

Evaluation of Guided Bone Regeneration Using Xenograft/A-PRF Mixture in Atrophic Posterior Mandible (Clinical and Radiographic Study)

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[Doi:10.19044/esj.2023.v19n36p9](https://doi.org/10.19044/esj.2023.v19n36p9)

Submitted: 31 October 2023

Accepted: 23 December 2023

Published: 31 December 2023

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Cite As:

Richa R., Osman E., Attia N., Arakji H. & Shokry M. (2023). *Evaluation of Guided Bone Regeneration Using Xenograft/A-PRF Mixture in Atrophic Posterior Mandible. (Clinical and Radiographic Study)*. European Scientific Journal, ESJ, 19 (36), 9.

<https://doi.org/10.19044/esj.2023.v19n36p9>

Abstract

Introduction: The rehabilitation of the posterior mandible with dental implants represents a hard challenge for clinicians today due to the lack of supporting bone. Different surgical techniques are currently being used to augment the posterior mandible, where GBR is considered the most commonly used. **Materials and Methods:** Fifteen patients were selected to treat mandibular alveolar ridge resorption with guided bone regeneration using a titanium-reinforced membrane and a filling mixture of xenograft bovine bone and PRF. The membrane was fixed using a Meisinger pin control kit and Profix 3mm microscrews. A PRF membrane was used to cover the Ti-d-ptfe.

Results: Swelling, pain, and numbness were evaluated using the mixture of PRF/xenograft as well as PRF membranes. The results showed promising results in terms of primary wound healing, whereas a significant bone quantity with a mean bone volume of 5.78 ± 0.81 was reported after 6 months. The primary implant stability recorded high values and significantly increased at a period of 6 months post-insertion ($p = 0.037$). Conclusion: It could be concluded that the PFR/xenograft mixture can be promising when used with the titanium-reinforced d-ptfe membrane in 3D ridge reconstruction of the atrophic posterior mandible; moreover, using the PRF membrane to cover the TI-d-ptfe membrane could enhance soft tissue healing as well as prevent soft tissue dehiscence due to the concentration of growth factors that can be released during primary wound healing. The xenograft/PRf mixture can be consistently utilized for the creation of new bone in severely atrophic ridges if used in GBR. The high ISQ at primary implant placement and at a period of 6 months post-insertion, according to Osstell, can explain the successful application of this mixture in 3D bone augmentation of the atrophic posterior mandible.

Keywords: Guided bone regeneration, A-PRF, Xenograft, Posterior mandible, implant stability

Introduction

After tooth loss, alveolar ridge resorption proceeds. Following the extraction of a tooth, the alveolar ridge width and height decrease at a high rate during the first year and mainly during the first few months (Kingsmill, 1999). During the healing phase after extraction, the mean changes recorded based on data from several studies show that the clinical loss in width is greater than the loss in height (Van der Weijden & Dell'Acqua, 2009).

Dental implants are currently the treatment of choice for the restoration of edentulous areas. Depending on the edentulous period, the difficulty of implant surgery varies. According to the width, height, and quality of the bone, the surgeon would assess the possibility of placing the implants. In long periods of edentulism, it is often mandatory to perform hard tissue ridge augmentation to enhance bone volume before implant placement (Toscano, et al., 2010).

The reconstruction of alveolar ridge abnormalities concurrently with or staged before implant placement has been extensively documented using guided bone regeneration, where the function of the barrier membrane aims to promote bone formation while acting as a passive barrier to preclude soft tissue in-growth. Moreover, the effect of the barrier membrane has been further shown to promote bone formation as it induces molecular and cellular events. (Urban, et al., 2022)

Guided bone regeneration for vertical ridge augmentation is a highly technique-sensitive therapy (Rocchietta, et al., 2008). The application of a moldable barrier membrane in conjunction with a bone substitute that can securely build up a durable biological structure that mimics native tissues and provides enough volume is required for space creation and maintenance to function reliably. These requirements are met by non-resorbable titanium-reinforced barrier membranes, which have been proposed as a successful means of achieving vertical ridge augmentation in big defects (Merli, et al., 2014). Non-resorbable (frequently polytetrafluoroethylene-PTFE) or resorbable (frequently collagen-based) membranes are usually used to contain the grafting material, preventing graft resorption and preventing the surrounding soft tissues from migrating and infiltrating into the surgery site (Urban & Monje, 2019). The local anatomy and desired clinical outcome, the type of graft used, and the healing biology—all these factors drive the choice of a specific membrane. However, the main disadvantages faced using this technique are the anatomical limitations and the high resorption rate of the graft material (Drăgan, 2022)

Vertical GBR is technique-sensitive and limits clinical success; failure is usually associated with wound dehiscence. The ability to develop bone along the axis of applied forces is another limitation (Rocchietta, Fontana, & Simion, 2008). Although the titanium membrane shows a specific problem where the fibrous tissues grow into the wide holes of the membrane, this leads to its exposure. (Urban, et al., 2014) (Rakhmatia, et al., 2013)

(Choukroun, et al., 2006) developed platelet-rich fibrin (PRF), a second-generation platelet concentrate that promotes hard and soft tissue repair. It contains large quantities of collected platelets, allowing for the delayed release of growth factors (GFs) (Kang, et al., 2011). These GFs include vascular endothelium growth factor (VEGF), platelet-derived growth factor (PDGF), fibroblast growth factor (FGF), epidermal growth factor (EGF), hepatocyte growth factor (HGF), insulin-like growth factor (IGF), and transforming growth factor- β (TGF- β). All of this helps to replace damaged tissue, resurface wounds, and restore vascular integrity. In comparison to other platelet concentrates, PRF releases these factors at a slower pace over a longer period of time, improving wound healing (Blair & Flaumenhaft, 2009)

PRF has been demonstrated to enhance the formation of osteoblasts and periodontal ligament cells, both of which are important for periodontal defect healing (Ehrenfest, et al., 2010); (Sharma & Pradeep, 2011); (Mazor, et al., 2009); (Simonpieri, et al., 2011).

For more predictable bone regeneration, autografts can be combined with platelet concentrates. This clinical case letter reports a case of Siebert's class I ridge defect, which was treated with the staged guided bone regeneration (GBR) approach using autogenous block graft and platelet-rich

fibrin. It demonstrates the efficacy of using a block graft along with PRF, which stimulates new bone formation and successful placement of a dental implant in the augmented site (Datla, et al., 2018)

The rationale for conducting this study was to evaluate the effect of xenograft mixed with A-PRF as a biological mediator on restoring the resorbed posterior mandible for the placement of a fixed implant-supported prosthesis.

Therefore, the primary objectives of this study were to evaluate the implant stability of dental implants placed in the augmented site by measuring the implant stability quotient (ISQ), and the secondary objective was to assess post-operative sequelae (swelling, numbness, and pain) and radiographically the bone gained in the surgical site through cone beam computed tomography.

Material and Methods:

This study was accomplished as a randomized clinical trial following the consort guidelines. The study was carried out at the Oral Surgery Division, Faculty of Dentistry, Beirut Arab University, Lebanon, between February 2022 and September 2023. Ethical approval was obtained by the institutional review board (2023-H-0121-D-P-0534) before the start of the study. The study was completed in accordance with the Helsinki Declaration of 1975, revised in 2013. Before the initiation of the work, patients who participated in this trial signed informed consent and were well-informed about all the steps of the procedure and any complications that might result during or after the procedure.

The sample size was estimated using the sample size calculator website, <http://epitools.ausvet.com.au>, by adjusting the power of the study to 80% and regulating the alpha error to 5%. This yielded a total of 13 patients; two patients were added to the final calculated sample size to avoid sample attrition that might occur throughout the follow-up period of the study. A total of 15 patients of both genders with an age range of 30–60 years fulfilled the inclusion and exclusion criteria. Patients who were included in this trial should have unilateral or bilateral mandibular posterior partial edentulism, a bone height crestal to the canal of <7 mm, and good oral hygiene. Patients that have uncontrolled or untreated periodontal disease involving residual dentition, uncontrolled systemic conditions that jeopardize the surgery, radiotherapy to the head/neck district performed within the past 24 months, chemotherapy for treatment of malignant tumors at the time of the surgical procedure, patients with present or past treatment with intravenous bisphosphonates, patients having psychological problems, heavy smoking (>10 cigarettes per day), alcohol or drug abuse, and pregnant patients were excluded from this study. (Ronda et al., 2014):

All patients underwent a thorough clinical examination; the health of the periodontium and oral hygiene level were inspected. A prosthetic assessment was performed for the future prosthesis. Preoperative cone beam CT was requested from all patients to quantitatively measure the available bone and the distance between the alveolar crest and the mandibular canal (Figure 1). Moreover, all patients received proper prophylactic treatment and were given adequate oral hygiene instructions.

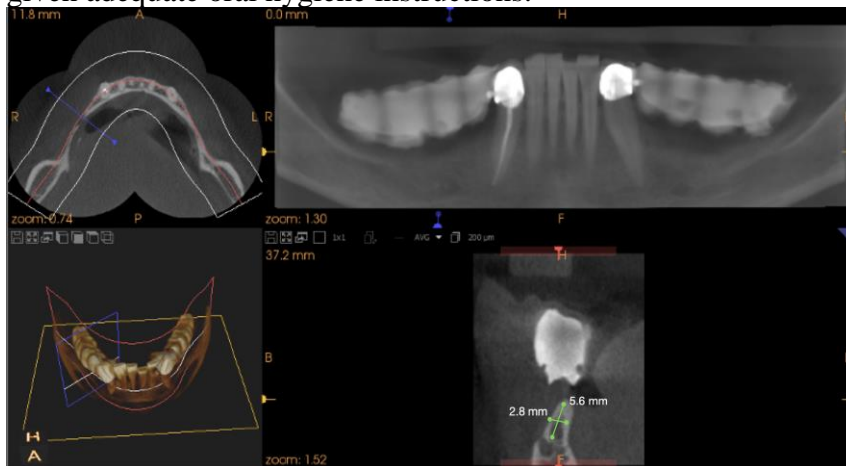


Figure 1. Preoperative CBCT showing the mandibular deficiency

One hour prior to the surgical procedure, all patients were instructed to take 2 g of antibiotics (875 mg amoxicillin and 125 mg clavulanic acid). As for patients allergic to penicillin, 600 mg of clindamycin was prescribed. All patients were told to rinse their mouths with chlorhexidine gluconate 0.2% mouthwash 30 minutes before the initiation of the procedure.

Under complete aseptic and sterile conditions, the patients received inferior alveolar and buccal block anesthesia using Articaine 4% and 1:100,000 epinephrine (Septanest, Septodont). At the recipient site, crestal incisions were made over the edentulous alveolar ridge and extended from the retromolar area (distally) to the mesial aspect of the adjacent tooth. A full-thickness flap was reflected on the buccal and lingual sides, exposing the posterior atrophic mandible. With a 1mm round bur mounted on a straight surgical handpiece, the bone was decorticated under copious irrigation (Figure 2). Afterward, A-PRF was prepared (Choukroun, et al., 2006) by withdrawing the patient's own blood from the median cubital or cephalic vein into empty plastic vacuum tubes, and they were immediately centrifuged at a speed of 1300 rpm for 7 min. A-PRF was collected and placed in its specific box to produce the A-PRF membrane. A-PRF membranes were cut, and together with serum exudates, they were mixed with the graft material (Cerabone, Botiss, Germany).



Figure (2). Preparation of the recipient site with decortication

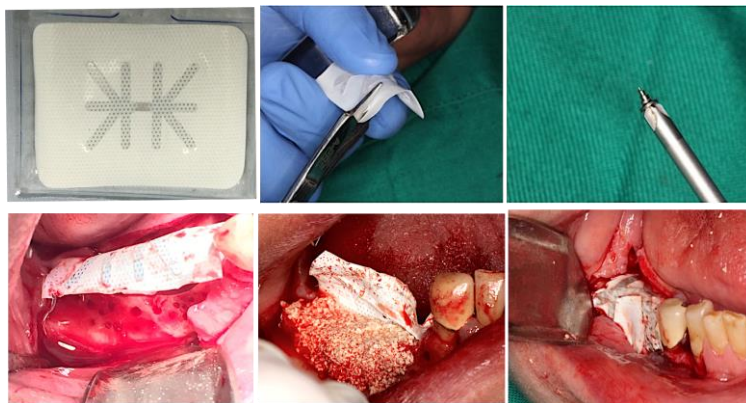


Figure (3). Total fixation procedure of the membrane overlying the A-PRF/Xenograft mixture

Using Cytoplast™ Ti-250 Titanium-Reinforced Non-Resorbable High-Density PTFE Membrane of 250 microns thick, which is ideal for ridge augmentation and grafting bony defects missing one or more walls. The membrane was molded and shaped for tenting and space maintenance, and the titanium frame was trimmed and shaped to create additional space for bone growth. The textured Regentex™ surface of the membrane is designed to increase the surface area available for cellular attachment, thereby assisting in stabilization of the membrane and prevention of soft tissue retraction (Osteogenics Biomedicals, USA). The membrane fixation was achieved using bone tacs (Meisinger Master pin kit, Germany), Profix kit, and fixation screws (3mm length) (Osteogenics Biomedicals, USA) on the lingual side of the mandible. Furthermore, the Xenograft-A-PRF mixture was delivered to the recipient site using a bone carrier to fill under the membrane, and the titanium-reinforced membrane was properly adapted over the bone graft material, ensuring that no empty spaces were present (Figure 3).

The membrane was then fixed on the crestal and buccal sides using the membrane tacs and fixation screws. The non-resorbable titanium-reinforced membrane was trimmed 1 mm away from the adjacent tooth, and the previously prepared membrane was adapted over the non-resorbable titanium-reinforced membrane (Figure 4). After proper releasing of the flaps, horizontal mattress sutures at 5mm with interrupted sutures were used to ensure primary closure of the surgical site.

Patients were directed to strictly follow the standard post-operative instructions. Dexamethasone 8mg injection was prescribed immediately postoperatively. Antibiotics were continued, and NSAID medication (Bruffen 400 mg) was administered to all patients twice daily for 5 days. Patients were requested to continue the chlorhexidine mouthwash for the following 10 days. All patients did postoperative CBCT to check the augmented site as a baseline (Figure 5).

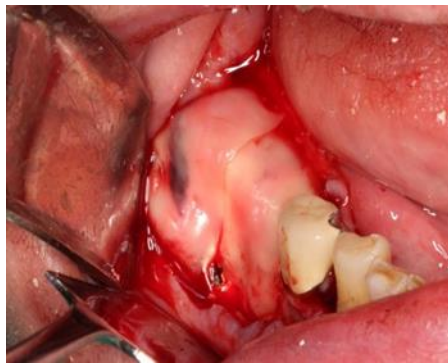


Figure (4). Application of A-PRF the membrane overlying Ti d-ptfe

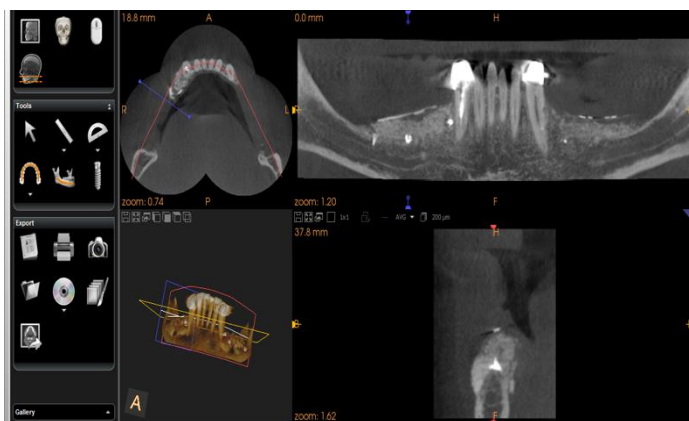


Figure (5). Immediate postoperative CBCT (baseline)

Clinically, soft tissue healing (presence or absence of infection and dehiscence of the flap) was evaluated over a period of two weeks postoperatively. Also, swelling was assessed on the 4th, 7th, and

14th postoperative days. Evaluation of pain was performed using a visual analog scale (VAS) on the 2nd, 7th, and 14th postoperative days. As for paresthesia, it was evaluated according to the Two Point Discrimination Test (TPD) on the 2nd, 7th, and 14th postoperative days.

6 months postoperative, reentry to the augmented site for the purpose of removal of the titanium-reinforced membrane, clinical evaluation of the grafted site for volume as well as bone formation, and implant placement according to the surgical protocol of the Zimvie 3i implant system.

Primary implant stability was measured using RFA (radio frequency analysis) by means of the Osstell system at the time of placing the implants, while delayed measurement of implant stability was performed 4 months later.

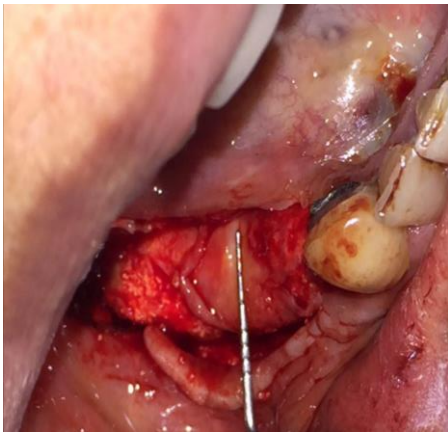


Figure (7). Healed mature bone

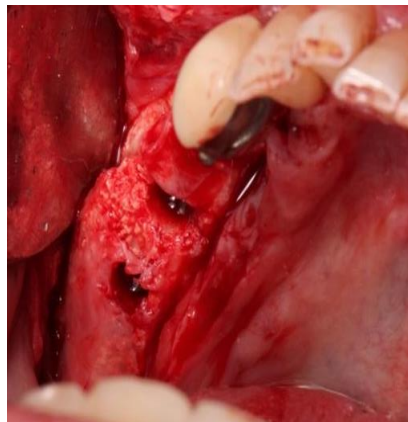


Figure (8). Implant placement

Radiographically, cone beam computed tomography (CBCT) was done directly postoperatively (baseline) and after 6 months to check the amount of new bone volume before implant placement. All radiographs were evaluated by the same investigator. CBCT analysis was executed using a software program (CS 9600, Carestream, Atlanta, USA). The same sagittal cut on the area with the greatest defect was used at all follow-up periods to measure the bone width and height until the inferior alveolar nerve canal. Figure (9)

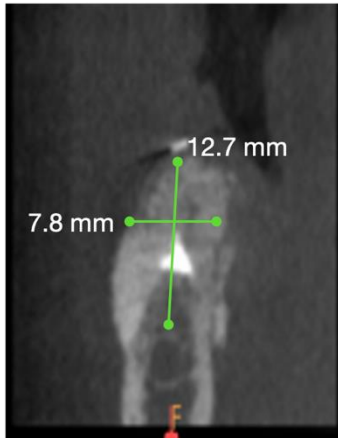


Figure (9). 6 months postoperative CBCT to evaluate bone density and volume before implant placement

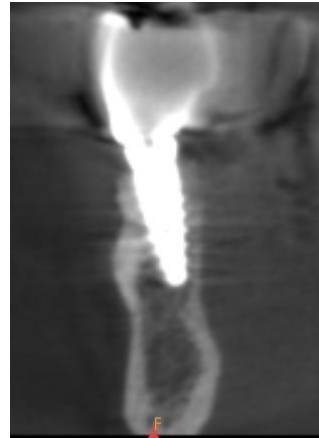


Figure (10). 6 months CBCT after implant placement showing stable bone in 3D

Furthermore, a CBCT was performed at 6 months to evaluate the stability of grafted bone around implants. Figure (10)

The obtained data were fed to the computer using the IBM SPSS software package, version 24.0, to be analyzed and interpreted (Armonk, NY: IBM Corp.). Numbers and percentages were used to describe qualitative data. The Kolmogorov-Smirnov test was employed to ensure that the distribution was normal. Range (minimum and maximum), mean, standard deviation, and median were used to characterize quantitative data. The significance of the acquired results was assessed at a 5% level.

Results

The fifteen participants consisted of 8 females and 7 males, ranging in age from 42 to 55 years, with a mean of 47.76 ± 3.65 years. All the surgeries were done without any complications. All operative sites showed uneventful healing without infection or flap dehiscence during the follow-up period.

Figure 11 compares swelling over the follow-up period. A statistically significant difference existed in swelling values between baseline (postoperative swelling measures) and all the follow-up periods. A non-statistically significant difference existed between the 4th and 7th days, while there was a statistically significant difference between the 4th and 14th days and the 7th and 14th days.

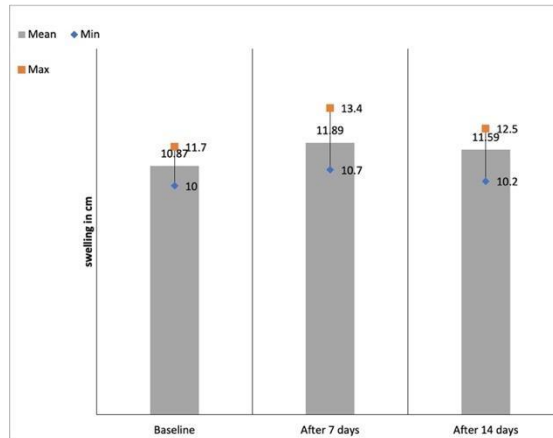


Figure 11. Comparison between the different studied periods according to swelling

Figure 12 compares pain over the two weeks follow up period, statistically significant difference between all the follow up periods. Pain reached a maximum value score (8) on the 2nd postoperative day and started to decrease gradually on the 7th and 14th days respectively.

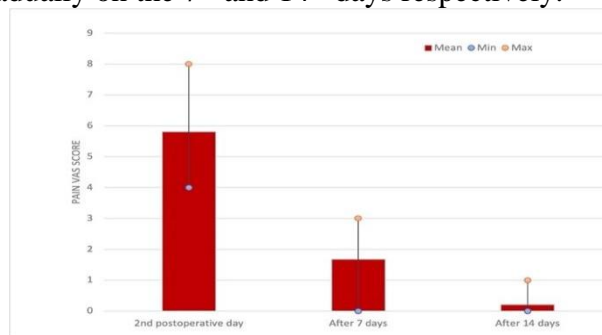


Figure 12. Comparison between the different studied periods according to pain

Table 1 shows the comparison of paresthesia throughout the follow up. Statistically significant differences existed between all tested periods. All patients had a full sensation recovery after 2 months.

Table 1. Comparison between the three studied periods according to numbness

	Numbness		
	4 th post-operative	After 7 days	After 14 days
(n = 15)			
Mean ± SD.	3.47 ± 0.61	3.22 ± 0.47	2.93 ± 0.41
Median (Min. – Max.)	3.50 (2.50 – 4.50)	3.0 (2.50 – 4.0)	3.0 (2.50 – 4.0)
Sig. bet. periods.	p ₁ =0.026*, p ₂ =0.010*, p ₃ =0.025*		

p₁: p value for comparing between 4th post-operative and After 7 days, p₂: p value for comparing between 4th post-operative and After 14 days, p₃: p value for comparing between After 7 days and After 14 days, *: Statistically significant at p ≤ 0.05

Table 2 evaluates the bone quantity between three studied periods. Comparing preoperative bone quantity to baseline (immediate postoperative) and after 6 months, statistically significant difference existed. Non-statistical significant difference was present between the readings of bone quantity between baseline and 6 months.

Table 2. Comparison between the three studied periods according to bone quantity

	Bone quantity		
	Pre-operative	Baseline	6 months post-operative
(n = 15)			
Mean ± SD.	6.04 ± 0.97	11.92 ± 0.85	11.82 ± 0.81
Median (Min. – Max.)	6.0 (4.0 – 7.0)	12.0 (10.0 – 13.0)	12.0 (10.0 – 13.0)
Sig. bet. Periods.	P ₁ <0.001*, p ₂ <0.001*, p ₃ =0.206		

p₁: p value for comparing between **Pre-operative** and **Baseline**, p₂: p value for comparing between **Pre-operative** and **6 months post-operative**, p₃: p value for comparing between **Baseline** and **6 months post-operative**, *:Statistically significant at p ≤ 0.05

Table 3, compares the ISQ values at implant placement and after 6 months. Statistically significant differences existed between the two-time intervals. ISQ values increased after 6 months, showing increased implant stability.

Table 3. Comparison between the two different periods for implant stability according to ISQ

	ISQ at implant placement (n = 15)	ISQ 6 months after implant placement (n = 15)	p
ISQ			
Mean ± SD.	61.07 ± 1.39	78.33 ± 1.95	0.0370*
Median (Min. – Max.)	63.0 (59.0 – 66.0)	81.0 (72.0 – 85.0)	

*:Statistically significant at p ≤ 0.05

Discussion

The lack of sufficient bone quantity in sites selected for implant placement is a challenge that frequently faces implantologists (Garaicoa-Pazmiño, et al., 2014). However, several surgical methods to create sufficient bone volume have been developed, such as autogenous onlay bone blocks, guided bone regeneration, distraction osteogenesis, and ridge expansion, as well as many other techniques that have been shown to be successful in the reconstruction of the atrophic posterior mandible.

This study is a randomized, controlled clinical trial. Fifteen consecutive patients from the outpatient clinic of the Oral Surgical Sciences Department, Faculty of Dentistry, Beirut Arab University, Beirut, Lebanon, needing dental implants in the posterior mandible were enrolled in this study with an age range of 30 to 60 years. Mandibular partial edentulism involving

the premolar/molar area is associated with the presence of crestal bone height <7 mm coronal to the mandibular canal. The sample was randomly allocated to receive 3D ridge reconstruction that was performed using the conventional GBR technique with the use of an A-PRF-Cerabone mixture as a filling material, which was covered with non-resorbable titanium-reinforced d-PTFE (dense polytetrafluoroethylene). The membrane was fixed with bone tacs and fixation screws, and then A-PRF membranes were used overlying the d-PTFE. Assessment of soft tissue healing took place by evaluating the color of the mucosa, soft tissue dehiscence, and infection over different follow-up periods. There was no statistically significant difference regarding the change in color throughout the evaluation period of this study.

This outcome can be agreed with (Al-Hamed, et al., 2019) who suggest that enhancing the biological capacities, tissue creation, and healing of the regenerated region through the increased concentration of growth factors and other molecules associated with angiogenesis, stem cell migration, and osteogenic differentiation is what makes PRF biologically plausible. Furthermore, (Miron, et al., 2017) who conducted a study to evaluate the benefits of using PRF in alveolar ridge augmentation, demonstrated that the presence of an A-PRF membrane can improve soft tissue healing and reduce tissue dehiscence.

Upon evaluating swelling, the results revealed a statistically significant difference between the follow-up periods of 4th, 7th, and 14. The conclusion was reached by Romanos (Romanos, 2010) who suggested that periosteal and vertically releasing incisions are frequently employed in vertical GBR to raise a tensionless flap. However, depending on the augmentation approach, this flap design frequently leads to problems such as flap perforation and graft exfoliation in 2.5–10% of instances, as well as edema, bleeding, and patient discomfort (Ogata, et al., 2013). The location of deep periosteal incisions, which disrupt periosteal blood vessel circulation, is likely one of the primary causes of severe problems. Tension at the crestal incision site is caused by increased tissue swelling brought on by postoperative blood stasis. This tension can hinder wound healing and cause premature membrane exposure (Maridati, et al., 2016).

A statistically significant difference was recorded among patients at different time intervals, as pain was manageable and subsided at day 14 in all patients. Pain scored its maximum value on the second postoperative day, and this is due to the body reaction to the surgical procedure and the release of prostaglandin and cytokines. The pain score started to decrease gradually throughout the follow-up period. These results run in parallel with (Windisch, et al., 2021), who found that pain was moderate in all GBR cases.

(Pacifici, et al., 2015) suggested that the use of plasma-rich fibrin membranes is indicated to improve soft-tissue healing, reduce tissue

dehiscence, reduce postoperative pain and swelling, and minimize infection in the surgical area.

A statistically significant difference was noticed while assessing the bone quantity at baseline and at 6 months in comparison to preoperative bone quantity. These results run parallel with those of (Tunkel et al., 2021) who showed comparable results regarding vertical and horizontal augmentation gain when using autologous and allogenic bone shells. However, a systematic review and meta-analysis (Urban, et al., 2019) affirmed that GBR and bone shells can both significantly increase bone quantity in the augmented sites. Also, devices that have form-stable growth, such as titanium-reinforced non-resorbable membranes, may increase vertical bone and enhance vertical bone gain.

In a review article (Urban, et al., 2023) the authors stated that the majority of trials using titanium-reinforced polytetrafluoroethylene membranes, which are thought to be perfect for 3D augmentation surgery since they can create a private zone for long-term space maintenance and can halt the soft tissue from collapsing,.

Resonance frequency analysis (RFA), which evaluates the lateral support of the implant in bone, was used for more accountable and trustworthy results that were patient-friendly, according to (Huang, et al., 2020).

The implant stability quotient was compared at the time of implant placement as well as at 6 months post-implant insertion. The results yielded significant differences in the ISQ values, which explain the better bone maturation and integration with implants over time. Both periods showed high ISQ readings where the implants placed had high primary stability, which means that the bone was hard and mature, and it can predict a successful survival of the implants if the prosthetic part is well planned and oral hygiene is well maintained.

Moreover, (Mendoza-Azpur, et al., 2019) conducted a randomized controlled clinical trial comparing guided bone regeneration with xenografts and bone blocks with xenografts, the authors declared that implants were 100% successful after a follow-up period of 18 months.

The investigators encountered limitations in this study, including the availability of the participants. Also, the follow-up period, which was considered a long period for some of the patients, Additionally, there was no financial support for this research, which made it difficult for some participants to be enrolled in this research due to the high cost of the materials used.

Conclusion

Considering the limitations of this study, the findings showed that the PRF/Xenograft mixture may show promise in conjunction with the titanium-

reinforced d-ptfe membrane for 3D ridge reconstruction of the atrophic posterior mandible. Bone quantity increased significantly after 6 months of placing a standard-sized implant. Furthermore, the concentration of growth factors that may be released during primary wound healing suggests that covering the TI-d-ptfe membrane with the PRF membrane may promote soft tissue healing and prevent soft tissue dehiscence. Implant stability showed promising results at the implant placement phase, with high ISQ values and an increase in ISQ after 6 months of follow-up. A more extensive follow-up study involving a larger sample size and a histomorphometry study is necessary to validate the encouraging results. Last but not least, a reliable method for restoring the atrophied posterior mandible is guided bone regeneration.

Conflict of Interest: The authors declare that there was no conflict of interest during conducting this research work.

Data availability: All dataset used and/or analyzed during the current study are available from the corresponding author (Rami Richa, r.risha@bau.edu.lb) upon reasonable request. (Rami Richa: <https://www.bau.edu.lb/Dentistry/Clinical-Academic-Staff>)

Funding statement: The authors did not obtain any funding for this research

Declaration for human participants/ Ethical Approval: This study was approved by the international review board at Beirut Arab University, code: (2023-H-0121-D-P-0534), (<https://www.bau.edu.lb/Research/Approval-Codes>)

Ethical principles of research: This research was completed in accordance with the Helsinki Declaration of 1975, revised in 2013.

References:

1. Al-Hamed, F., Mahri, M., Al-Waeli, H., Torres, J., & Badran, Z. a. (2019). Regenerative effect of platelet concentrates in oral and craniofacial regeneration. . *Frontiers in cardiovascular medicine*, 126.
2. Amaral Valladão, C., Freitas Monteiro, M., & and Joly, J. (2020). Guided bone regeneration in staged vertical and horizontal bone augmentation using platelet-rich fibrin associated with bone grafts: a retrospective clinical study. . *International journal of implant dentistry*, 6, 1-10.
3. Blair, P., & Flaumenhaft, R. (2009). Platelet alpha - granules: basic biology and clinical correlates. *Blood Reviews*, 23, 177-189.

4. Choukroun, J., Diss, A., & Simonpieri, A. (2006). Platelet-rich fibrin (PRF): a second-generation platelet concentrate. Part V: histologic evaluations of PRF effects on bone allograft maturation in sinus lift. *Oral Surgery Oral Medicine Oral Pathology Oral Rad Endod.*, 101, 299-303.
5. Coulthard, P., Patel, N., Bailey, E., & Coulthard, M. (2014). Measuring pain after oral surgery . *Oral Surgery.*, 203-208.
6. Datla, M., Chellathurai, B., & Thiagarajan, R. a. (2018). Platelet-rich Fibrin Application in Guided Bone Regeneration Using Autogenous Block Graft in Staged Dental Implant Placement: A Case Report. *Int J Oral Implantol Clin Res.*, 9, 1-3.
7. Drăgan, E. a. (2022). Review of the Long-Term Outcomes of Guided Bone Regeneration and Autologous Bone Block Augmentation for Vertical Dental Restoration of Dental Implants. *Medical Science Monitor: International Medical Journal of Experimental and Clinical Research*, , 28(1), 937433-1.
8. Ehrenfest, D., Corso, M., Diss, A., Mouhyi, J., & Charrier, J. (2010). Three-dimensional architecture and cell composition of a Choukroun's platelet-rich fibrin clot and membrane. *Journal of Periodontology*, 81, 546-555.
9. Garaicoa-Pazmiño, C., Suárez-López del Amo, F., Monje, A., Catena, A., Ortega-Oller, I., & Galindo-Moreno, P. a. (2014). Influence of crown/implant ratio on marginal bone loss: a systematic review. . *Journal of periodontology*, 85(9), 1214-1221.
10. Huang, H., Wu, G., & and Hunziker, E. (2020). The clinical significance of implant stability quotient (ISQ) measurements: A literature review. *Journal of oral biology and craniofacial research*, 10(4), 10(4), pp.629-638.
11. Kang, Y., Jeon, S., & Park, J. (2011). Platelet-rich fibrin (PRF) is a bioscaffold and reservoir of growth factors for tissue regeneration. *Tissue Engineering*, 17, 349-359.
12. Kingsmill, V. (1999). Post-extraction remodeling of the adult mandible. *Critical Reviews in Oral Biology & Medicine*, 10(3), pp.384-404., 10(3), 384-404.
13. Maridati, P., Cremonesi, S., Fontana, F., & Cicciù, M. a.-P.-2. (2016). Management of d-PTFE membrane exposure for having final clinical success. . *Journal of Oral Implantology*, 42(3), 289-291.
14. Mazor, Z., Horowitz, R., Corso, M., Prasad, H., Rohrer, M., & Ehrenfest, D. (2009). Sinus floor augmentation with simultaneous implant placement using Choukroun's platelet-rich fibrin as the sole grafting material: a radiologic and histologic study at 6 months. *Journal of Periodontol*, 80, 2056-2064.

15. Mendoza-Azpur, G., de la Fuente, A., Chavez, E., & Valdivia, E. a. (2019). Horizontal ridge augmentation with guided bone regeneration using particulate xenogenic bone substitutes with or without autogenous block grafts: A randomized controlled trial. *Clinical implant dentistry and related research. . A randomized controlled trial. Clinical implant dentistry and related research.*, 21(4), 521-530.
16. Merli, M., Moscatelli, M., Mariotti, G., Rotundo, R., & Bernardelli, F. a. (2014). Bone level variation after vertical ridge augmentation: resorbable barriers versus titanium-reinforced barriers. A 6-year double-blind randomized clinical trial. *Int J Oral Maxillofac Implants*, 29, 905-913.
17. Meshram, V., Meshram, V., & Lambade, P. (2013). Assessment of Nerve Injuries after Surgical Removal of Mandibular Third Molar: A Prospective Study. *Asian Journal of Neuroscience*, 1-6.
18. Miron, R., Fujioka-Kobayashi, M., Bishara, M., Zhang, Y., & Hernandez, M. a. (2017). Platelet-rich fibrin and soft tissue wound healing: a systematic review. . *Tissue Engineering Part B: Reviews*, 23(1), 83-99.
19. Mourão, A., Valiense, H., ER., M., NBMF., M., & MD-C., M. (2015). Obtention of injectable platelets rich-fibrin (i-PRF) and its polymerization with bone graft: technical note. *Rev Col Bras Cir [Internet].*, 42(6), 21–3.
20. Ogata, Y., Griffin, T., Ko, A., & Y, H. (2013). Comparison of double-flap incision to periosteal releasing incision for flap advancement: a prospective clinical trial. . *Int J Oral Maxillofac Implants* , 26(2), 597–604.
21. Pacifici, A., Carbone, D., Soda, G., & Polimeni, A. a. (2015). Guided bone regeneration procedure with platelet rich fibrin (PRF) membranes in the resolution of a severe maxillary bone defect: report of a case. *Senses and Sciences*, 2(1), 64-70.
22. Rakhmatia, Y., Ayukawa, Y., Furuhashi, A., & Koyano, K. (2013). Current barrier membranes: Titanium mesh and other membranes for guided bone regeneration in dental applications. *J. Prosthodont. Res.*, 57, 3-14.
23. Rocchietta, I., Fontana, F., & Simion, M. (2008). Clinical outcomes of vertical bone augmentation to enable dental implant placement: A systematic review. *J. Clin. Periodontol.*, 35, 203-215.
24. Romanos, G. (2010). Periosteal releasing incision for successful coverage of augmented sites. A technical note. *Journal of Oral Implantology*, 36(1), 25-30.
25. Ronda, M., Rebaudi, A., Torelli, L., & Stacchi, C. (2014). Expanded vs. dense polytetrafluoroethylene membranes in vertical ridge

- augmentation around dental implants: a prospective randomized controlled clinical trial. *Clin. Oral Impl. Res.*, 25, 859-866.
26. Sharma, A., & Pradeep, A. (2011). Autologous platelet rich fibrin in the treatment of mandibular degree II furcation defects: a randomized clinical trial. *Journal of Periodontol*, 82, 1396-1403.
 27. Simonpieri, A., Choukroun, J., Corso, M., Sammartino, G., & Ehrenfest, D. (2011). Simultaneous sinuslift and implantation using microthreaded implants and leukocyte and platelet-rich fibrin as sole grafting material: a six-year experience. *Implant Dentistry*, 20, 2-12.
 28. Szolnok, G., Szendi-Horváth, K., Seres, L., Boda, K., & Kemény, L. (2007). Manual lymph drainage efficiently reduces postoperative facial swelling and discomfort after removal of impacted third molars. *Lymphology*, 40, 138-142.
 29. Toscano, N., Shumaker, N., & Holtzclaw, D. (2010). The art of block grafting: A review of the surgical protocol for reconstruction of alveolar ridge deficiency. *Journal of Implant and Advanced Clinical Dentistry*, 2(2), 45-47.
 30. Tunkel, J., de Stavola, L., & Kloss-Brandstätter, A. (2021). Alveolar ridge augmentation using the shell technique with allogeneic and autogenous bone plates in a split-mouth design—a retrospective case report from five patients. *Clin Case Rep.*, 9(2), 947-959.
 31. Urban, I., & Monje, A. (2019). Guided bone regeneration in alveolar bone reconstruction. *Oral and Maxillofacial Surgery Clinics*, 31(2), 331-338.
 32. Urban, I., Lozada, J., Jovanovic, S., Nagursky, H., & Nagy, K. (2014). Vertical ridge augmentation with titanium-reinforced, dense-PTFE membranes and a combination of particulated autogenous bone and anorganic bovine bone-derived mineral: A prospective case series in 19 patients. *Int. J. Oral Maxillofac. Implant.*, 29, 185-193.
 33. Urban, I., Montero, E., & Monje, A. a.-S. (2019). Effectiveness of vertical ridge augmentation interventions: A systematic review and meta-analysis. *Journal of Clinical Periodontology*, 46, 319-339.
 34. Urban, I., Montero, E., Amerio, E., & Palombo, D. a. (2023). Techniques on vertical ridge augmentation: Indications and effectiveness. *Periodontology 2000*.
 35. Urban, I., Tattan, M., Ravida, A., Saleh, M., & Tavelli, L. a.-O. (2022). Simultaneous Alveolar Ridge Augmentation and Periodontal Regenerative Therapy Leveraging Recombinant Human Platelet-Derived Growth Factor-BB (rhPDGF-BB): A Case Report.

International Journal of Periodontics & Restorative Dentistry, 42(5), 42(5).

36. Van der Weijden, F., & Dell'Acqua, F. (2009). Alveolar bone dimensional changes of post-extraction sockets in humans: a systematic review. *Journal of Clinical Periodontology.*, 36(12), 1048-1058.
37. Windisch, P. O. (2021). Vertical-guided bone regeneration with a titanium-reinforced d-PTFE membrane utilizing a novel split-thickness flap design: a prospective case series. *Clinical oral investigations*, 25, 2969-2980.