Autologous leucocyte and platelet rich in fibrin (L-PRF) – is it a competitive solution for bone augmentation in maxillary sinus lift? A 6-month radiological comparison between xenografts and L-PRF

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Abstract

Maxillary lateral sinus floor elevation, or external sinus lift, is a widespread surgical intervention in the dental field. Insertion of implants in the posterior region of the maxilla often requires reconstruction of the remaining native bone that has insufficient volume.

Background and aims. Much of the research published involves using artificial products, like xenografts and resorbable collagen membranes, after a prior Cone Beam Computer Tomography (CBCT) investigation. Nowadays, more accessible access, less financial costs, a biological approach, and faster healing are objectives that surround this procedure. Leucocytes and platelets rich in Fibrin (L-PRF) are a natural component with a high concentration of growth factors. Due to its regenerative properties and lack of complications, it is used in several medical fields, like orthopedics, dermatology, and oral surgery. This retrospective study aims to compare results in bone height and volume obtained through external sinus lift, either by using xenografts or autologous plasma rich in fibrin, by evaluating the quantity of new bone formation from a radiological point of view.

Methods. Fifty-eight Caucasian patients were included in this retrospective study; 48 were submitted to xenograft procedure, and 10 were selected for L-PRF grafting material with simultaneous implant placement. Lack of clinical and histological studies performed on patients with L-PRF surgeries limited us in choosing a larger group for the radiological analysis. CBCT evaluation was performed before surgery and 6 months after. All patients selected for the study presented good general and oral health, acute oral and sinus infections excluded; smoking and periodontal disease were also criteria of exclusion. Two operators performed the measurements in pre-established landmarks in different time frames. The two independent groups were compared with the Wilcoxon rank-sum test for quantitative data. Qualitative characteristics were described as counts and percentages. All analyses were performed in an R environment for statistical computing and graphics.

Results. Mean bone height gain in the xenograft group in the regions was as follows: 7.44 for the anterior landmark, 12.14 for the median and 8.28 for the distal. The mean group height gained for the L-PRF group was 0.1 anteriorly, -0.18 for the median measurement, and 0.23 distally. We obtained excellent overall reliability for all the height measurements between the two operators.

Conclusions. Further studies must be conducted to establish new sets of surgical protocols in case L-PRF alone is found to be a reliable, stable, biological alternative to the well-documented xenografts in external sinus lifts. Radiological results, although promising, must be further applied in long term clinical survival of the implants in the grafted sites. Also, studies combining L-PRF in conjunction with xenograft might bring improved clinical results in terms of reduced postoperative complications and accelerated healing.

Keywords: dental implant, bone grafting, xenograft material, L-PRF, sinus lift, radiological imaging

Background and aims

Maxillary sinus augmentation (MSA), also known as sinus lift (SL), is a predictable surgical manoeuvre to reconstruct the atrophic posterior maxillary alveolar ridge, for future implant placement in edentulous patients, ensuring final fixed restorations [1,2,3]. Following tooth loss, pneumatisation of the maxillary leads to the necessity of a bone grafting surgery. This procedure involves the elevation of the Schneiderian membrane through either a lateral window on the alveolar ridge (lateral sinus lift) or a transalveolar (internal) sinus lift [4].

The decision between the two techniques depends on the quantity of the remaining native bone, skills and experience of the practitioner, and anatomical conditions of the sinus: presence of cysts within the sinus cavity, presence of one or more septa, acute palatal-nasal recess, trajectory of the superior posterior alveolar artery and its branches (alveolar antral artery) [5-7]. To accurately assess the anatomical conditions of the sinus, the golden standard imagistic evaluation is considered the CBCT (Cone Beam Computer Tomography) [8,9]. CBCT provides valuable and significant information to the surgeon, apart from the ones mentioned before, such as lateral bone wall thickness, Schneiderian membrane thickness, maxillary sinus angle, and maxillary sinus septa [8].

Once the sinus membrane is elevated, the missing bone can be reconstructed through several approaches. Many techniques have been described, and the implant success and survival rates have been counted. Bone grafts are divided into four main categories: xenografts, allografts, alloplasts and autologous grafts. Various combinations were studied: recombinant human bone morphogenetic protein-2 in an absorbable collagen sponge carrier, recombinant human platelet-derived growth factor-BB in combination with freeze-dried bone allograft or beta-tricalcium phosphate, autologous cell therapy [10,11]. In most cases, the quantity required for autologous bone is too significant. It involves a secondary surgical site, such as the iliac crest, which is a more painful, higher-risk approach for the patient. This is the main reason researchers worldwide focused their attention on different alternatives. One of the most scientifically studied and documented commercial xenografts of bovine origin is Bio-Oss® (Geistlich Pharma AG, Wolhusen, Switzerland), used for bone regeneration. Therefore, it is frequently compared to other alternatives and combinations [12,13]. One treatment alternative to xenograft might be the autologous growth factors obtained from platelet concentrate, which is leucocyte and platelet-rich fibrin (L-PRF). This "bioactive" material might be another option in sinus lift procedure , used as a sole grafting material or in conjunction with bone substitutes [14]. There are two very different approaches: one that has excellent clinical results over the years but involves certain cost materials and fewer biological components, and the second, which compensates for the first one's drawbacks, but fewer studies are published on the amount of bone obtained and its stability. L-PRF alone, in maxillary sinus lift with simultaneous implant placement, is a procedure that lacks clinical, radiological and histological outcomes. Concise, repeatable surgical procedures must be established to have evidenced-based results.

This study compared the effectiveness of two different grafting materials for the maxillary sinus floor augmentation regarding radiographical outcomes. The comparison implied the analysis of the 3D images captured by the CBCT of pre-operative residual alveolar ridge with the postoperative situation of lateral sinus floor augmentation performed either with xenografts (Bio-Oss, Geitslich Pharma AG) together with resorbable collagen membrane (Bio-Gide, Geitslich Pharma AG) or with Leucocyte Platelet Rich In Fibrin (PRF) with simultaneous implant placement. L-PRF was chosen over other platelet derivatives for this study due to its obtention process: without any anticoagulants, bovine thrombin, additives or any jellifying agents during the centrifugation process [15]. Many platelet concentrates were investigated for their potential in regenerative medicine, having angiogenic properties [16]. Diminishing external components brings accuracy in evaluating L-PRF alone strength in promoting tissue repair. This pure, bioactive, autologous material needs to be investigated more, especially in bone formation, where there is less evidence. Nevertheless, we added one more objective to our study: establishing repetitive landmarks in several points for overall reliability between two or more raters.

Methods

Patients. The retrospective study included 58 patients (26 males and 32 females) with insufficient native bone in the posterior alveolar ridge. The surgical procedure chosen for this group of patients was sinus floor elevation through the lateral window technique. CBCT evaluation was performed on all the patients before surgery. Residual native bone was measured, anatomical particularities were noted, and the number of implants for future prosthodontic treatment was discussed with the patient.

All patients signed an informed consent, and the study was approved by the Ethical Committee of the Iuliu Hatieganu University of Medicine and Pharmacy 81/11.03.2019. A group of 48 patients benefitted from the same xenografts' materials, Bio-Oss from Geitslich Pharma AG combined with resorbable collagen membrane (Bio-Gide, Geitslich Pharma AG), and 10 patients were treated with Platelet Rich in Fibrin and simultaneous implant placement in all cases included.

We included two groups in the study, in order to compare two types of materials used in sinus floor augmentation. The xenograft group included 48 patients. The bovine bone material used for the sinus lift procedure is considered the gold standard for xenograft material in maxillary sinus augmentation [17,18]. The l-PRF group is still under research

according to the literature, consequently fewer patients were selected. Expanding the testing group is considered depending on the long-term stability of these results.

The inclusion criteria were:

1. Patients missing more than one tooth on the posterior maxillary site and consent to receive implant therapy and regenerative procedures,
2. Good oral health, with no dental or periodontal active diseases that might have a negative impact on postoperative healing,
3. Class V – VI Cawood atrophy, with 5-7 mm in height, vertically measured between the mid buccal to oral distance of the alveolar crest and the sinus floor, and horizontally, at equal distance between the most anterior and posterior points of the sinus delimitating the edentulous space.
4. Less than 5 mm Schneiderian membrane thickness,
5. After the procedure, during the 240-day healing time, the patients did not wear any provisional removable partial denture or fixed prosthesis.

The exclusion criteria were the following:

1. Dentures after the surgery,
2. Maxillary sinus diseases, including chronic sinusitis, infection of the ear, nose, throat,
3. Systemic diseases, like uncontrolled diabetes and osteoporosis, treated with bisphosphonates, anticoagulants, and chemo-radio therapy,
4. Long-term smokers,
5. Pregnancy.

Surgical procedure for the xenograft

Patient preparation: Before surgery, patients were given oral antibiotics, amoxicillin with clavulanic acid, 1 gram twice a day, starting 24 hours before the surgery, CBCT evaluation of the sinus performed to exclude any sinus infection that might affect the outcome, preoperative disinfection of the skin with an antiseptic solution and mouth rinses with chlorhexidine 0.12% for 2 minutes, use of sterile draping and infection-control protocol, salivary-contamination prevention for bone graft and collagen membrane, avoiding of bone overheating, by using a rinse of the surgical area with sterile saline solution, use of two sets of sterile surgical instruments, one for the flap elevation and the other one for the grafting step. A conventional lateral approach was performed for all the patients. The full-thickness flap was elevated. A lateral trap door was designed in the lateral sinus wall with the aid of piezosurgery to minimize the risks of perforating the sinus membrane. Several curettes were used to detach the sinus membrane from the walls. A double-layer technique was used, and a resorbable collagen membrane was placed inside the sinus to protect the intact detached sinus membrane. Simultaneous implant placement was performed. In our xenograft sinus lift cases, we used Bio-Oss (Geitslich Pharma AG), size L particles (1-2 mm), collagen resorbable membrane, pins from Frios, and Dentsply. After grafting, before the sutures were in place, the bone lateral window harvested at the beginning of the surgery was placed into its initial position. Resorbable sutures were used from Glycolon, Resorba. Postoperative medication included antibiotic therapy with amoxicillin/Clavulanic acid 1 gram twice a day for 7 days combined with Metronidazole 250 mg three times a day, non-steroidal anti-inflammatory drugs, mouthwash with chlorhexidine for two weeks.

The technique used for the preparation of L-PRF

Patient preparation: identification of the vein, placing a tourniquet 3-4 cm above the puncture place, disinfection of the prelevation site with alcohol swabs, peripheral blood collection from the median cubital, cephalic, or basic veins from the antecubital fossa by using a bevelled needle or butterfly needle, inserted at 30 degrees into the vein (according to the world health organization blood draw guideline) [19]. Blood preparation: A-PRF matrix 10 ml glass, free from any additives (Pro-Cell) tubes, was used in a DLAB DM0412 Centrifuge (Figure 1). The original L-PRF protocol from Choukroun and Dohan [20,21], describes an RCF (relative centrifugal force) of 408 g and a centrifugation time of 12 minutes for an IntraSpin Centrifuge set to 2700 rpm. We applied the formula set by Pinto and Quirynen, Miron et al. [22], RCF = 11.18 x r x $(N/1000)^2$. The L-PRF clot obtained in the middle of the tube depends on the angulation of the tube in the centrifuge, the time of spinning, the speed and the g-force. For the above equation, r is the centimetres radius from the rotor's centre to the sample during centrifugation, and N is the rotor speed in rpm. Considering all this, we set our centrifuge to 2300 rpm and 15 minutes. The PRF clots obtained through the centrifugation process were separated from the red blood cells, placed in the PRF box and compressed. The result was several membranes of L-PRF, which were carefully inserted inside the sinus. The surgical technique used for elevating the sinus membrane was the same as for the xenograft group. Simultaneous implant placement was performed. The lateral trap door detached from the sinus wall was placed into its initial harvested site. L-PRF membranes were used as much as possible, with a minimum of 8 to 10 membranes per sinus, to ensure proper support for the naturally detached sinus membrane. The literature lacks evidence regarding a specific number or quantity of L-PRF membranes to be used in such cases.

The surgeries for all the cases studied went without any accidents or immediate complications. All patients received professional cleaning one day before surgery to lower intraoral bacteria levels. No postoperative complications were noted for the patients included in the study.

(a) **(b)**

Figure 1. L-PRF preparation. (a) PRF Box specially designed to press the L-PRF clot; (b) Removal of the L-PRF clot from the other components of the blood.

CBCT measurments

This study used CBCT data (OnDemand3D Dental, CyberMed, Korea, Soredex-Cranex) obtained before surgery and six months after. According to the instructions provided by the manufacturer, we used a field of view of 9x12 cm, an X-ray tube voltage of 85KV, an X-ray tube current of 4mA, and a section thickness of 0.5 mm. Residual native bone was measured on the CBCT sections before starting the surgery, in both cases, xenografts or L-PRF. The OnDemand 3D software presents a Dental module that offers the practitioner multiple measurement sections, including axial and cross-sectional. In the axial arch/curve function, we used the midpoints of the present teeth, including the midpoint of the tooth pulp chamber, mesial and distal surfaces, continuing with the midpoint of the alveolar ridge, ensuring equal distance to the buccal and lingual wall of the crest. Then, we evaluated the height of the residual crest in three points: the anterior landmark corresponded to the anterior wall of the sinus or the distal surface of the adjacent tooth (Figure 2 a, b, c), if present, the median milestone corresponded to the middle of the edentulous site, the posterior landmark was measured to the most posterior benchmark grafted or mesial surface of the adjacent tooth, if present (Figure 3). The height of the native residual bone was measured from the alveolar crest and maxillary sinus floor in the previously mentioned points. The distance between the crest edge and the sinus floor was performed in the axis of the crest, at an equal distance between the buccal and oral bone cortical.

Two clinicians, both oral surgeons, performed the measurements but in different time frames.

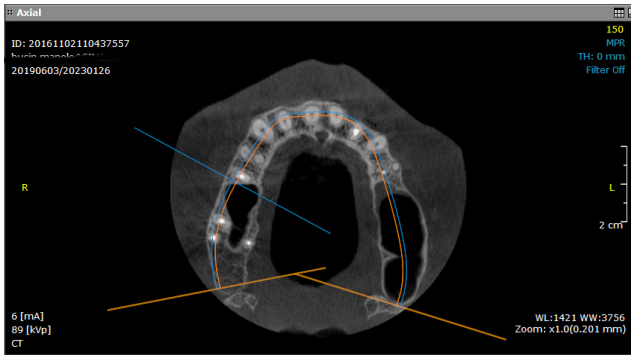

Figure 2. (a) Axial view of the anterior landmark – distal surface of the adjacent tooth.

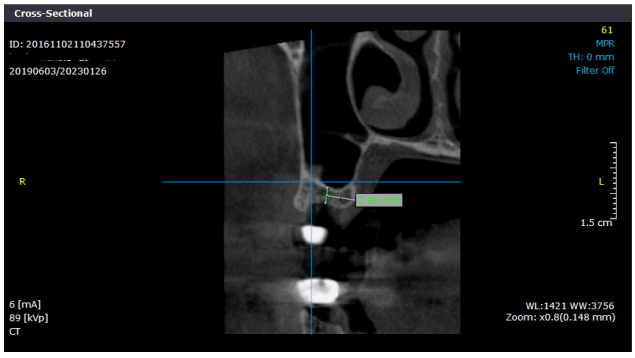

Figure 2. (b) Cross sectional measurement of the anterior landmark, distal surface of the adjacent tooth – between the mid-distance of the buccal and oral cortical of the edentulous crest and the sinus floor.

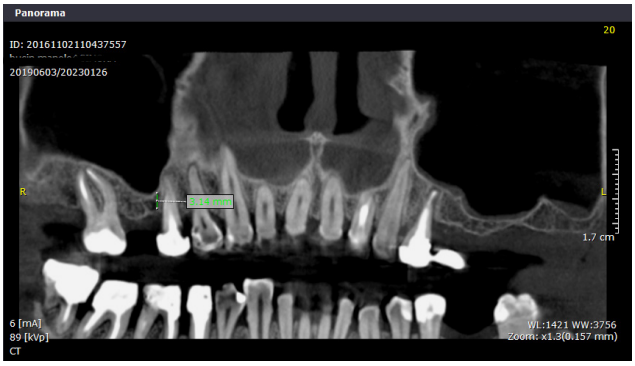

Figure 2. (c). Panorama view of the measurement made on the distal surface of the adjacent tooth.

Six months after the surgery, new CBCT data were acquired for all the cases. The radiological measurements were performed before loading the implants. The same clinicians were responsible for the measurements at different time points. The same software was used. In the axial plane of the CBCT, we marked the midpoint of the mesial and distal surfaces of the present teeth, including the mid-point of the implant, if placed. On the axial and coronal axis section we re-measured the new anterior, median and posterior height obtained after the grafting, starting from the same point of the alveolar crest, having the same anterior landmark, corresponding to the anterior wall of the sinus, or distal surface of the tooth (Figure 4); median distance corresponds to the highest top of the sinus grafted (dome) or the apical point of the implant for the L-PRF sinus with simultaneous implant placement (Figure 5), posterior landmark corresponded to the most posterior wall of the sinus grafted, or the mesial surface of the adjacent tooth (Figure 6).

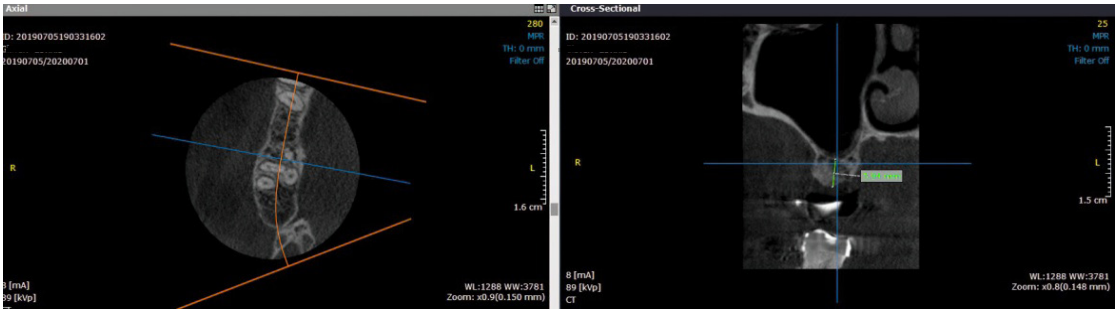

Figure 3. Preoperative CBCT evaluation of distal bone height of the edentulous site.

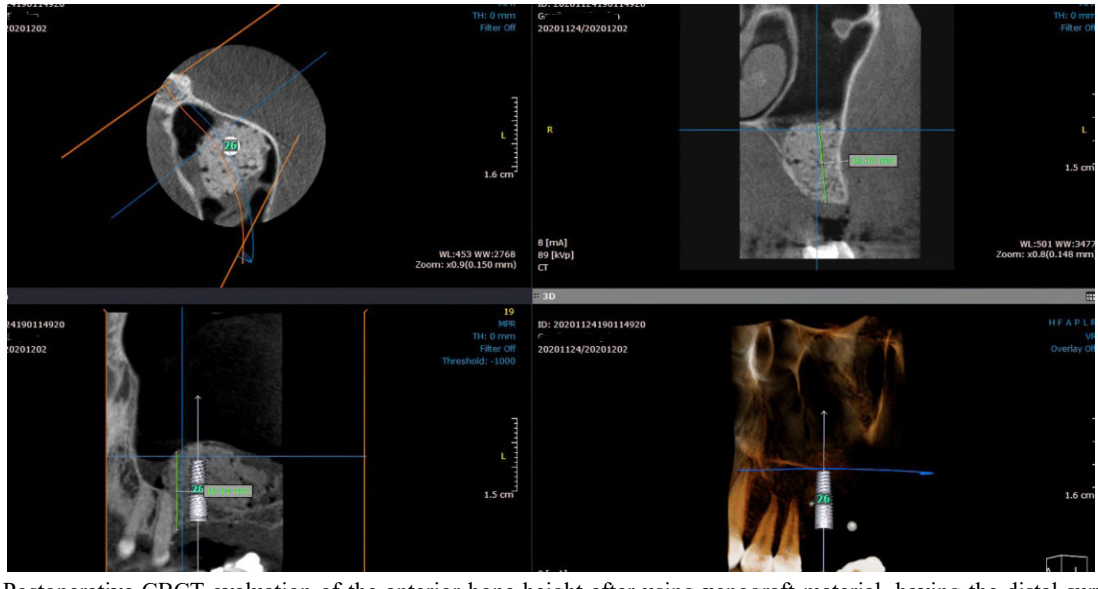

Figure 4. Postoperative CBCT evaluation of the anterior bone height after using xenograft material, having the distal surface of the adjacent tooth as a landmark.

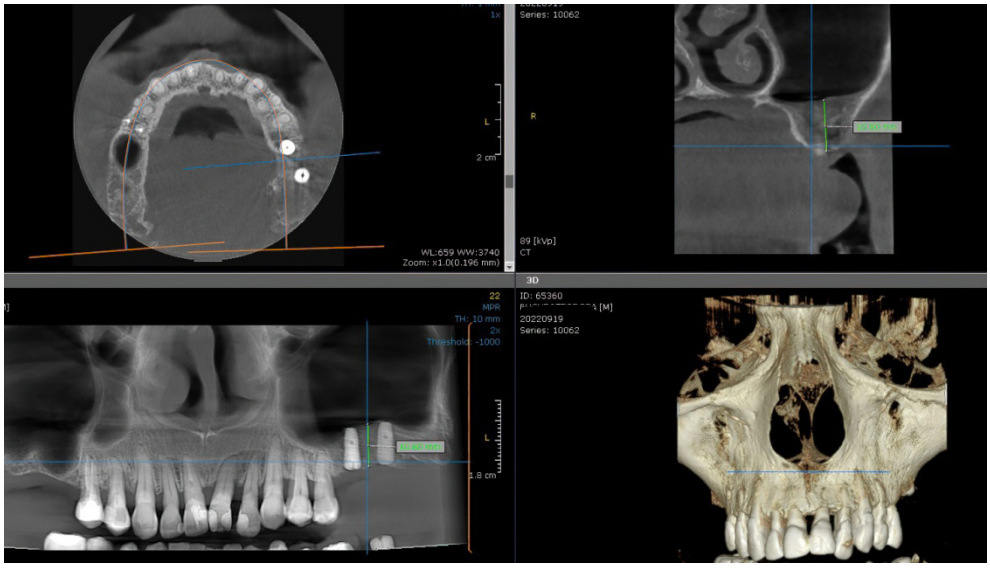

Figure 5. Postoperative CBCT measurement of the median distance that corresponds to the highest top of the sinus grafted (dome) or the apical point of the implant for the L-PRF sinus with simultaneous implant placement. The CBCT sotware provides multiple types of sections, cross-sectional, axial, panoramic.

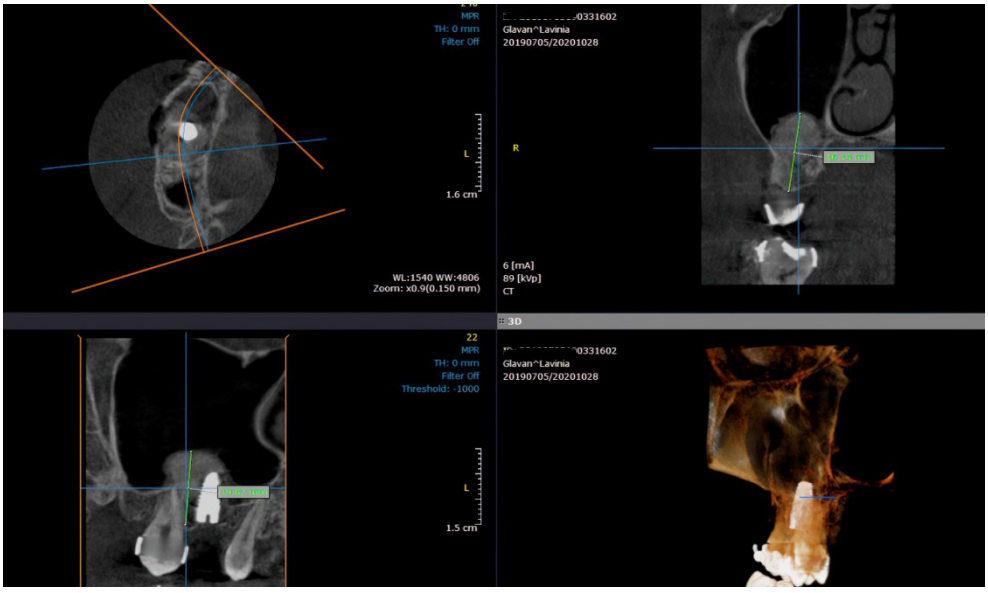

Figure 6. Postoperative CBCT measurement of the distal bone height of the edentulous site using xenograft materials.

Statistical analysis

Qualitative characteristics were described as counts and percentages. Quantitative characteristics were described by medians and the first and third quartiles (IQR). The two independent groups were compared with a chi-square test for qualitative data. Comparisons between the two independent groups were conducted with the Wilcoxon rank-sum test for quantitative data that did not follow the normal distribution. The intrarater reliability between the two raters was computed with the interclass correlation coefficient (computed considering agreement, a single unit of analysis, and the two-way model). We considered values between 0.50 and 0.75, indicating moderate reliability; values between 0.75 and 0.90, indicating good reliability; and values above 0.90, indicating excellent reliability [23]. A p-value less than 0.05 was considered statistically significant. The two-tailed p-values were computed for all statistical tests. All

analyses were performed in R environment for statistical computing and graphics (R Foundation for Statistical Computing, Vienna, Austria), version 4.3.1 [24]. A post-hoc power analysis was performed in GPower 3.1.9.7, for each of the three comparisons regarding post-preoperatory height differences (anterior, distal, median), between the two groups (L-PRF and xenograft). The parameters of the power analyses were: a Mann-Whitney test, with a two-tailed p-value, an alpha level of 0.05, the two sample sizes, with a difference between the two sample sizes, the observed means on the study data, as well as the standard deviation within each group.

Results

The preoperative values for anterior, distal, and median heights were statistically significantly lower for the xenograft participants than the PRF participants. The postoperative values for anterior, distal, and median height were statistically significantly higher for the xenograft participants than the PRF participants. The differences between the postoperative and preoperative values for anterior, distal, and median height were statistically significantly higher for the xenograft participants than the PRF participants (Table I).

Due to imbalances between samples we performed a post-hoc power analysis for each of the three comparisons regarding post-preoperative height differences (anterior, distal, median), between the two groups (L-PRF and xenograft). The power values for the three tests were: 0.999, 0.997, and 0.999, all beeing very high.

The mean bone height gain for the xenograft group in the anterior region was 7.44 mm (Figure 7), for the median landmark, 12.14 mm (Figure 8) and 8.28 mm for the distal one (Figure 9).

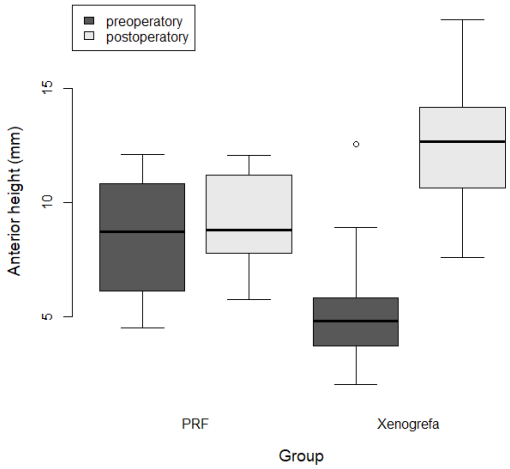

Figure 7. Anterior height pre-postoperative evolution by group.

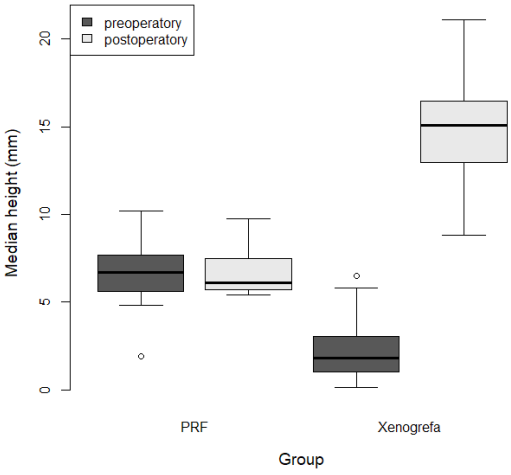

Figure 8. Median height pre-postoperative evolution by group.

Table I. Patient characteristics.

Characteristics	L-PRF (n=10)	Xenograft (n=48)	Difference (95% CI)	P
Age (years), median (IQR)	52.5 (35.75 - 63)	44.5 (36.75 - 52)	8 (-5 - 15)	0.313
Sex (F), n (%)	7 (70)	25 (52.08)		0.487
Anterior height (mm), median (IQR)				
preoperative	8.72 (6.58 - 10.49)	4.78 (3.73 - 5.76)	3.93 (2.08 - 5.51)	< 0.001
postoperative	8.78 (7.94 - 10.96)	12.69 (10.68 - 14.16)	3.9 (-5.19 - -1.73)	< 0.001
Difference post-preoperative	0.1 (-0.16 - 0.74)	7.44 (5.67 - 9.21)	7.34 (-8.66 - -5.59)	< 0.001
Distal height (mm), median (IQR)				
preoperative	6.05 (4.42 - 7.18)	3.4 (2.26 - 4.52)	2.65 (0.72 - 3.85)	0.005
postoperative	6.46 (5.16 - 7.19)	12.56 (10.46 - 13.92)	6.1 (-7.39 - -3.82)	< 0.001
Difference post-preoperative	0.23 (-0.06 - 0.79)	8.28 (6.54 - 10.61)	8.05 (-9.71 - -6.06)	< 0.001
Median height (mm), median (IQR)				
preoperative	6.69 (5.7 - 7.53)	1.79 (1 - 3.02)	4.9 (3.37 - 5.87)	< 0.001
postoperative	6.12 (5.76 - 7.17)	15.08 (13.02 - 16.41)	8.96 (-9.59 - -6.19)	< 0.001
Difference post-preoperatoy	-0.18 (-0.53 - 0.07)	12.14 (10.86 - 13.96)	12.32 (-13.47 - -11.06)	< 0.001

L-PRF, platelet rich in fibrin; IQR, interquartile range; CI, confidence interval.

Table II. Reliability between two raters.

Characteristic	ICC 95% CI	p-value
Anterior preoperative height (mm)	0.764 (0.632 - 0.853)	< 0.001
Median preoperative height (mm)	0.628 (0.405 - 0.773)	< 0.001
Distal preoperative height (mm)	0.66 (0.485 - 0.784)	< 0.001
Anterior postoperative height (mm)	0.77 (0.632 - 0.859)	< 0.001
Median postoperative height (mm)	0.861 (0.767 - 0.918)	< 0.001
Distal postoperative height (mm)	0.841 (0.746 - 0.903)	< 0.001
Overall heights	0.921 (0.896 - 0.939)	< 0.001
Postoperative volume (cc)	0.948 (0.909 - 0.97)	< 0.001

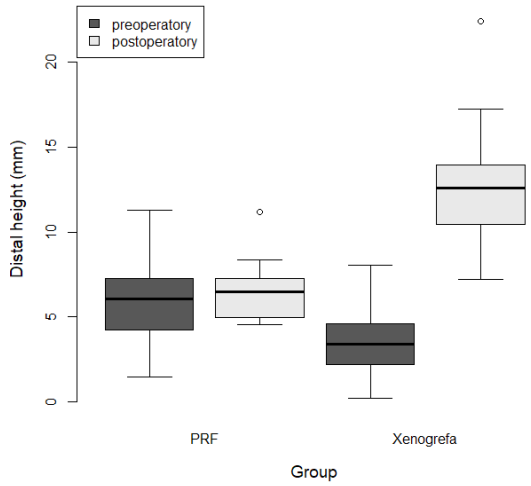

Figure 9. Distal height pre-postoperative evolution by group.

For the PRF group, the anterior and distal landmarks present a mean height gain of bone between 0.1 and 0.23 mm, with a mean loss in the median region of 0.18 mm.

There were no statistically significant differences between the participants receiving L-PRF and Xenograft concerning age and sex.

There was moderate reliability between the two raters concerning the measuring of preoperative median and distal heights, good reliability for the anterior preoperative heights and all the postoperative heights (anterior, median, and distal), and excellent reliability for the postoperator volume. Concerning the overall reliability for all height measurements, it was excellent (Table II).

Discussion

A resorption of the alveolar process follows tooth loss in width and height, which subsequently translates into insufficient bone for implant treatment. In the posterior region of the maxilla, apart from the resorption of native bone, a process called pneumatization (positive air pressure during respiration) accentuates the lack of bone for the implant insertion due to the migration of the maxillary sinus floor to a more inferior position, close to the alveolar mucosa [25,26]. Grafting procedures are mandatory to ensure the proper implant placement. In the 80s`, we found the first authors to publish scientific work on sinus floor elevation with autologous bone harvested from extraoral donor sites and later with bone from intraoral sites [27,28]. Although considered a gold standard in bone reconstruction procedures due to its unique osteoinductive properties, autologous bone sampling comes with certain inconveniences, such as: the second operation site and its morbidity, unpredictable resorption, and limited available quantities [29]. Alternative techniques have been developed and studied, from guided bone regeneration (GBR), using different grafting materials, to, more recently, using growth factors and stem cells [30]. These bone substitutes are divided into three major categories: allografts when the donor and the recipient come from the same species, xenografts, obtained from different species than humans, alloplasts, and synthetic bone graft substitutes [31].

The inclusion criteria for the present study refer to patients with class V – VI Cawood atrophy, with 5-7 mm in height available native bone. Practitioners have two options: either sinus lift graft alone or with simultaneous implant placement. In the case of xenograft materials, one can perform a bone graft without any implant placement and in situations with almost no residual native bone. However implant placement is required to support the lifted Schneiderian membrane in the case of the L-PRF grafting material for the sinus lift. We have obtained significantly higher values for the xenograft materials in all point measurements (anterior, median, posterior). Still, it is also true that in the case of the L-PRF grafting material, one is limited by the height of the chosen implant.

The mean bone height gain for the xenograft group for the anterior landmark was 7.44 mm, taking into consideration that the highest gain was of 14.16 mm. Great results were achieved for the other measurements as well, starting from 1 mm, for example, in the median region, up to 16 mm in some of the cases.

Xenografts are materials commonly used in dentistry, derived from animal origin, with osteoconductive characteristics [32]. One of the most studied and well-

documented products used by dentists is Bio-Oss (Geitslich Pharma AG), obtained from bovine hydroxyapatite, with no cellular or organic content, having a chemical composition of calcium/phosphate ratio of 1.67 identically to the one of the human skeleton [33-35]. In terms of dimension, the Bio-Oss calcium crystals matrix is 100 µm in diameter, similar to the human matrix [36].

The Bio-Oss comes in two size particles – small (0.25-1 mm) and large (1-2 mm). For the sinus floor augmentation surgery, a comparison of the newly formed bone and angiogenesis-related bone healing was made in several studies. After 6 months of healing, new bone formation and higher bone volume with a greater angiogenesis expression by means of vascular endothelial growth factor (VEGF) expression were obtained with larger size particles, using micro-computed tomography and histomorphometrically analysis [37].

In the present research, we obtained 6 months postoperative volumes corresponding to the quantity of xenograft material used for recontouring the lack of native bone. We, therefore, highlight the utility of performing CBCT evaluations of the grafted sites to properly evaluate the stability of the results, as sustained in most recent studies [38] and to exclude any pathology that might affect the outcome [39].

Our study included more patients who benefitted from the external sinus lift with xenograft materials than implants and L-PRF alone as the sole biomaterial. Although, in the last decade, many studies have been published on the sinus augmentation topic, where the grafting material used was combined with platelet-rich in fibrin concentrate [40-44], fewer exist that used only L-PRF as a single grafting material [45,46]. For example, the study of Dominiak compared two small groups of patients - only 30 implants in total, xenograft versus PRF, ensuring a 3 year retrospective, but only panoramic evaluation, not CBCT [47]. We, therefore had a larger group that was submitted to an enhanced studied technique.

L-PRF is an easy blood concentrate obtained through centrifugation in tubes without anticoagulants or additives, a fibrin matrix that reunites growth factors, leucocytes and cytokines [48]. It is considered a bioscaffold for tissue regeneration due to its slow release of growth factors by promoting differentiation of the human alveolar bone marrow stem cells [49]. Due to its biological properties, L-PRF has been studied in many dentistry fields, including implantology and bone regeneration [50-52]. Its characteristics of a temporary matrix that mediates cellular activity by inducing angiogenesis and osteogenesis in bone regeneration make it appealing in bone tissue engineering [53].

Our study proved a mean bone height gain of 0.23 mm with a maximum of 2 to 3 mm gain compared to other research, which showed greater bone height gain. The mean gain in bone height of the sinus floor augmentation in the study conducted by Barbu et al. was 6.43 mm, with a maximum of 9 mm [54], or between 7 and 13 mm [mean +/- SD: 10.1 +/- 0.9 mm] in the Mazor et al study [55]. Simonpeiri states higher bone gain, ranging between 8.5 to 12 mm in a study of sinus lift augmentation with simultaneous implants and L-PRF as sole grafting material [45]. However, our study did not include long implants, the longest being 10 mm and the measurements included in the study for the postoperative evaluation were performed 6 months after the surgery. Although we had bone height loss of a mean value of 0.18 mm for the median measurement, one must consider that the median landmark was measured between two inserted implants or at the apical point of one implant. If we translate it not only in radiological results but also in clinical, the loss level is insignificant for the implant stability, including bone stability at 6 months. Aoki points out a significant information in his study, that sinus floor elevation with L-PRF alone should be perfomed in cases with a residual bone height of minimum 4 mm [56].

Our study, within its limitations, proves that, from a radiological point of view, higher bone values in terms of height are obtained when xenograft materials are used, compared to L-PRF. We acknowledge that we had a small group of patients integrated into the L-PRF study and that higher-length implants should be inserted for a more accurate evaluation of the bone volume obtained when a L-PRF graft is used. Nevertheless, CBCT evaluation after 6 months brings to our attention that the quantity of PRF graft material, regardless of the amount in place, positively impacts bone height gain. A recent study reported contradictory data, showing no results in terms of bone gain after tooth extraction with L-PRF, but their histogical and radiological data were performed only 8 weeks after the surgical procedure [57]. Another study compared external sinus lift procedure with L-PRF and without any other material and found a 1.42 mm bone height gain for the group treated with L-PRF [58].

However, modern medicine is searching for biological alternatives. L-PRF could become a real option, but further studies need to be performed, including histological ones, in order to confirm or not its role in bone formation. We emphasize the need to expand clinical research within the study's limitations. It would be of utmost interest to further evaluate the stability of the results obtained by performing long-term CBCT examinations and expanding the L-PRF group. Also, considering the L-PRF properties on soft tissue healing, clinical studies on sinus lift procedures combining xenograft in conjunction with L-PRF versus xenograft alone should be performed.

In terms of clinical outcomes, all implants had primary stability, and after 6 months of healing, prosthodontics was in place without any implant loss. It also shows that to properly evaluate the bone height after surgery, 3D examinations are required. Moreover, CBCT proves to be an objective tool since two raters in

the present study obtained overall reliability for all height measurements.

Conclusions

The present study comes with more than one benefit. It proves that how landmarks were chosen for the radiological assessment brought good to excellent reliability between the operators. L-PRF group showed stable radiological results after six months, before implant loading. Although our study confirmed that significant volume and overall heights were higher for the surgical procedure accompanied by xenograft materials, L-PRF could be a valuable alternative, safe and predictable in certain, precisely defined preoperative clinical and radiological situations. L-PRF is far from being considered an equivalent for the xenograft material, which has excellent results in all cases, from mild to severe atrophy of the residual bone.

Institutional Review Board Statement

The study was conducted following the Declaration of Helsinki and was approved by the Institutional Ethics Committee of Iuliu Hatieganu University of Medicine and Pharmacy (UMPh), no. 81, from 11 March 2019.

Informed Consent Statement

Written informed consent was obtained for all subjects involved in the study.

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