. Collagen could also offer initial structural and mechanical support to the coagulum in the early stages of healing, preventing premature collapse and being sufficient for space preservation and further bone formation.<sup>13,22</sup> Sampath and Reddi<sup>47</sup> have reported that the type I cross-linked collagen is the most suitable carrier to promote the activity of the osteoinductive signal to support and guide bone regeneration.

This study compared I-PRF with collagen carrier to  $\beta$ -TCP, as clinical, radiographic, and histological studies showed supporting evidence that  $\beta$ -TCP is a good synthetic bone substitute with very similar development to an autogenous graft and can be reabsorbed and replaced by new bone within a short interval of time like 6 months.<sup>18,19,41,48</sup> This is

the primary reason for the utilization of radiographic assessment following 6 months of graft placement in many studies and the same has been followed in the present study.

Simultaneous implant placement with MSFA was applied in this study, with the advantages of no second surgery, decreasing the costs, procedure time, and risk of infection. It also allows for the preservation of the graft as earlier loading can be achieved.<sup>49</sup>

In the present study, none of the cases showed any infection. Clinically and radiographically all surgical areas exhibited normal healing without complications. The overall implant survival rate was 100 %, which is similar to Leighton et al.<sup>50</sup> study which used autologous fibrin glue with collagen carrier in MSFA. This could be related to the antimicrobial effect of I-PRF and the safety range of 6 months of loading time used in this study, which is considered an appropriate period for bone maturation and osseointegration.

Patients included in this study had RBH from 3 to 5 mm with a mean of 4.45  $\pm$  0.89 mm for group I and 4.28  $\pm$  0.94 mm for group II with no statistically significant difference between the two groups (P = 0.700), in agreement with indications for lateral MSFA in literature as the study by Thor et al.,<sup>51</sup> who reported a mean RBH of 4.6 mm.

Within each group, there was a statistically significant difference comparing stability over time from T<sub>0</sub> to T<sub>6</sub> (P < 0.001), yet there was no

statistically significant difference between the two groups at  $T_0$  and  $T_6$  ( $P = 0.300$ ), this could be related to comparable RBH between the two groups ( $P = 0.700$ ), and the use of same implant length of 10 mm for all sites. The high ISQ values could be attributed to the replacement of the graft by a new bone formation in a short period, increasing osseointegration (bone–implant contact), and consequently implant stability.

This is in agreement with a study by Han et al.<sup>52</sup> with mean ISQ values of 75.3 and 75.4 after lateral MSFA simultaneous with implant placement. Different than this study, Leighton et al.<sup>50</sup> reported a lower mean ISQ value of  $66 \pm 3.8$ , in the third year of assessment.

Although the median of ABH for the I-PRF group decreased from 13.2 with a range of 5.5–20 at  $T_0$  to 0 with a range of 0–4.5 at  $T_6$ , better radiographic results were obvious, and new bone formation was evident and surrounded all fixtures from all sides up to the most apical point of the implants with sufficient quantity. The sinus membrane was not collapsed and the implant's apexes were not protruded inside the sinus.

The mean VBG was  $6.52 \pm 1.71$  for the I-PRF group and  $9.81 \pm 2.47$  for  $\beta$ -TCP group after 6 months ( $T_6$ ). This is in agreement with the study by Gülsen and Dereci<sup>37</sup> who evaluated bone regeneration after MSFA with I-PRF carried by collagen plugs simultaneous with implant placement, after 6 months, CBCT revealed considerable mesial and distal bone growth. The same results were reported in a study by Leighton et al.<sup>50</sup> who used autologous fibrin glue with a collagen carrier as a sole filling material in lateral MSFA simultaneous with implant placement, the average VBG was 7.75 mm. Similarly in a study by Berberi et al.,<sup>53</sup> MSFA with ambient blood and an absorbable collagen sponge reported VBG of  $8.48 \pm 1.4$  anteriorly,  $7.98 \pm 1.04$  medially, and  $7.46 \pm 0.99$  posteriorly after 6 months before implant insertion.

VBG achieved in the  $\beta$ -TCP group agreed with a larger sample size study that reported VBG  $8.5 \pm 0.3$  mm at 6 months following MSFA with  $\beta$ -TCP and immediate implant placement.<sup>18</sup>

On the other hand, this study was not in agreement with Ahn et al.<sup>54</sup> study; where little to no new bone formed 6 months following MSFA with blood-soaked collagen sponges, but this could be due to delayed implant placement.

The mean FBH in the I-PRF group was  $10.96 \pm 1.50$  mm which coincident with the implant length (10 mm) with adequate new bone covering implants apexes. This is the same as Leighton et al.<sup>50</sup> who reported 12 mm FBH similar to the

length of implants simultaneously placed with lateral MSFA.

The mean FBH for the  $\beta$ -TCP group was  $14.08 \pm 2.32$  mm. Not in agreement with a study reported FBH of 12.03 mm after a two-stage MSFA with 100 %  $\beta$ -TCP, this could be due to the absence of implant support to the graft material during the 6 months of the healing period.<sup>55</sup>

In this context, it was considered important to preserve blood clot stability through the simultaneous implant placement and the association of the collagen sponge to maintain the space under the elevated sinus membrane.

Similar several studies that used collagen in MSFA showed the same encouraging results.<sup>56</sup> Also in a case study, the results obtained from an equine collagen sponge used in MSFA simultaneous with implant placement have been found comparable to those achieved with biomaterial application.<sup>57</sup>

Different than this study; no advantages were reported of the application of I-PRF to particulate bone graft,<sup>58</sup> or PRF to deproteinized bovine bone mineral in MSFA after a healing period of 6 months.<sup>59,60</sup> Similarly blood-derived GFs did not improve bone repair when associated with calcium phosphate in MSFA.<sup>61</sup>

In conclusion according to clinical and radiographic results of this study, using I-PRF with collagen carrier as a filling material in MSFA simultaneous with implant placement would have a mechanical function through preservation of the created space and prevention of premature sinus membrane collapse allowing time for the provisional matrix to develop into new bone tissue.

Furthermore, it has a biological function, as the concentrated GFs and leukocytes present in I-PRF can control the inflammatory process with an antimicrobial effect, enhance healing, cell proliferation, and differentiation, promote angiogenesis, and encourage remodeling.

#### 4.1. Conclusion

I-PRF with collagen carrier is an economical biomaterial that preserves the created subantral space with adequate new bone formation congruous to implant apexes. So, lateral MSFA using I-PRF and collagen carrier with simultaneous implant placement could be a simple, reliable, and predictable surgery with a high success rate that could be comparable to using  $\beta$ -TCP.

#### Conflicts of interest

There are no conflicts of interest.

## References

- [1] Awadalkreem F, Khalifa N, Satti A, Suleiman AM. The influence of immediately loaded basal implant treatment on patient satisfaction. *Int J Dent* 2020;2020:6590202.
- [2] Lekholm U, Zarb GA. Patient selection. In: Branemark PI, Zarb GA, Albrektsson T, editors. *Tissue Integrated Prostheses*. Chicago: Quintessence; 1985.
- [3] Buser D, Sennerby L, De Bruyn H. Modern implant dentistry based on osseointegration: 50 years of progress, current trends and open questions. *Periodontol* 2000 2017;73:7–21.
- [4] Starch-Jensen T, Aludden H, Hallman M, Dahlin C, Christensen AE, Mordenfeld A. A systematic review and meta-analysis of long-term studies (five or more years) assessing maxillary sinus floor augmentation. *Int J Oral Maxillofac Surg* 2018;47:103–16.
- [5] Al-Dajani M. Recent trends in sinus lift surgery and their clinical implications. *Clin Implant Dent Relat Res* 2016;18:204–12.
- [6] Jensen OT. Report of the sinus consensus conference of 1996. *Int J Oral Maxillofac Implant Quintessence Dent Implant* 1999;6:330–52.
- [7] Kawakami S, Lang NP, Ferri M, Alccayhuaman KAA, Botticelli D. Influence of the height of the antrum in sinus floor elevation assessed by cone beam computed tomography: a randomized clinical trial. *Int J Oral Maxillofac Implants* 2019;34:1.
- [8] Cricchio G, Palma VC, Faria PE, de Olivera JA, Lundgren S, Sennerby L, et al. Histological outcomes on the development of new space-making devices for maxillary sinus floor augmentation. *Clin Implant Dent Relat Res* 2011;13:224–30.
- [9] Schweikert M, Botticelli D, de Oliveira JA, Scala A, Salata LA, Lang NP. Use of a titanium device in lateral sinus floor elevation: an experimental study in monkeys. *Clin Oral Implants Res* 2012;23:100–5.
- [10] Omori Y, Botticelli D, Ferri M, Delgado-Ruiz R, Ferreira Balan V, Porfirio Xavier S. Argon bioactivation of implants installed simultaneously to maxillary sinus lifting without graft. An experimental study in rabbits. *Dent J* 2021;9:105.
- [11] Ye M, Liu W, Cheng S, Yan L. Outcomes of implants placed after osteotome sinus floor elevation without bone grafts: a systematic review and meta-analysis of single-arm studies. *Int. J. Implant Dent*. 2021;7:1–14.
- [12] Ekhlasmandkermani M, Amid R, Kadkhodazadeh M, Hajizadeh F, Abed PF, Kheiri L, et al. Sinus floor elevation and simultaneous implant placement in fresh extraction sockets: a systematic review of clinical data. *J Korean Assoc Oral Maxillofac Surg* 2021;47:411–26.
- [13] Busenlechner D, Huber CD, Vasak C, Dobsak A, Gruber R, Watzek G. Sinus augmentation analysis revised: the gradient of graft consolidation. *Clin Oral Implants Res* 2009;20:1078–83.
- [14] Shahidi S, Zamiri B, Danaei SM, Salehi S, Hamedani S. Evaluation of anatomic variations in maxillary sinus with the aid of cone beam computed tomography (CBCT) in a population in south of Iran. *J Dent* 2016;17:7.
- [15] Dobeles I, Kise L, Apse P, Kragis G, Bigestans A. Radiographic assessment of findings in the maxillary sinus using cone-beam computed tomography. *Stomatol Balt Dent Maxillofac J* 2013;15:119.
- [16] Stern A, Green J. Sinus lift procedures: an overview of current techniques. *Dent Clin* 2012;56:219–33.
- [17] Ogose A, Kondo N, Umezu H, Hotta T, Kawashima H, Tokunaga K, et al. Histological assessment in grafts of highly purified beta-tricalcium phosphate (OSferion®) in human bones. *Biomaterials* 2006;27:1542–9.
- [18] Aragonese Lamas JM, Sánchez MG, González LC, Suárez García A, Aragonese Sánchez J. Vertical bone gain after sinus lift procedures with beta-tricalcium phosphate and simultaneous implant placement—a cross-sectional study. *Medicina (B Aires)* 2020;56:609.
- [19] Loin J, Kün-Darbois JD, Guillaume B, Badja S, Libouban H, Chappard D. Maxillary sinus floor elevation using Beta-Tri-calcium-Phosphate (beta-TCP) or natural bone: same inflammatory response. *J Mater Sci Mater Med* 2019;30:1–6.
- [20] Zhang D, Wu X, Chen J, Lin K. The development of collagen based composite scaffolds for bone regeneration. *Bioact Mater* 2018;3:129–38.
- [21] Tabata Y. Biomaterial technology for tissue engineering applications. *J R Soc Interface* 2009;6(suppl\_3):S311–24.
- [22] Marconcini S, Denaro M, Cosola S, Gabriele M, Toti P, Mijiritsky E, et al. Myofibroblast gene expression profile after tooth extraction in the rabbit. *Materials* 2019;12:3697.
- [23] Cosola S, Di Dino B, Traini T, Kim YS, Park YM, Marconcini S, et al. Radiographic and histomorphologic evaluation of the maxillary bone after crestal mini sinus lift using absorbable collagen—retrospective evaluation. *Dent J* 2022;10:58.
- [24] Saluja H, Dehane V, Mahindra U. Platelet-rich fibrin: a second generation platelet concentrate and a new friend of oral and maxillofacial surgeons. *Ann Maxillofac Surg* 2011;1:53.
- [25] Borie E, Olivé DG, Orsi IA, Garlet K, Weber B, Beltrán V, et al. Platelet-rich fibrin application in dentistry: a literature review. *Int J Clin Exp Med* 2015;8:7922.
- [26] Jeon YR, Kim MJ, Kim YO, Roh TS, Lee WJ, Kang EH, et al. Scaffold free bone regeneration using platelet-rich fibrin in calvarial defect model. *J Craniofac Surg* 2018;29:251–4.
- [27] Kim J, Ha Y, Kang NH. Effects of growth factors from platelet-rich fibrin on the bone regeneration. *J Craniofac Surg* 2017;28:860–5.
- [28] Ali S, Bakry SA, Abd-Elhakam H. Platelet-rich fibrin in maxillary sinus augmentation: a systematic review. *J Oral Implantol* 2015;41:746–53.
- [29] Castro AB, Meschi N, Temmerman A, Pinto N, Lambrechts P, Teughels W, et al. Regenerative potential of leucocyte- and platelet-rich fibrin. Part B: sinus floor elevation, alveolar ridge preservation and implant therapy. A systematic review. *J Clin Periodontol* 2017;44:225–34.
- [30] Choukroun J, Ghanaati S. Reduction of relative centrifugation force within injectable platelet-rich-fibrin (PRF) concentrates advances patients' own inflammatory cells, platelets and growth factors: the first introduction to the low speed centrifugation concept. *Eur J Trauma Emerg Surg* 2018;44:87–95.
- [31] Wend S, Kubesch A, Orłowska A, Al-Maawi S, Zender N, Dias A, et al. Reduction of the relative centrifugal force influences cell number and growth factor release within injectable PRF-based matrices. *J Mater Sci Mater Med* 2017;28:1–11.
- [32] Wang X, Zhang Y, Choukroun J, Ghanaati S, Miron RJ. Behavior of gingival fibroblasts on titanium implant surfaces in combination with either injectable-PRF or PRP. *Int J Mol Sci* 2017;18:331.
- [33] de Almeida VH, de Araujo RF, Vasconcelos RC, Garcia VB, de Souza LB, de Araujo AA. Histological preparation technique of blood derivative injectable platelet-rich fibrin (I-Prf) for microscopic analyzes. *J Cytol Histol* 2018;9:1000506.
- [34] Thanasisuebwong P, Surarit R, Bencharit S, Ruangwasdi N. Influence of fractionation methods on physical and biological properties of injectable platelet-rich fibrin: an exploratory study. *Int J Mol Sci* 2019;20:1657.
- [35] Hwang D, Wang HL. Medical contraindications to implant therapy: part I: absolute contraindications. *Implant Dent* 2006;15:353–60.
- [36] Pignataro L, Mantovani M, Torretta S, Felisati G, Sambataro G. ENT assessment in the integrated management of candidate for (maxillary) sinus lift. *Acta Otorhinolaryngol Ital* 2008;28:110.
- [37] Gülsen U, Ö Dereci. Evaluation of new bone formation in sinus floor augmentation with injectable platelet-rich fibrin—soaked collagen plug: a pilot study. *Implant Dent* 2019;28:220–5.
- [38] Rahpeyma A, Kajeahmadi S. Open sinus lift surgery and the importance of preoperative cone-beam computed

- tomography scan: a review – PubMed. *J Int Oral Heal* 2015; 127:7–9.
- [39] Pinto N, Quirynen M. RE: optimized platelet-rich fibrin with the low-speed concept: growth factor release, biocompatibility, and cellular response. *J Periodontol* 2019;90:119–21.
- [40] Raghoobar GM, Onclin P, Boven GC, Vissink A, Meijer HJA. Long-term effectiveness of maxillary sinus floor augmentation: a systematic review and meta-analysis. *J Clin Periodontol* 2019;46:307–18.
- [41] Sheikh Z, Hamdan N, Ikeda Y, Grynypas M, Ganss B, Glogauer M. Natural graft tissues and synthetic biomaterials for periodontal and alveolar bone reconstructive applications: a review. *Biomater Res* 2017;21:9.
- [42] Ahmed TAE, Dare EV, Hincke M. Fibrin: a versatile scaffold for tissue engineering applications. *Tissue Eng Part B Rev* 2008;14:199–215.
- [43] Watanabe T, Isobe K, Suzuki T, Kawabata H, Nakamura M, Tsukioka T, et al. An evaluation of the accuracy of the subtraction method used for determining platelet counts in advanced platelet-rich fibrin and concentrated growth factor preparations. *Dent J* 2017;5:7.
- [44] Atalay B. Sinus lifting and leucocyte- and platelet-rich fibrin [Internet]. In: *Challenging Issues on Paranasal Sinuses*. IntechOpen; 2019. <https://doi.org/10.5772/intechopen.81163>. Available from: . [Accessed 15 June 2023].
- [45] Ghanaati S, Booms P, Orlowska A, Kubesch A, Lorenz J, Rutkowski J, et al. Advanced platelet-rich fibrin: a new concept for cell-based tissue engineering by means of inflammatory cells. *J Oral Implantol* 2014;40:679–89.
- [46] Miron RJ, Fujioka-Kobayashi M, Hernandez M, Kandalam U, Zhang Y, Ghanaati S, et al. Injectable platelet rich fibrin (i-PRF): opportunities in regenerative dentistry? *Clin Oral Invest* 2017;21:2619–27.
- [47] Sampath TK, Reddi AH. Importance of geometry of the extracellular matrix in endochondral bone differentiation. *J Cell Biol* 1984;98:2192–7.
- [48] Fernandez de Grado G, Keller L, Idoux-Gillet Y, Wagner Q, Musset AM, Benkirane-Jessel N, et al. Bone substitutes: a review of their characteristics, clinical use, and perspectives for large bone defects management. *J Tissue Eng* 2018;9: 2041731418776819.
- [49] Blomqvist JE, Alberius P, Isaksson S. Retrospective analysis of one-stage maxillary sinus augmentation with endosseous implants. *Int J Oral Maxillofac Implants* 1996;11:4.
- [50] Leighton Y, Weber B, Rosas E, Pinto N, Borie E. Autologous fibrin glue with collagen carrier during maxillary sinus lift procedure. *J Craniofac Surg* 2019;30:843–5.
- [51] Thor A, Sennerby L, Hirsch JM, Rasmusson L. Bone formation at the maxillary sinus floor following simultaneous elevation of the mucosal lining and implant installation without graft material: an evaluation of 20 patients treated with 44 astra tech implants. *J Oral Maxillofac Surg* 2007;65(7, Supplement):64–72.
- [52] Han JJ, Moon JE, Lee EH, Yang HJ, Hwang SJ. Clinical and radiographic outcomes of dental implant after maxillary sinus floor augmentation with rhBMP-2/hydroxyapatite compared to deproteinized bovine bone. *PLoS One* 2022;17: e0273399.
- [53] Berberi A, Nader N, Assaf RB, Fayyad-Kazan H, Khairallah S, Moukarzel N. Sinus floor augmentation with ambient blood and an absorbable collagen sponge: a prospective pilot clinical study. *Implant Dent* 2017;26:674–81.
- [54] Ahn JJ, Cho SA, Byrne G, Kim JH, Shin HI. New bone formation following sinus membrane elevation without bone grafting: histologic findings in humans. *Int J Oral Maxillofac Implants* 2011;26:1.
- [55] Jelusic D, Zirk ML, Fienitz T, Plancak D, Puhar I, Rothamel D. Monophasic  $\beta$ -TCP vs. biphasic HA/ $\beta$ -TCP in two-stage sinus floor augmentation procedures - a prospective randomized clinical trial. *Clin Oral Implants Res* 2017;28: e175–83.
- [56] Triplett RG, Nevins M, Marx RE, Spagnoli DB, Oates TW, Moy PK, et al. Pivotal, randomized, parallel evaluation of recombinant human bone morphogenetic protein-2/ absorbable collagen sponge and autogenous bone graft for maxillary sinus floor augmentation. *J Oral Maxillofac Surg* 2009;67:1947–60.
- [57] Chipaila N, Marini R, Sfasciotti GL, Cielo A, Bonanome L, Monaco A. Graftless sinus augmentation technique with contextual placement of implants: a case report. *J Med Case Rep* 2014;8:1–11.
- [58] Noronha Oliveira M, Varela HA, Caramês JM, Silva F, Henriques B, Teughels W, et al. Synergistic benefits on combining injectable platelet-rich fibrin and bone graft porous particulate materials. *Biomed Mater Devices* 2022;1:426–42.
- [59] Zhang Y, Tangl S, Huber CD, Lin Y, Qiu L, Rausch-Fan X. Effects of Choukroun's platelet-rich fibrin on bone regeneration in combination with deproteinized bovine bone mineral in maxillary sinus augmentation: a histological and histomorphometric study. *J Cranio-Maxillofacial Surg* 2012; 40:321–8.
- [60] Nizam N, Eren G, Akcalı A, Donos N. Maxillary sinus augmentation with leukocyte and platelet-rich fibrin and deproteinized bovine bone mineral: a split-mouth histological and histomorphometric study. *Clin Oral Implants Res* 2018;29:67–75.
- [61] de Almeida Barros Mourão CF, Lourenço ES, Nascimento JRB, Machado RCM, Rossi AM, Leite PEC, et al. Does the association of blood-derived growth factors to nanostructured carbonated hydroxyapatite contributes to the maxillary sinus floor elevation? A randomized clinical trial. *Clin Oral Invest* 2019;23:369–79.