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Research Article

Nine Different Applications for Platelet-Rich Fibrin, Two Centrifugation Protocols

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Abstract

Introduction: PRF or Platelet-Rich Fibrin is a platelet concentrate obtained from a patient's venipuncture brought to a blood collection tube, without any blood thinners (anticoagulant), that goes through a centrifugation process and results into different types of growth factors that stimulate the cellular proliferation, it has been widely used on regenerative medicine because its biological qualities.

Objective: Establish the clinical and biological use of the A-PRF and I-PRF on the bone regenerative field through two different centrifugation protocols.

Materials and Methods: Sample of 8 surgical cases managed between October 2018 and January 2020, where both centrifugation protocols were applied to perform nine surgical procedures: alveolar preservation, immediate implants, second phase surgery, maxillofacial pathologies, maxillary sinus floor lift, dento-alveolar surgery, cover up palatal graft donor site and peri-implantitis, throughout a clinical and radiographic evaluation establishing a pre and post-surgical comparison.

Results: Bone neoformation, lack of infection, edema and bleeding, emergence profile improvement and keratinized gingiva formation was obtained in all 8 cases.

Discussion: The use of PRF in different scenarios on Oral and Maxillofacial Surgery is a useful tool for the operator because of its biological and immunological characteristics shown in the postoperative results.

Keywords: *PRF; Utilities; Centrifuge; Clot*

Introduction

The main goal for today's Oral Surgery is to achieve better results in molecular biology generating less invasive surgical procedures for patients. Based on this, many authors have guided their studies to find a mechanism that uses tissue's engineering biological principles to regenerate tissue and restore the function and structure lost in some anatomic element.

In accordance with previously mentioned, in the last thirty years there has been an evolution on different technologies that aim to stimulate regenerative medicine, which combines different aspects of medicine, cellular and molecular biology and tissue engineering, to repair or replace tissues. This is where different protocols were created to obtain PRP (Platelet-rich plasma), PRF (Platelet-rich Fibrin) among others [1].

PRF or Platelet-rich Fibrin is a platelet concentrate which preparation technique does not require the use of any kind of anticoagulants, so the platelets are immediately activated by contact with the blood collection tube initiating the coagulation process. The fi-

brinogen initially concentrates on the top of the collection tube so that at contact with the thrombin, normally found in blood, it turns to fibrin which works as a matrix to retain platelets [1]. When the centrifugation process is over, three layers are obtained, red blood cells as a base, and intermediate layer where the PRF clot is and the acellular plasma on top. The PRF clots contain growth factors such as, the Transforming growth factor beta 1 (TGFb-1), its *in vitro* effects have allowed to demonstrate the stimulation of the osteoblast's proliferation and the ability to induce fibrosis in the wound healing process, Platelet-derived growth factor (PDGF-AB) is an essential regulator for the migration, proliferation and survival of the mesenchymal cells, Vascular endothelial growth factor (VEGF), Insulin-derived growth factor (IGF) which results into a positive regulator of almost every type of cell's proliferation, acting as a cytokine and matrix proteins such a fibronectin, thrombospondin-1, among other that have a 7 days life [2-4].

The platelet cytokine's quantification in the PRF clot play an important role in its understanding because its soluble molecules are key to the inflammation and the wound healing mediators [4]. Platelets come from the megakaryocytes formed in the bone marrow, they have a life between 7 and 10 days and are distinguished for being formed by alfa granules that contain fibronectin, beta thromboglobulin, thrombospondin, fibrinogen, immunoglobulin, among others [4,5]. Platelet's activation allows cytokines release that stimulates cellular migration and proliferation inside the previously formed fibrin's matrix [4,5].

Another important characteristic of the PRF clot is the leucocyte degranulation as a result of the low speed centrifugation process. This leads to catch the leucocyte cytokines in the fibrin matrix besides the platelet cytokines. In the leukocyte cytokine range are: Interleukin-1beta (IL-1b) produced by the activation of macrophages, neutrophils, endothelial cells, fibroblast and keratinocyte, Interleukin 6 (IL-6) stimulates monocytes, fibroblasts and endothelial cells, is produced by macrophages, lymphocytes T and B, granulocytes, masticates, chondrocytes and osteoblasts, Tumor necrosis factor alpha (TNF-a) secreted by monocytes and macrophages, neutrophils, lymphocytes T, their function is to stimulate monocytes and the ability of fibroblast's remodeling. PRF does not only represents a platelet concentrate, it also participates as a mediator to stimulate defense mechanisms [6,7].

The use of PRF in our country has been growing through time because of its properties and different therapeutic uses, that is why it has led to investigations about centrifugation protocols and manufacture of centrifuges with technical details that offer better results compared to its competition. Therefore this investigation's objective is to establish the cellular composition, clinical and biological uses in the bone regeneration field by obtaining A-PRF, L-PRF, S-PRF with three different centrifugation protocols, establishing as definitive the 9 uses achieved for the regenerative field in dental implants.

Materials and Methods

Develop two centrifugation protocols described by Joseph Choukroun8, where the platelet concentrates were placed in wounds using the body's natural would healing capacity to obtain nine regenerative uses on Oral and Maxillofacial surgery. A sample of eight (8) surgical cases managed between October 2018 and January 2020 were included. Dr Joseph Chouckoun A-PRF-I-PRF protocol was applied in all 08 cases, using autografts from the Retromolar Trigone (ACm Bone Collector - Neobiotech) in some cases and xenografts (Matrix Oss) in others. Nine different surgical procedures were made in various stages: Alveolar preservation technique, Guided Bone Regeneration, Maxillary Sinus floor Lift, Immediate Implant placement, Second Phase surgery in Dental Implants, coverup defects made by taking a palatal epithelial graft, Oral and Maxillofacial Pathology cases, Dento-alveolar surgery complex cases and resolving Peri-implantitis cases. This study was conducted in accordance with the standards of the Declaration of Helsinki of 1983. The patients were informed about the aim and design of the study and a written consent was obtained from all of them. Inclusion criteria: ASA I patients without any previous systemic, immunological or surgical disease, patients with a history of drug abuse were excluded. Also, a blood concentration within the normal range and absence of a history of maxillary sinus inflammations were considerate as inclusion criteria. To review the pre-surgical condition of the patients a clinical and radiographic examination, and in some cases CBCT was made.

The PRF was obtained by the venipuncture of every patient, it was made in the pre-surgical phase before entering the operation room, all the samples were taken and managed by the same operator and four blood collection tubes were obtained by patient. The blood collection tubes should always be placed opposed to each other to balance forces in the centrifuge and avoid unwanted vibrations during the process. For the A-PRF the centrifugation speed

used was 1300 rpm for 8 minutes and for I-PRF the speed used was 700 rpm for 3 minutes. The clinical success of the PRF protocol depends on how quick the collection of blood and its transfer to the centrifuge is made because blood will start the coagulation process 1 - 2 minutes after extracted.

Once the centrifugation process is over, the sample preparation for A-PRF consists in extract the acellular plasma on top with a syringe without touching the clot. This A-PRF clot is removed with the kit's tweezers that does not puncture its content, it is dragged out without cutting the red blood cells in the bottom, separating them from the clot. At this moment the A-PRF clot is obtained, then put on the PRF Box and it is compressed for at least five minutes to obtain the A-PRF membrane. Different studies have shown that significant amounts of growth factors are released during the first 20 minutes after its preparation, also it has been known that it can last for a 4-hour period (Figure 1). For I-PRF, once the centrifugation is over, the liquid part on top of the tube is extracted with a syringe, a totally liquid sample is obtained. Merging A-PRF, I-PRF and a biomaterial (autologous or xenograft) results into sticky-bone (Figure 1).

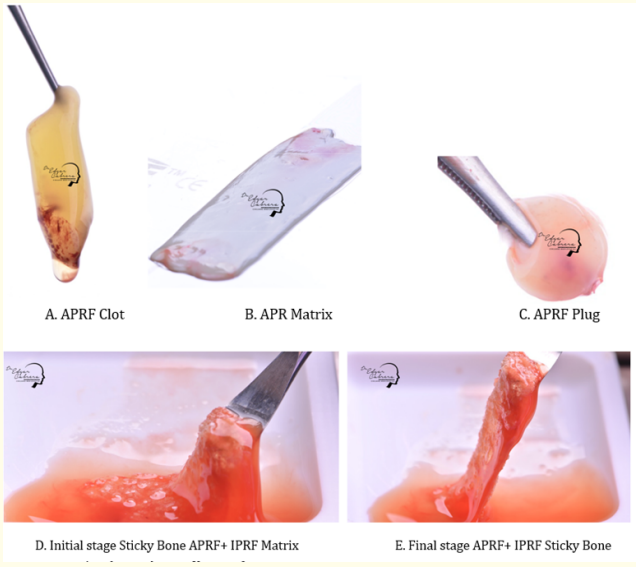

Figure 1

The two different types of PRF obtained, A-PRF for a matrix and I-PRF for an injectable solution, were applied for different surgical techniques, a total of nine (9) new clinical uses:

1. **Alveolar preservation and guided bone regeneration:** In this case a DFDBA bone graft was used, it was soaked up with an A-PRF liquid membrane taken after the membrane's compression and placed directly in the left maxillary central incisor alveolus zone, considering the importance of previously placing a collagen membrane with the tunnel technique on the vestibular cortical bone and on top of that a A-PRF membrane was placed to achieve alveolus closure with an A-PRF plug and sutured with a 5-0 inter-proximal monofilament suture (Figure 2).

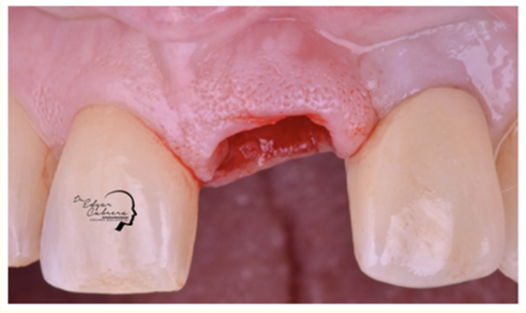

Figure 2A: Alveolar preservation.

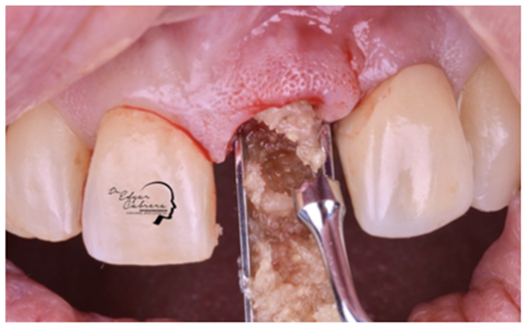

Figure 2B: GBR+APRF (Guided bone regeneration).

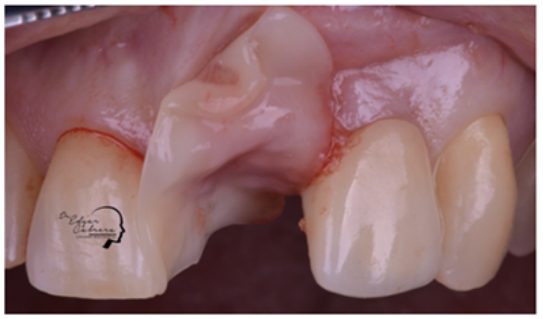

Figure 2C: APRF matrix positioning.

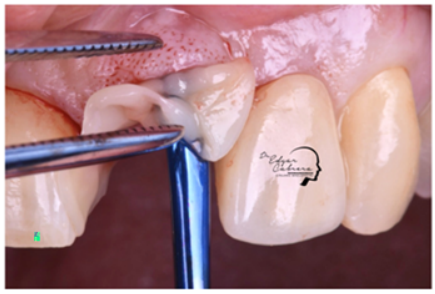

Figure 2D: APRF matrix Stabilization.

2. **Immediate implants and guided bone regeneration:** The same surgical technique applied in cases of atraumatic extractions and immediate implant placement but in this case the vestibular gap is filled (between the vestibular surface and the bone cortical) with the A-PRF soaked up biomaterial, this liquid allows to fill up all the alveolar length. In maxillary and mandibular molars extractions the guided bone regeneration is made in the alveolar bone around the implant and for the final closure a punched A-PRF plug can be use with the prosthetic abutment or healing screw to isolate the alveolar healing process (Figure 3).

3. **Second phase surgery:** A punched A-PRF plug with the second phase screw or healing screw seeks to isolate the alveolar healing process to obtain a better emergence profile with the soft tissue healing. In cases where the primary stability is not reached or in deferred implants, the Roll technique [9] is used to improve the vestibular profile applying the same procedure of A-PRF punched in the healing screw (Figure 4).

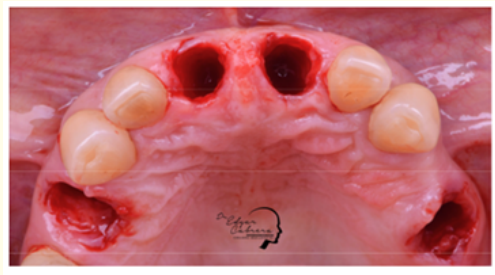

Figure 3A: Atraumatic extractions.

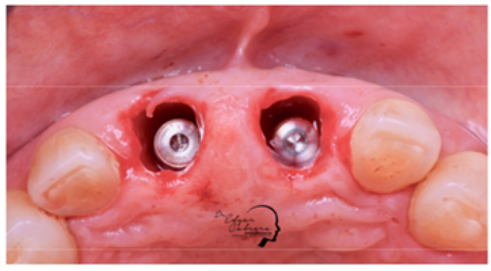

Figure 3B: Immediate implant placement.

Figure 4A: Healing´s screw + APRF plug.

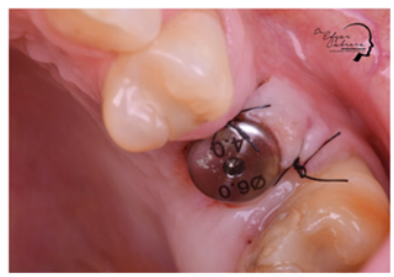

Figure 4B: Roll technique.

4. **Oral and maxillofacial pathology cases:** A patient is initially diagnosed with Cementoblastoma, with the use of trephine the resection of the alveolar bone cortical of the first and second mandibular molars was made. 6 A-PRF clots were placed and it was sutured with monofilament suture. After 6 months with a postoperative evaluation implants were placed and loaded, showing the 5 year follow up (Figure 5).

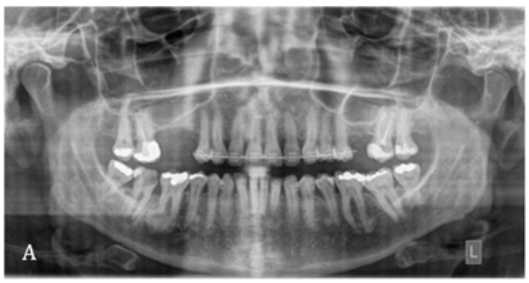

Figure 5A: Oral pathology case: Initial radiography where the diagnosis of cementoblastoma is established.

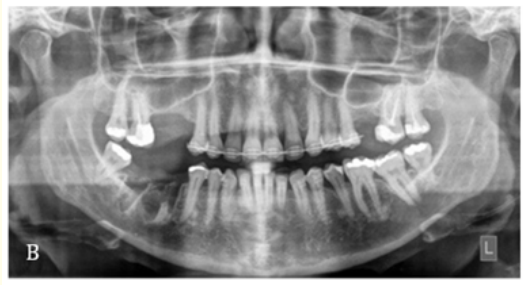

Figure 5B: Post-surgical Healing process after the management with the APRF Plug´s.

5. **Maxillary sinus floor lift:** First the surgical site where the regeneration will take place has to be prepared, then an autologous graft from the retromolar trigone with bone collector drills (ACM bone collector Neobiotech) were obtained and mixed 50:50 with xenografts, both soaked in A-PRF previously cut membrane which was then mixed with I-PRF liquid plasma to change its final consistency to be completely firm. Finally, a collagen membrane was used to cover the lateral window (Figure 6).

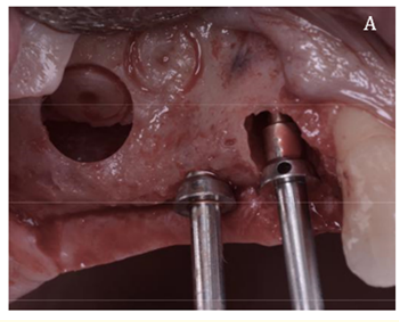

Figure 6A: Sinus Lift (surgical view).

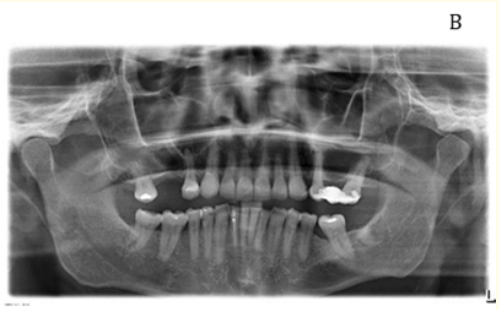

Figure 6B: RX pre-surgical condition.

6. **Dento-alveolar Surgeries:** A-PRF plug was placed in the dental alveolus after a traumatic avulsion of the tooth and sutured with a monofilament 5-0 suture (Figure 7).

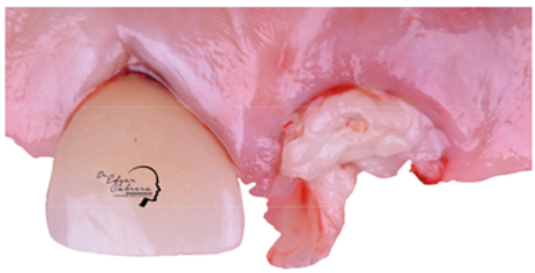

Figure 7A: Only APRF plug positioning

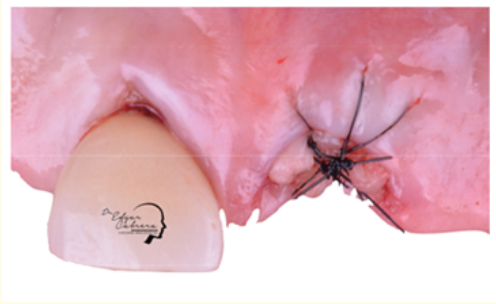

Figure 7B: Suture.

7. **Cover donor's site when a palatal epithelial graft is taken:** After taking the gingiva tissue palatal graft, 2 A-PRF membranes were placed between the suspension suture and the periosteum giving 2 proximal fixation sites to improve stability, reduce palatal's healing process to 21 days maximum and reduce patient's discomfort (Figure 8).

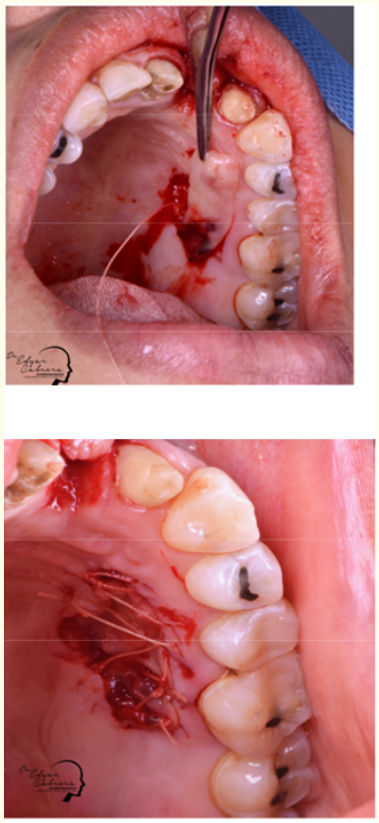

Figure 8

8. **Peri-implantitis cases:** The prosthetic, screw retained or cemented, crows were removed for 21 days placing healing abutments with A-PRF punched plug that performs as a biological barrier. Guided bone regeneration was performed on the peri-implantitis zone (Figure 9).

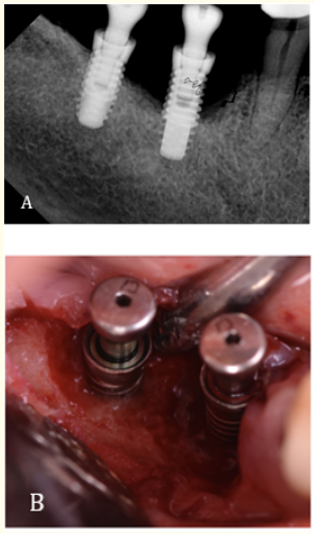

Figure 9A and 9B: Initial condition, RX Periapical imaging, clinical.

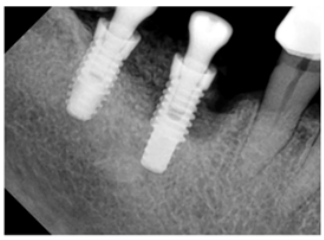

Figure 9C: IHealing condition, RX Periapical after surgery.

Results

A postoperative follow up was made in every surgical procedure showing the following results:

1. **Alveolar preservation and guided bone regeneration:** After 12 weeks a postoperative evaluation was made showing the alveolus healing, keratinized gingiva formation and bone neoformation which allowed placing a dental implant in the incisor's zone (Figure 10).

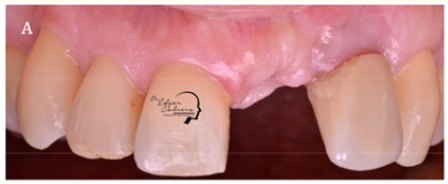

Figure 10A: Healing condition, clinical condition.

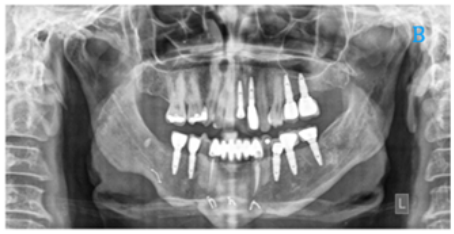

Figure 10B: Panoramic X-ray.

2. **Immediate implants and guided bone regeneration:** 2 postoperative evaluations were made,10 days and 45 days after, it showed a fibrin plug formation that allowed new keratinized gingiva to appear and works as a barrier between the bone regeneration zone and the mouth, also improved the implant's emergence profile. The new bone formation is seen around the dental implants (Figure 11).

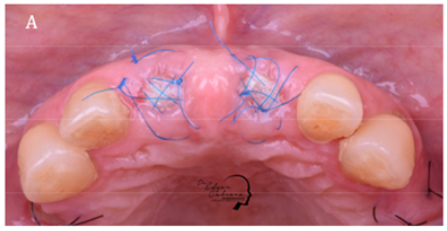

Figure 11A: Healing condition, 10 days after surgery.

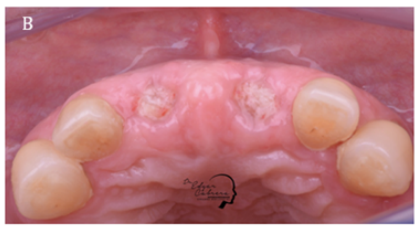

Figure 11B: Healing condition, 45 days after surgery.

3. **Second phase surgery:** 10 days after a postoperative control was made showing a wound healing process, no edema or bleeding and a good amount of keratinized gingiva that improves the implant's emergence profile (Figure 12).

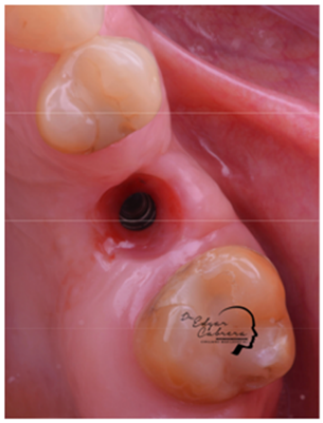

Figure 12: Healing Screw Poncho´s Technique, Second stage surgery.

4. **Oral and maxillofacial pathology cases:** A radiographic evaluation was made 4 months and 5 years after placing the implants, showing bone formation around implants and no signs of cementoblastoma relapse (Figure 13).

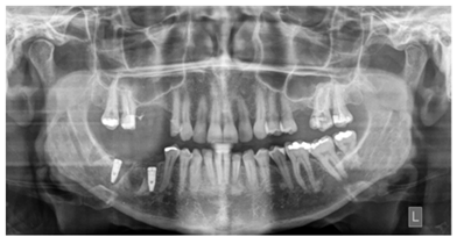

Figure 13A: 4 months after dental implant installation.

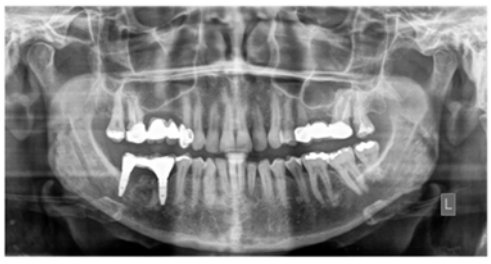

Figure 13B: 5 years follow-up.

5. **Maxillary sinus floor lift:** 6 months after the surgery a radiographic exam was made and a dental implant was placed in the zone of the maxillary first molar. The Rx showed new bone formation where the sinus lift was made gaining 8 mm that allowed the primary stability of the placed implant (Figure 14).

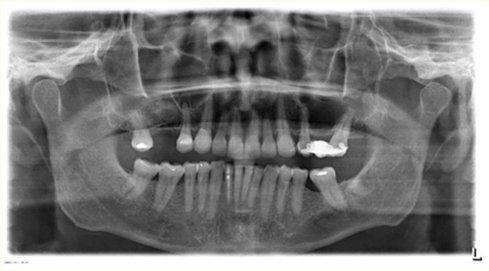

Figure 14

6. **Dento-alveolar surgery:** 7 days after the surgery a fibrin plug was formed in the avulsion zone with evidence of keratinized gingiva (Figure 15).

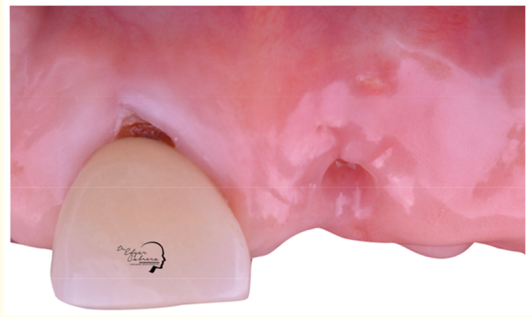

Figure 15

7. **Cover donor's site when a palatal epithelial graft is taken:** 18 days after the surgery a total healed keratinized gingiva where the graft was taken was seen, no evidence of edema or bleeding, patient referred a minor discomfort that lasted 3 days (Figure 16).

8. **Peri-implantitis cases:** 3 and 6 months after the surgery new bone formation around implants was shown, no bleeding, no edema and the implant body was not showing (Figure 17).

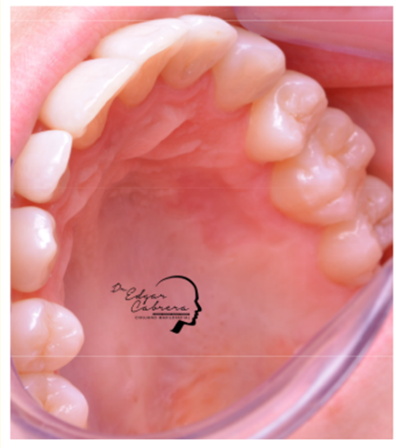

Figure 16: Healing process 18 days.

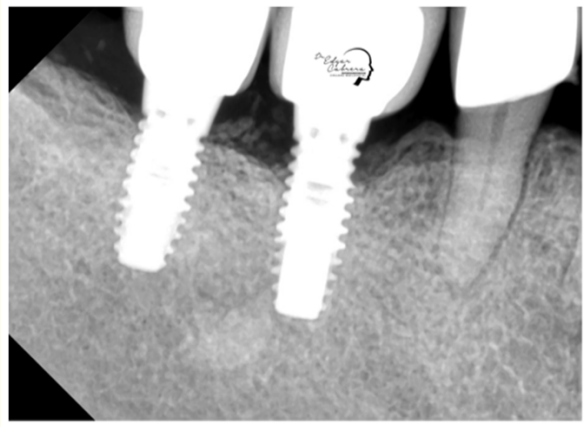

Figure 17

Discussion

The PRF technique was first described in France by Choukroun. This technique did not require using blood thinners which allowed the activation of the platelets contended in a blood collection tube in a few minutes just by being in contact with the walls of the red collection tube, putting the fibrinogen concentrate on the top of the tube before the thrombin transformed into fibrin. The result is a fibrin clot in the middle of the tube between the erythrocyte concentrate and the acellular plasma on the top [8].

The fibrin's biological activity is enough to induce a healing capacity in any tissue where it is put. Slow polymerization gives the

PRF membrane a favorable architecture to pit up with the wound healing process [8].

Growth factors have shown their capacity to accelerate bone repair and promote osteoblast's proliferation, they also increase vascularity, mesenchymal, endothelial and osteoblast cell's mitosis which allows membrane formation that supports mesenchymal cells for bone regeneration [10].

Because of PRF's biological composition that shows a great amount of growth factors, such as PDGF (platelet derived growth factor). TGF-b (transforming growth factor), VEGF (vascular endothelial growth factor) others like fibrinogen, fibronectin, vitronectin, PRF receives the property to change phases in the wound healing process and angiogenesis [11], obtaining clinical results as mentioned in this article: alveolar preservation, bone guided regeneration, maxillary sinus floor lift, immediate implants, second phase surgery, to cover donor's site when a palatal epithelial graft is taken, Oral and Maxillofacial Pathology cases, dento-alveolar surgeries and peri-implantitis cases.

PRF used for alveolar preservation in post-operative alveolus and on immediate implant placement represents a useful tool to improve post-operative pain and soft tissue healing process, especially on the first day, reducing inflammation effects. The fibrin membrane promotes the mechanical protection of the surgical site and interacts biologically with the angiogenesis mechanism and immune process because of its leucocyte concentration, important to prevent post-operative infections [11].

Regarding PRF's potential as a tissue regenerator used on second phase surgeries and to cover up defects caused by taking palatal grafts, it has been shown that it is capable to act as a biological barrier helping primary closure of the surgical site protecting it for external aggressions, it accelerates the healing process from 3 - 4 weeks to just 18 days and helps with patient's pain [12].

Recent studies have also shown its capacity on bone regeneration, even as being the only material used to sinus lifting, generating up to 7.5 - 10.1 mm of new bone. Its properties have also been used on handling sinus membrane ruptures during the sines lift [13].

PRF's clinical and immune characteristics have allowed to establish the nine uses mentioned in this article, however, it is possible to add other like management of third molar post-operative complications, periodical lesions, management of oro-sinusal communication, dental infection treatment, among others.

Conclusion

Finally, it can be concluded that the right management of these platelet concentrates and their knowledge regarding its biological activity, is a useful tool on different clinical scenarios that can occur in the daily practice of all dental specialties.

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