

Use of platelet-rich fibrin (PRF) in periodontology: A review

Aslı Sağsöz¹ , Filiz Acun Kaya^{1,2} 

¹ Firat University, Faculty of Dentistry, Department of Periodontology, Elazığ, Turkey

² Dicle University, Faculty of Dentistry, Department of Periodontology, Diyarbakır, Turkey

Received: 20 February 2023

Accepted: 10 April 2023

Published: 1 June 2023

Correspondence:

Dr. Aslı SAĞSÖZ

Firat University, Faculty of Dentistry,
Department of Periodontology, Elazığ,
Turkey.

E-mail: sgszasli1@gmail.com



How to cite this article:

Sağsöz A, Acun Kaya F. Use of platelet-rich fibrin (PRF) in periodontology: A review. J Med Dent Invest 2023;4:e230317.
<https://doi.org/10.5577/jomdi.e230317>

Abstract

Platelets play an essential role in wound healing and periodontal regeneration, so using platelet concentrates can speed up wound healing after periodontal treatment. Platelet-rich fibrin (PRF), an autogenous concentrated blood product, is a fibrin matrix comprising molecular and cellular elements that allow for optimum improvement and PRF also increases the production of osteoprotegerin, which causes osteoblast proliferation and acts as an osteoconductive and osteoinductive material, initiating bone regeneration. Platelet-rich plasma (PRP) and PRF are platelet concentrates prepared from the patient's own blood. Recent studies have focused on the development of therapeutic alternatives that are simple to prepare, non-toxic or biocompatible to living tissues, and inexpensive, with the potential to result in the local release of growth factors that accelerate hard and soft tissue healing. PRP is a plasma fraction that contains a high concentration of growth factors. PRF is a natural fibrin-based biomaterial derived from an anticoagulant-free blood harvest without any artificial biochemical modification, allowing fibrin membranes enriched with platelets and growth factors to be obtained. It facilitates the application of growth factors to the surgical area in a concentrated form, thereby accelerating wound improvement and regeneration. Platelet concentrates are used in many areas of dentistry, including soft tissue improvement, plastic periodontal surgery, gingival enlargement, ridge preservation, regeneration of bone defects, drug-related osteonecrosis of the jawbone, sinus augmentation, immediate implant placement, and implant osseointegration. Their use is preferred due to their ease of application and low cost. This paper reviews the current literature concerning the utilization of platelet-rich fibrin in periodontology.

Keywords: Platelet-rich fibrin, platelet-rich plasma, regeneration, autogenous blood product, growth factors

Introduction

1. Purpose of autogenous concentrated blood products

Platelets represent the main source of the growth factor complex, which plays a fundamental role in natural wound improvement. More specifically, platelets contain growth factors and cytokines that initiate wound improvement. Both platelet-rich plasma (PRP) and platelet-rich fibrin (PRF), which have been developed in recent years, enable the application of growth factors in a concentrated form to the surgical area, thereby accelerating wound improvement and regeneration [1]. Blood draws attention as the most important autogenous source used by the body in its own repair, both in soft tissue healing and hard tissue healing [2].

The molecular structure of PRF, a fibrin biomaterial with a low thrombin concentration, is considered an optimum matrix for the migration of endothelial cells and fibroblasts. It has previously been stated that PRF membranes can be used for all kinds of superficial cutaneous and mucosal healing processes, as PRF provides rapid angiogenesis and allows for the easier remodeling of fibrin [3]. PRF is not merely a simple fibrin membrane; rather, it is a matrix containing all the molecular and cellular elements that allow for optimum improvement. The matrix has been determined to carry all the beneficial components found in a blood sample [3]. These components can be obtained without any additions or manipulations. Thus, PRF has been recognized as a healing biomaterial. Moreover, it has been emphasized that a polymerized fibrin matrix with a tetramolecular structure consists of platelets, leukocytes, and cytokines, and it indicates the presence of circulating stem cells. Despite the gradual release of the cytokines retained within PRF having the potential to accelerate cellular events, it has been observed that the fibrin network structure is essential for all advanced PRF recovery processes [3].

1.1. Autogenous Concentrated Blood Products

The platelet concentrates of autogenous blood products can be divided into four categories on the basis of their fibrin and leukocyte contents [4]:

- Pure platelet-rich plasma (P-PRP)
- Leukocyte- and platelet-rich plasma (L-PRP)
- Pure platelet-rich fibrin (P-PRF)
- Leukocyte- and platelet-rich fibrin (L-PRF)

1.2. Platelet-Rich Plasma

To prevent platelet activation and degranulation, the venous blood taken with anticoagulant is separated into 3 layers following the initial centrifugation. The red blood cells located at the bottom of the tube constitute 55% of the total volume. By contrast, at the top of the

tube, the cell-free plasma layer mainly consists of circulating plasmatic molecules (especially fibrinogen) and a low percentage of platelets. This upper layer is known as platelet-poor plasma (PPP) and constitutes 40% of the total volume. Between the two aforementioned layers, the platelet concentrations are greatly increased, with the interlayer constituting just 5% of the total volume [5]. This interlayer includes the bulk of the concentrated platelet-rich plasma (cPRP), although there is no easy scientific process for separating it from the other layers at this stage. Instead, using a sterile syringe, it is necessary to aspirate the PPP, PRP, and some red blood cells (systemically removed during surgery). This material, which is transferred to a tube that does not contain anticoagulant, is then subjected to longer and faster centrifugation in the second tube than in the first. This process ensures that the platelets are concentrated at the bottom of the tube, meaning that three different layers are again obtained. It is easier to collect the PRP at this stage. Most PPP can be removed using a syringe, leaving only enough serum to place the concentrated platelets in suspension. Next, the unit should be gently shaken to obtain ready-to-use cPRP. Red blood cells trapped at the bottom of the tube are also involved during the shaking, which explains the pink aspect of the finish. The cPRP must then be mixed with both bovine thrombin and calcium chloride using a mixing syringe. The gelation of the platelet concentration occurs rapidly. The fibrinogen also condenses during the cPRP preparation, with its polymerization forming a fibrin matrix with particularly interesting hemostatic and adhesive properties. The fibrin polymerization is completed within a few minutes during the cPRP application, which can be made into a gel or spray [5] (Fig. 1).

The benefits of using PRP in relation to medicine have been extensively studied, although most reviews are found in the fields of orthopedics and sports medicine [6]. In terms of oral and maxillofacial surgery, PRP is used in the treatment of periodontal bone defects and sinus elevation techniques, as well as for hard and soft tissue augmentation, especially following the extraction of third molars. PRP is used in this type of surgery to accelerate the vascularization of the graft, enhance the soft tissue improvement and bone regeneration, and reduce the incidence of postoperative morbidity. However, prior results in this regard have proved inconclusive. To increase its effectiveness, the preparation protocol for this platelet concentrate has been modified and adapted several times over the years [6]. Despite this, the number of studies concerning the effectiveness of PRP is considered insufficient. Moreover, there has been no standardization with regard to the study designs, such as patient-control groups or comparison preparation protocols [6].

In addition, it has been established that the use of PRP has a number of significant disadvantages, including the fact that the preparation protocol involves a costly, complex, and practitioner-dependent phase, while the use of animal thrombin as a coagulator raises legal concerns [7].

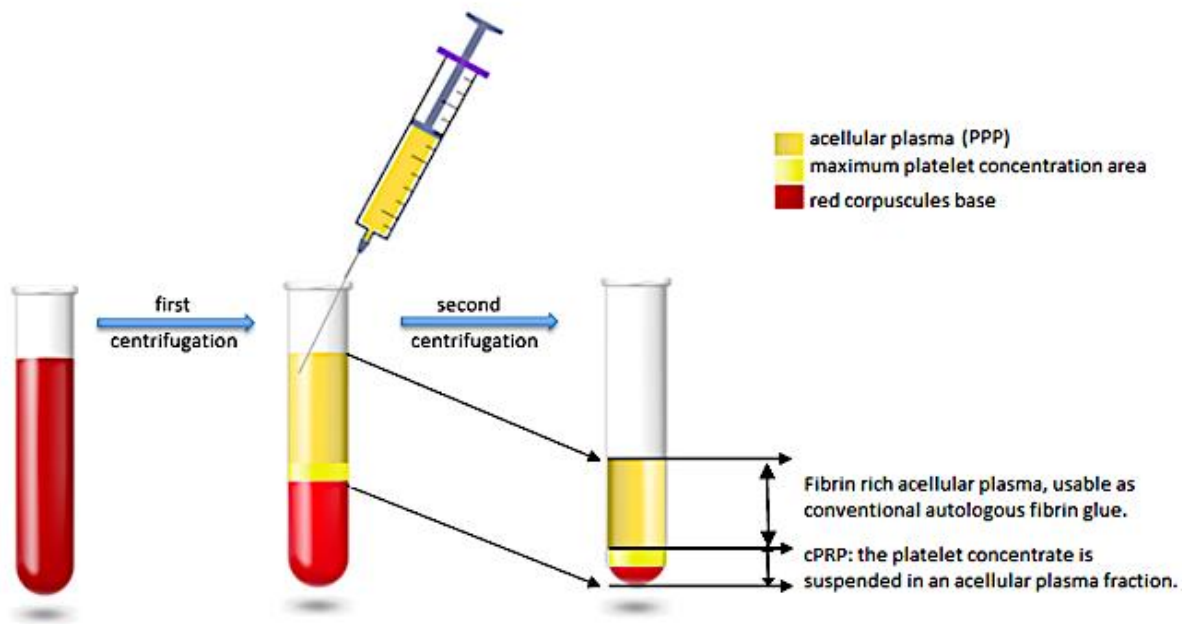


Figure 1. Getting platelet-rich plasma

1.2.1. Platelet-Rich Fibrin

The disadvantages of first-generation concentrated blood products have prompted the development of new products. In this regard, without disrupting the natural coagulation mechanism, blood samples (9-10 mL) are transferred into glass-lined, completely glass, plastic-lined or titanium tubes (Fig. 2a) [8].

The tubes are placed in pairs and centrifuged for 12 minutes under 400 g relative centrifugal force (RCF) using the Nuve centrifuge (Nuve, Ankara, Turkey); 400 g RCF is equivalent to 2700 revolutions per minute (RPM) (Fig. 2b). The centrifugation process leads to the activation of the physiological coagulation cascade and subsequent formation of fibrin clots enriched with blood cells. L-PRF clots and membranes produced using higher RCFs such as 400 and 600 RCFs are significantly larger and have higher bone regenerative potential, whereas clots originating from lower RCFs such as 200 RCFs potentially have a weaker and less polymerized fibrin chain and smaller sized L-PRF clots [9].

It is vital that the blood collection and insertion of the tubes into the centrifuge be as quick as possible so that it is achieved before the spontaneous coagulation process takes place. It is important at this point that the tubes are centrifuged within 60 seconds of starting the IV line. This usually requires loading the centrifuge with the tubes in twos or one at a time. In the latter case, a tube filled with the same amount of glycerin or saline should be used to balance centrifugation. No additional treatment is applied to the blood; no anticoagulants are used in the tubes, and therefore animal thrombin and calcium chloride are not required for fibrin

polymerization. Plastic tubes are coated with silica and silicone to activate coagulation. In the absence of anticoagulants, the activation of platelets in contact with the inner walls of the tube is allowed. After a few minutes, a coagulation cascade is initiated. Initially, the fibrinogen is positioned at the top of the tube. However, due to the activation of autologous thrombin after centrifugation, it is converted to fibrin, and a fibrin clot is formed.

Three different layers can be seen in the tube after centrifugation (Fig. 3) [6]. There are red blood cells in the lower part of the tube, PPP in the upper part of the tube, and between those two layers, there is a fibrin clot consisting mostly of leukocytes and platelets. The leukocyte- and platelet-rich fibrin (L-PRF) clot can be removed from the tube using forceps. The red blood cell fraction can be gently separated from the fibrin clot with a spatula-like instrument. The growth factor-rich exudate contained within the clot can be removed with approximately five minutes of gentle pressure on the clot to obtain stronger L-PRF membranes. This pressure can be achieved with a box containing a weighted pressure plate that removes the serum from the L-PRF clot. In this way, standard 1-mm-thick L-PRF membranes are obtained. Membranes remain stable for several hours at room temperature. It has also been demonstrated that membranes containing an intense fibrin network can withstand a load of approximately 400 g without tearing [8]. L-PRF provides a fibrin scaffold that supports cellular migration, which is an important aspect of the regeneration process [10]. It has been noted that L-PRF membranes continuously excrete copious amounts of growth factor for a period of 7 to 14 days [10].

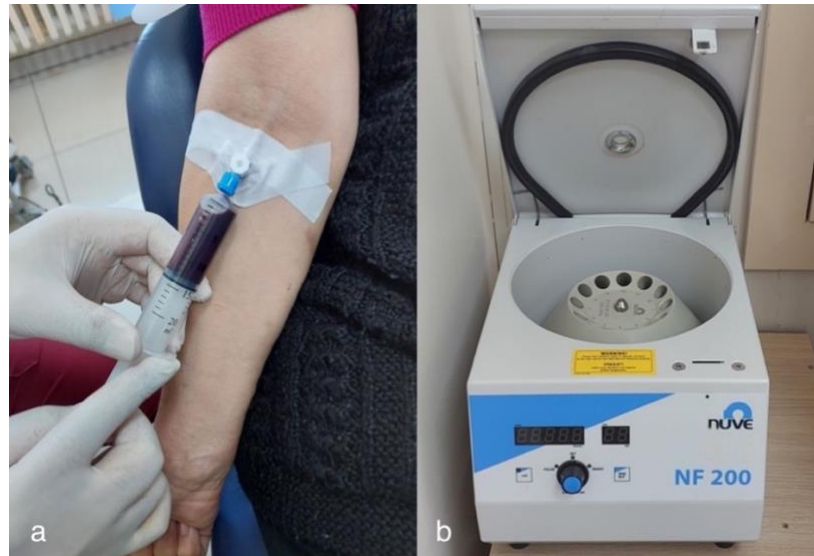


Figure 2. (a) Obtaining venous blood from the vascular access, (b) Centrifuge device.

Concentrated growth factors (CGF), advanced platelet-rich fibrin (A-PRF), and injectable platelet-rich fibrin (I-PRF) were found to improve the properties of PRF. By changing the centrifugation time and speed, better autogenous biological material can be obtained [11, 12]. In their study comparing PRP, PRF, and A-PRF after 15-60 minutes of incubation, Kobayashi et al. routinely found that A-PRF released the highest total growth factors at later time points up to 10 days. They noted that when compared to traditional PRP or PRF, A-PRF released significantly higher total quantities of growth factors accumulated over a 10-day period [13]. Plastic tubes in I-PRF are intended to be used in liquid form without PRF membrane formation. Unlike L-PRF, the main purpose of these products is to obtain good biological material that can be used with graft materials [2].

To overcome the disadvantages of PRP, new techniques were investigated, and in 2001, Choukroun et al. [14] introduced PRF. Platelets have an important function in the release of growth factors. Alpha granules

in platelets include: platelet-derived growth factor (PDGF), which initiates wound improvement by attracting and activating macrophages, fibroblasts, and endothelial cells, insulin-like growth factor-1 (IGF-1), epidermal growth factor (EGF), vascular endothelial growth factor (VEGF), and transforming growth factor β (TGF- β). L-PRF membranes continuously (≥ 7 days) secrete large amounts of growth factor. A significant amount of these growth factors is produced by platelets. These growth factors are also present in the PRP gel. However, it is released especially in the first hours and is completely dissolved in the environment after three days due to the chemical activation of the platelet content. This difference can be explained by differences in fibrin architecture between the PRF families. PRF has a natural polymerization with the intrinsic growth factor mesh, whereas PRP gel families have artificially initiated polymerization with the extrinsic growth factor mesh, leading to their immediate release and use or destruction [5, 15, 16].

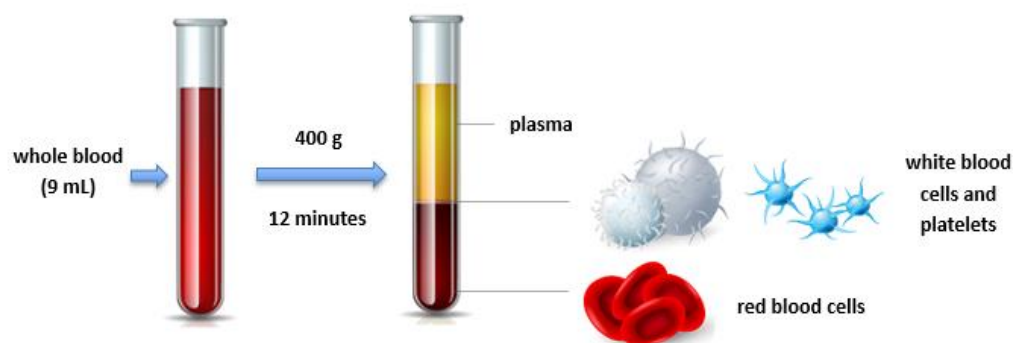


Figure 3. L-PRF with three components after centrifugation.

PRF can be viewed as an autologous biomaterial made from a fibrin matrix containing the highest platelet concentration; the maximum concentration of growth factors (including VEGF, PDGF, and TGF); a representative concentration of thrombospondin, fibrin, fibronectin, and vitronectin; and a leukocyte concentration of approximately 65% [16].

Being completely autogenous and containing no foreign matter, wound improvement with PRF allows natural inflammation [16]. During glass tube centrifugation, silica in the glass or glass-coated tube (which acts only as a catalyst in platelet activation) has side effects, and glass-activated fibrin is resorbed in human tissues in 7-11 days. It has been stated that this resorption time is sufficient for soft tissue healing, but the osteoconductive feature when used alone in hard tissue healing is still a question mark.

However, PRF stands out as a superior biological material when used with autogenous or non-autogenous graft materials [17]. Tunalı et al. [18] stated that it is not correct to talk about the natural inflammation of PRF

when it is used with non-autogenous products and that the foreign substance reactions of the graft with which it is used in the body resorptive affect wound improvement in the region and prevent physiological inflammation, which impairs the properties of PRF.

Tunalı et al. found that a tighter fibrin network structure was formed by using titanium instead of silica in platelet activation, and that this tight fibrin structure was also used as a stand-alone autogenous graft material by increasing the resorption time of the titanium-platelet-rich fibrin (T-PRF) membrane in the tissue (Fig. 4) [19]. This is the first human study to identify T-PRF as an autogenous leukocyte- and platelet-rich fibrin product. In their studies [19], it was shown that T-PRF can remain without resorption for more than 30 days after it is placed into the tissue, and it has been pointed out that T-PRF provides the controlled release of growth factors. It has also been shown to activate bone improvement mechanisms in the body due to its long resorption time and natural matrix structure [20].



Figure 4. Transporting the T-PRF to the PRF box after centrifugation.

CLINICAL AND RESEARCH CONSEQUENCES

2. Use of Platelet-Rich Fibrin (PRF) in periodontology

Today, the least costly and most up-to-date way to obtain platelet concentrate is PRF production. PRF is classified as L-PRF or pure platelet-rich fibrin (P-PRF) based on its leukocyte content. L-PRF contains up to 90% of platelets and at least 75% of leukocytes in the patient's blood [6]. L-PRF is the most recent development in blood-derived platelet concentrations.

L-PRF is used in many areas, such as the treatment of periodontal bone defects, protection of the alveolar ridge, elevation of the sinus floor, periodontal mucogingival surgery, and implant surgery. L-PRF can be used in the treatment of periodontal or bone defects by filling into the defect for regenerative purposes (Fig. 5). When applied in this way, it is expected to act similarly to directed tissue regeneration and directed bone regeneration [21]. By keeping the epithelium and connective tissues away from the intraosseous crater, cells from the periodontal ligament or periosteum have time to regenerate the cementum, bone, and ligaments. It has been point out that L-PRF supports the

proliferation and differentiation of osteoblasts and bone marrow stromal cells in vitro [22]. It can be used during the PRF augmentation process to take advantage of this feature (Fig. 6). An analysis examining the application of L-PRF in regenerative procedures found decreased

pocket depth, increased clinical attachment levels, and bone defect filling [23]. Some studies have combined L-PRF with a bone graft, and an additional benefit has been noted.

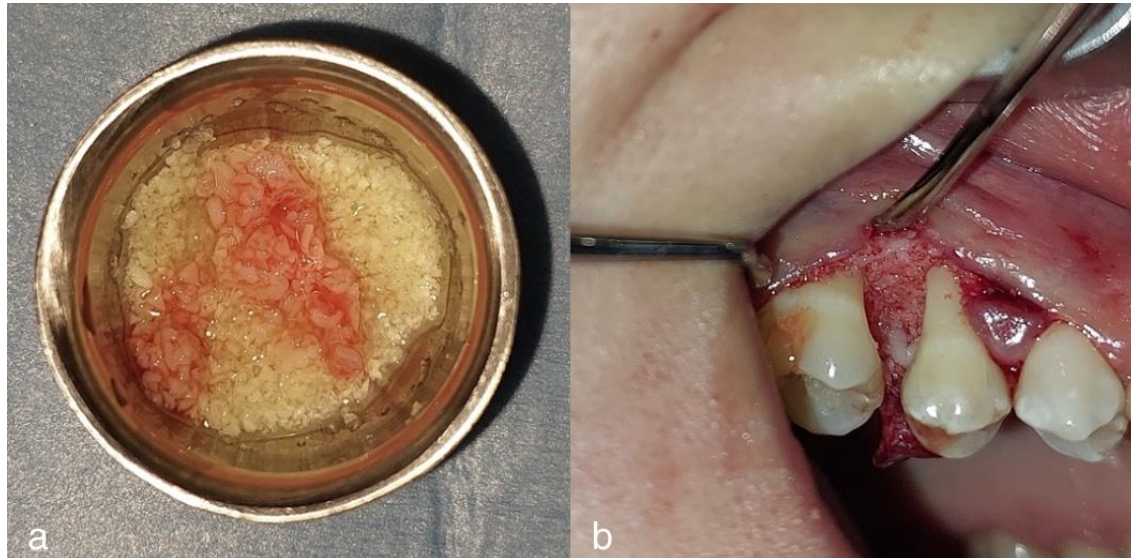


Figure 5. (a) Allogeneic bone graft with fragmented L-PRF, (b) Application of L-PRF combined with bone grafting to the bone defect.

Sharma et al. [24] showed the effect of PRF on the healing potential of hard and soft tissue in the treatment of Class 2 furcation problems. Only open flap operation was performed in the control group patients, and PRF application was performed together with the open flap operation in the test group. At the nine-month clinical and radiographic measurements, statistically important gains were recorded in the test group compared to the control group in all clinical and radiographic parameters compared to the baseline, confirming that PRF can be an effective treatment method in the regenerative treatment of furcation defects.

After tooth extraction and loss of the bundle bone, the alveolar ridge undergoes remodeling in both the vertical and horizontal directions. This process often makes it difficult to place implants in an ideal position. Many surgical techniques have been developed to prevent or at least minimize osteoporosis. The use of L-PRF in an extraction socket may be a less costly, simpler, and more effective treatment alternative, but standardization of the protocol is required to obtain reproducible results. The use of adequate L-PRF clots or membranes appears to be crucial for achieving an optimum effect [25]. In their systematic review, Castro et al. [25] showed that L-PRF application alone resulted in less buccal bone resorption and preservation of alveolar width compared to natural healing. Hauser et al. [26] concluded that L-PRF application after tooth

extraction resulted in better preservation of alveolar crest width and better intrinsic bone quality (measured by bone biopsies with microcomputed tomography). A study by Temmerman et al. [27] that compared natural improvement of extraction sockets and improvement between sockets filled with L-PRF saw significantly less horizontal and vertical resorption, more socket filling, higher bone quality, and faster soft tissue and bone improvement. It has been shown that L-PRF, as a filling material, has a beneficial effect on soft tissue improvement and postoperative pain [28]. The PRF clot provides rapid neoangiogenesis and compensates for bone trauma caused by extraction, with bone regeneration induced by growth factors.

L-PRF is useful as a graft for the sinus (alone or in combination with a bone graft), as a membrane to close the lateral window, as protection for the Schneiderian membrane after separation from the underlying bone, or for closing a membrane rupture in the sinus region. After the external lateral sinus lift procedure, the window in the maxillary sinus is usually closed with a resorbable collagen membrane. This membrane reduces the proliferation of connective tissue and the reabsorption rate of the graft material. Gassling et al. [29] conducted a randomized controlled trial with a split-mouth design in which a bilateral external sinus augmentation procedure was performed. The sinus was filled with a mixture of deproteinized bovine bone mineral (DBBM)

and autologous bone. On one side (control), the lateral window was closed with a resorbable collagen membrane; on the other side (test), it was covered with L-PRF membranes. The authors concluded that there was no difference in the rate of new bone formation and

residual bone replacement between the two groups. From this study, it can be concluded that an L-PRF membrane is a potential option for covering the lateral window in the maxillary sinus.

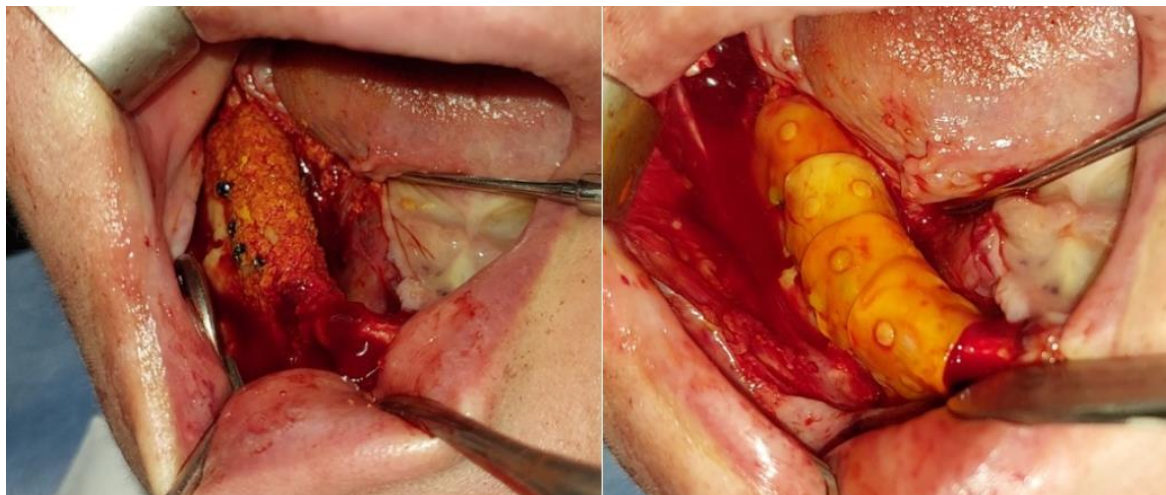


Figure 6. Covering the bone graft with T-PRF during augmentation.

L-PRF can be used as a stand-alone graft in sinus augmentation, or it can be applied with the lateral window technique or trans alveolar approach when used simultaneously with the placement of implants (with the tent effect protecting the cavity in bone regeneration). Each of these studies concluded that natural bone regeneration (approximately 10 mm with the window technique and 3.5 to 4 mm with the trans alveolar approach) occurs around the implants when L-PRF is used as the sole filling material [25]. L-PRF can also be used when implants need to be placed in a second stage (due to insufficient residual bone height) but must be mixed with a bone graft to delay resorption. The bone graft acts as a placeholder and provides an additional osteoinductive matrix. Although Lambert et al. [30] concluded that the use of pure autologous bone resulted in a greater loss of augmentation volume after five weeks, it does not appear to matter which bone graft is used in these procedures. A mixture of DBBM and L-PRF resulted in more new bone formation than when using DBBM alone [31]. As a result, recovery time can be reduced after implant placement. Concomitant use of L-PRF also reduced the amount of bone replacement, accelerated bone formation, and decreased the amount of remaining bone graft particles. A similar study by Toffler et al. reported that PRF alone can be used successfully in sinus wall elevations with an osteotome [32].

L-PRF can be used in mucogingival surgery because of its strong three-dimensional fibrin network. The slow release of growth factors and matrix proteins means that triggering cell induction would take time; however, in L-PRF, growth factors stimulate periosteal cell proliferation, new blood vessels develop within the fibrin matrix, and gingival fibroblasts migrate to the fibrin

matrix and induce remodeling and membrane surface epithelialization [6]. These processes facilitate rapid wound closure and healing and may result in more stable gingival recession and thicker gingiva in the long run. The possible advantages of this technique have prompted research whereby L-PRF is added during periodontal plastic surgery, or L-PRF membranes are used instead of connective tissue grafts (Fig. 7). To date, most studies have investigated the use of L-PRF in combination with the coronally advanced flap technique. It has been concluded that L-PRF can be successfully used instead of connective tissue graft, although long-term studies are needed to confirm the stability of the results [6]. Additional advantages have also been reported when performing a coronally advanced flap using L-PRF compared with a coronally advanced flap without L-PRF [33]. L-PRF applied to the donor site after free gingival graft removal results in faster healing compared with spontaneous healing; less postoperative pain has also been observed [34].

Another study that evaluated the effect of the PRF membrane used in combination with a coronally positioned flap (CPF) in the cure of multiple gingival recessions reported that the combined use of the CPF and the PRF membrane at the end of the sixth month did not provide any additional benefit in the closure of the root surface, although it increased the gingival thickness [35]. In a case report by Anilkumar et al. [36] in which they evaluated the combined use of PRF membrane with a laterally positioned flap (LPF) on the labial surfaces of mandibular anterior teeth for the treatment of gingival recession, it was reported that complete root surface closure was achieved with perfect tissue contour at the end of 6 months.

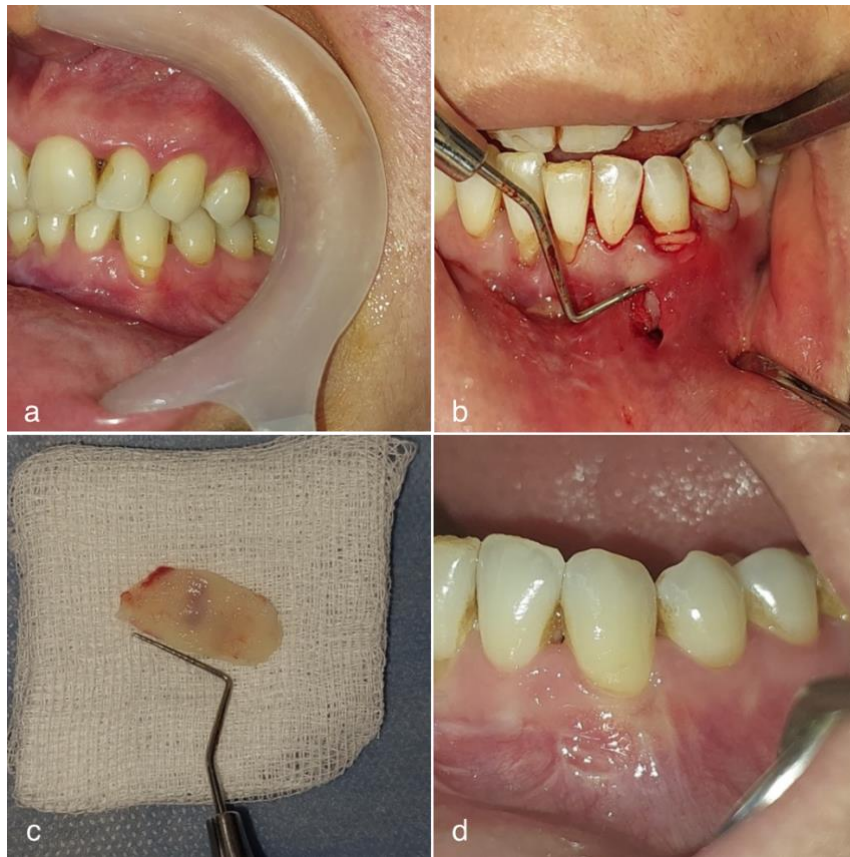


Figure 7. Covering the gingival recession in the mandibular canine tooth with T-PRF membrane and modified tunnel technique. (a) Gingival recession in the canine tooth, (b) Membranous double layer T-PRF, (c) Placing the T-PRF membrane in the prepared tunnel, (d) Postoperative 3rd month view.

In the study by Jankovic et al. [37] on the comparative evaluation of the clinical effect of the combination of a CPF with PRF or an enamel matrix derivative (EMD) in the cure of gingival recessions, after 12 months of follow-up, the PRF membrane was combined with CPF in the cure of gingival recessions. They reported that the combined use did not provide any superiority in terms of root surface closure compared with the use of the combination of KPF and enamel matrix products.

In a study by Öncü and Alaaddinoğlu [38], after the surgical preparation of the implant sockets, the PRF was randomly placed in one of the sockets, and the acellular plasma part of the PRF was also used to wet the implant placed in the PRF-coated socket. It was concluded that the implants showed a statistically higher Quotient of Implant Stability (ISQ; Osstell, Sweden) compared to the control group, measured after implant placement and at 1 week and 1 month after surgery. It has been shown that PRF application provides higher ISQ values and increases implant stability in the early healing period [38]. In addition, the initial amount of bone remodeling was significantly reduced when L-PRF was used in a single-stage implant application [39].

Bisphosphonates are inhibitors of osteoclastic bone resorption. They are used in the cure of osteoporosis (mainly in oral form), as well as in oncology (usually in intravenous form). However, patients treated with bisphosphonates are at risk of delayed bone and tissue improvement. In addition, drug-related osteonecrosis of the jaws/MRONJ may occur after extraction or oral surgery. The literature shows that the use of platelet concentrate at the surgical site can reduce this risk. L-PRF membranes can also be used to improve MRONJ lesions [40, 41].

Conclusion

Platelet concentrates are used in several domains, such as soft tissue improvement, plastic periodontal surgery, gingival enlargement, MRONJ, regeneration of bone defects, ridge preservation, sinus augmentation, immediate implant placement, and implant osseointegration. They are preferred in patient treatments because of their ease of use and low cost.

Disclosures

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - A.S.; Design - A.S., F.A.K.; Supervision - A.S.; Materials - A.S.; Data collection &/or processing - A.S., F.A.K.; Analysis and/or interpretation - A.S.; Literature search - A.S.; Writing - A.S.; Critical review - A.S., F.A.K.

Conflict of Interest: There is no any conflict of interest.

Funding: There is no any funding.

References

- Erdemir, HE, Özkan S. Trombositten zengin materyaller ve periodon-tolojideki kullanımı. Kırıkkale Üniversitesi Tıp Fakültesi Dergisi. 2014;16(1):18-30. <https://doi.org/10.24938/kutfd.124894>
- Kasnak G, Tunalı M, Fıratlı HE. Geçmişten günümüze kan kaynaklı ürünler ve trombositten zengin fibrinler. Türkiye Klinikleri J Periodontol-Special Topics, 2017;3(3):109-12.
- Choukroun J, Diss A, Simonpieri A, et al. Plate-let-rich fibrin (PRF): a second-generation platelet concentrate. Part IV: clinical effects on tissue improvement. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2006;101:e56-60. <https://doi.org/10.1016/j.tripleo.2005.07.011>
- Dohan DM, Andia I, Zumstein MA, et al. Classification of platelet concentrates (Platelet-Rich Plasma-PRP, Platelet-Rich Fibrin-PRF) for topical and infiltrative use in orthopedic and sports medicine: current consensus, clinical implications and perspectives. Muscles Ligaments Tendons J 2014;8(4):3-9.
- Dohan DM, Choukroun J, Diss A, et al. Platelet-rich fibrin (PRF): a second-generation platelet concentrate. Part I: technological concepts and evolution. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2006;101(3):37-44. <https://doi.org/10.1016/j.tripleo.2005.07.008>
- Newman MG, Takei H, Klokkevold PR, Carranza FA. (2018). Newman and Carranza's Clinical periodontology E-book. Elsevier Health Sciences.
- Kawase T. Platelet-rich plasma and its derivatives as promising bioactive materials for regenerative medicine: basic principles and concepts underlying recent advances. Odontology 2015;103:126-135. <https://doi.org/10.1007/s10266-015-0209-2>
- Schär MO, Diaz-Romero J, Kohl S, et al. Platelet-rich concentrates differentially release growth factors and induce cell migration in vitro. Clin Orthop Relat Res 2015;473:1635-1643. <https://doi.org/10.1007/s11999-015-4192-2>
- Giannini S, Cielo A, Bonanome L, et al. Comparison between PRP, PRGF and PRF: lights and shadows in three similar but different protocols. Eur Rev Med Pharmacol Sci 2015;19:927-930.
- Dohan Ehrenfest DM, Pinto NR, Pereda A, et al. The impact of the centrifuge characteristics and centrifugation protocols on the cells, growth factors, and fibrin architecture of a leu-kocyte and platelet-rich fibrin (L-PRF) clot and membrane. Platelets. 2018;17;29(2):171-84. <https://doi.org/10.1080/09537104.2017.1293812>
- Ghanaati S, Booms P, Orlowska A, et al. Advanced platelet-rich fibrin: A new concept for cellbased tissue engineering by means of in-inflammatory cells. J Oral Implantol 2014;40:679-89. <https://doi.org/10.1563/aaid-joi-D-14-00138>
- Kim TH, Kim SH, Sándor GK, Kim YD. Comparison of platelet-rich plasma (PRP), platelet-rich fibrin (PRF), and concentrated growth factor (CGF) in rabbit-skull defect improvement. Arch Oral Biol 2014;59:550-8. <https://doi.org/10.1016/j.archoralbio.2014.02.004>
- Kobayashi E, Flückiger L, Fujioka-Kobayashi M, et al. Comparative release of growth factors from PRP, PRF, and advanced-PRF. Clin. Oral Invest. 2016;20:2353-60. <https://doi.org/10.1007/s00784-016-1719-1>
- Choukroun J, Adda F, Schoeffer C, et al. Une opportunité en parodontologie: le PRF. Implantodontie 2001;42:55-62.
- Marrelli M, Tatullo M. Influence of PRF in the improvement of bone and gingival tissues. Clinical and histological evaluations. Eur Rev Med Pharmacol Sci 2013;17:1958-1962.
- Castro AB, Meschi N, Temmerman A, et al. Regenerative potential of leucocyte- and platelet-rich fibrin. Part A: intra-bony de-fects, furcation defects and periodontal plastic surgery. A systematic review and meta-analysis. Clin Periodontol. 2017;44:67-82. <https://doi.org/10.1111/jcpe.12643>
- Choukroun J, Diss A, Simonpieri A, et al. 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 Radiology Endodontics 2006;101:299-303. <https://doi.org/10.1016/j.tripleo.2005.07.012>
- Tunalı M, Ozdemir H, Kucukodacı Z, Fıratlı E. A novel platelet concentrate for guided bone regeneration: Titanium Prepared Platelet-Rich Fibrin (T-PRF). Gulhane Med J 2015;57:102- 6. <https://doi.org/10.5455/gulhane.173504>
- Tunalı M, Ozdemir H, Kucukodacı Z, et al. A novel platelet concentrate: Titanium prepared platelet-rich fibrin. BioMed Research International 2014;209548. <https://doi.org/10.1155/2014/209548>
- Tunalı M, Ozdemir H, Kucukodacı Z, Akman S, Yaprak E, Fıratlı E. In vivo evaluation of titanium-prepared platelet-rich fibrin (T-PRF): A new Platelet concentrate. British Journal of Oral and Maxillofacial Surgery 2013;51:438- 43. <https://doi.org/10.1016/j.bjoms.2012.08.003>
- Del Corso M, Vervelle A, Simonpieri A, et al. Current knowledge and perspectives for the use of platelet-rich plasma (PRP) and platelet-rich fibrin (PRF) in oral and maxil-lofacial surgery part 1: periodontal and dentoalveolar surgery. Curr Pharm Biotechnol 2012;13:1207-1230. <https://doi.org/10.2174/138920112800624391>
- Dohan DM, de Peppo GM, Doglioli P, Sammartino G. Slow release of growth factors and thrombospondin-1 in Choukroun's platelet-rich fibrin (PRF): a gold standard to achieve for all surgical platelet concentrates technologies. Growth Factors 2009;27:63-69. <https://doi.org/10.1080/08977190802636713>
- Castro AB, Meschi N, Temmerman A, et al. Regenerative potential of leucocyte- and platelet-rich fibrin. Part A: intra-bony defects, furcation defects and periodontal plastic surgery. A systematic review and meta analysis. J Clin Periodontol 2017a;44:67-82. <https://doi.org/10.1111/jcpe.12643>
- Sharma A, Pradeep AR. Autologous Platelet-Rich Fibrin in the Cure of Mandibular Degree II Furcation Defects: A Randomized Clinical Trial. J Periodontol, 2011;82:1396-1403. <https://doi.org/10.1902/jop.2011.100731>
- Castro AB, Meschi N, Temmerman A, et al. Regenerative potential of Leucocyte- and Platelet Rich Fibrin (L-PRF). Part B: sinus floor elevation, alveolar ridge preservation, and implant therapy. A systematic review. J Clin Periodontol 2017b;44:225-234. <https://doi.org/10.1111/jcpe.12658>
- Hauser F, Gaydarov N, Badoud I, Vazquez L, Bernard JP, Ammann P. Clinical and histological evaluation of

- postex-traction platelet-rich fibrin socket illing: a prospective randomized controlled study. *Implant Dent* 2013;22:295-303.
<https://doi.org/10.1097/ID.0b013e3182906eb3>
27. Temmerman A, Vandessel J, Castro AB, et al. The use of leucocyte and platelet-rich fibrin in socket management and ridge preservation: a split-mouth, randomized, controlled clinical trial. *J Clin Periodontol* 2016;43:990-999.
<https://doi.org/10.1111/jcpe.12612>
 28. Eshghpour M, Dastmalchi P, Nekooei AH, Nejat AH. Effect of platelet-rich fibrin on frequency of alveolar osteitis following mandibular third molar surgery: a double-blinded randomized clinical trial. *J Oral Maxillofac Surg* 2014;72:1463-1467.
<https://doi.org/10.1016/j.joms.2014.03.029>
 29. Gassling V, Purcz N, Braesen JH, et al. Comparison of two different absorbable membranes for the coverage of lateral osteotomy sites in maxillary sinus augmentation: a preliminary study. *J Craniomaxillofac Surg* 2013;41:76-82.
<https://doi.org/10.1016/j.jcms.2012.10.015>
 30. Lambert F, Leonard A, Drion P, Soruice S, Layrolle P, Rompen E. Influence of space-filling materials in subantral bone augmentation: blood clot vs. autogenous bone chips vs. bovine hydroxyapatite. *Clin Oral Implants Res* 2011;22:538-545.
<https://doi.org/10.1111/j.1600-0501.2010.02069.x>
 31. Tanaka H, Toyoshima T, Atsuta I, et al. Additional effects of platelet-rich fibrin on bone regeneration in sinus augmentation with deproteinized bovine bone mineral: Preliminary results. *Implant Dent* 2015;24:669-674.
<https://doi.org/10.1097/ID.0000000000000306>
 32. Toffler M, Toscano N, Holtzclaw D. Osteotome-mediated sinus floor elevation using only platelet-rich fibrin: an early report on 110 patients. *Implant Dent* 2010;19(5):447-456.
<https://doi.org/10.1097/ID.0b013e3181f57288>
 33. Castro AB, Meschi N, Temmerman A, et al. Regenerative potential of leucocyte- and platelet-rich fibrin. Part A: intra-bony defects, furcation defects and periodontal plastic surgery. A systematic review and meta-analysis. *J Clin Periodontol* 2017a;44:67-82.
<https://doi.org/10.1111/jcpe.12643>
 34. Femminella B, Iaconi MC, Di Tullio M, et al. Clinical comparison of platelet-rich fibrin and a gelatin sponge in the management of palatal wounds after epithelialized free gingival graft harvest: a randomized clinical trial. *J Periodontol* 2016;87:103-113.
<https://doi.org/10.1902/jop.2015.150198>
 35. Aroca S, Keglevich T, Barbieri B, Gera I, Etienne D. Clinical evaluation of a modified coronally advanced flap alone or in combination with a platelet-rich fibrin membrane for the cure of adjacent multiple gingival recessions: a 6-month study. *J Periodontol* 2009;80:244-252.
<https://doi.org/10.1902/jop.2009.080253>
 36. Anilkumar K, Geetha A, Umasudhakar, Ramakrishnan T, Vijayalakshmi R, Pameela E. Platelet-rich-fibrin: A novel root coverage approach. *J Indian Soc Periodontol* 2009;13:50-54.
<https://doi.org/10.4103/0972-124X.51897>
 37. Jankovic S, Aleksic Z, Milinkovic I, Dimitrijevic B. The coronally advanced flap in combination with platelet-rich fibrin (PRF) and enamel matrix derivative in the cure of gingival recession: a comparative study. *Eur J Esthet Dent* 2010;5(3):260-273.
 38. Öncü E, Alaaddinoglu EE. The effect of platelet-rich fibrin on implant stability. *Int J Oral Maxillofac Implants* 2015;30:578-582. <https://doi.org/10.11607/jomi.3897>
 39. Boora P, Rathee M, Bhorla M. Effect of Platelet Rich Fibrin (PRF) on peri-implant soft tissue and crestal bone in one-stage implant placement: a randomized controlled trial. *J Clin Diagn Res* 2015;9:ZC18-ZC21.
<https://doi.org/10.7860/JCDR/2015/12636.5788>
 40. Kim JW, Kim SJ, Kim MR. Leucocyte-rich and platelet-rich fibrin for the cure of bisphosphonate-related osteonecrosis of the jaw: a prospective feasibility study. *Br J Oral Maxillofac Surg* 2014;52:854-859.
<https://doi.org/10.1016/j.bjoms.2014.07.256>
 41. Lopez-Jornet P, Sanchez Perez A, Amaral Mendes R, et al. Medication-related osteonecrosis of the jaw: Is autologous platelet concentrate application effective for prevention and treatment? A systematic review. *J Craniomaxillofac Surg* 2016;44:1067-1072.
<https://doi.org/10.1016/j.jcms.2016.05.004>