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**Review Article**

# Role of Platelet-Rich Fibrin In Oral And Maxillofacial Surgery

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ABSTRACT

Platelet-rich fibrin (PRF) is an autogenous material that is derived from a person's own platelets and is used to enhance wound healing and tissue regeneration. PRF is a fibrin meshwork, in which platelet cytokines, growth factors, and cells are entrapped and discharged after a period and can serve as a resorbable film. PRF is proposed to have a direct effect on enhancing a patient's wound healing by suprasaturating the wound with growth factors that promote tissue healing. The autologous nature of PRF makes it preferred over a variety of allografts used in dentistry today. PRF in oral surgery are used for alveolar bone reconstruction, dental implant surgery, sinus augmentation, socket preservation, osteonecrosis, oroantral fistula closure, struggling with oral ulcers, preventing swelling and edema constitution. This article enriches the benefits and role of plasma-rich fibrin in oral surgery.

## Introduction

In recent years, the question how to increase patient comfort after surgical interventions became the main topic of oral surgical applications. As a result of various researches in recent years, the use of platelet concentrates give rise to improve patient comfort and enhance healing after the operation.

Platelet-rich fibrin (PRF) is actually a second-generation technology. It is anteceded by platelet-rich plasma (PRP), which is whole blood centrifuged to remove red blood cells, leaving behind a suspension rich in white blood cells and plasma components that are thought to be important in promoting wound healing. Both PRF and PRP use autologous blood. Both PRF and PRP aim to use blood growth factors to promote the body's own healing process.

As early as the 1950s, Kingsley[1] used the term PRP to describe a thrombocyte concentrate used for patients with thrombocytopenia. Hematologists started to widely use the term in the 1970s.[2] Choukroun's PRF is a matrix, in which cytokines and cells are entrapped which are released after a short period, and can serve as a resorbable membrane[3]. Whitman described the PRP for the first time in 1997 as a fibrin gel manufactured by Mantras[4]. PRP can be defined as a fraction of a volume of plasma with a higher concentration of platelets than in peripheral blood. PRP has three or four times more growth factors than peripheral blood[5]. Regenerative medicine is an augmentation or substitution of diseased or injured cells, almost 100 trillion cells are present in the human body[6].

## MECHANISM OF ACTION

When the body tries to repair itself, it will undergo 4 phases: *hemostasis, inflammatory phase, proliferative phase,* and the *remodeling phase.* At *hemostasis phase*, platelets are essential for blood clot formation and PRF with rich platelet granules is promotive to accommodate a strong fibrin network. This blood clot serves as a reservoir which allows cell migration, adhesion and proliferation. *Inflammatory phase* starts with the injury and takes 5–7 days approximately. During this phase, platelets are releasing various growth factors to the injured site that migrate inflammatory cells (Lymphocytes, macrophages and neutrophils). These factors are PDGF (Platelet-derived growth factor), VEGF

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(Vascular endothelial growth factor), TGF B (Transforming growth factor) and pro-inflammatory cytokines such as interleukins (IL-1, IL-6, IL-8) and tumor necrosis factor alpha (TNF-α), whose roles are enhancing angiogenesis and tissue healing. Within the comprising of new blood vessels with angiogenesis, acidic and hypoxic environment change. In the *proliferative phase,* MSCs (Mesenchymal stem cells) releasing from newly formed blood vessels, BMP's (Bone morphogenic protein) and TGF-β are playing an important role in MSCs organism. MSC's role is inducing osteoblast differentiation. The last but not the least, *remodeling phase* is characterized as maturation process. Within this process, vascularity ratio and collagen deposition decreases and mineral deposition increases with the replacement of woven bone into lamellar one[7,8].

Fibrin forms a matrix for the migration of cells such as fibroblasts and endothelial cells, which are crucial in angiogenesis and new tissue formation. PRF is a strong fibrin matrix structure, platelets and leukocytes attach on it and activate degranulated growth factors with the consequence of releasing cytokines. It has been suggested that PRF, a natural fibrin network, can protect the growth factors containing in its own structure from proteolysis. Thus growth factors may maintain their activity for a long time and stimulate tissue regeneration.

## TYPES OF PRF

The main purpose of using PRF is to release the rich content of alpha granules of platelets into the environment for therapeutic purposes. The main differences between PRF types are their centrifuge speed.

- ***Advanced platelet rich fibrin (A-PRF)****:* It is obtained with longer centrifugation time and lower rpm.

- ***Pure platelet rich fibrin (P-PRF):*** After the first centrifuge (6 min high speed), transferring the buffy coat and PPP (Platelet poor plasma) to the second tube, which contains CaCl2. After the second centrifuge starts and takes 15 min long, stable platelet-fibrin takes place. The authenticity of this method is the presence of separation gel at the first tube.

- ***Leukocyte and platelet rich fibrin (L-PRF):*** Blood samples are taken into glass tubes without any anticoagulant and centrifuged immediately at low speed. It forms 3 different layers with acellular plasma, platelet-rich fibrin and erythrocyte layer at the bottom, respectively. Thrombocyte rich fibrin matrix is very powerful and autologous biomaterial can be used in different fields in oral surgery.

- ***Injectable platelet rich fibrin (I-PRF):*** The use of I-PRF [Injectable] is at an early stage. But the results are very promising in terms of increasing vascularity and soft tissue healing.

- ***Liquid platelet rich fibrin (Liquid-PRF):*** Liquid-PRF was defined with low-speed centrifugation (LSC), which allows forming of a liquid-PRF formula of fibrinogen and thrombin rather than its conversion to fibrin.

## PREPARATION OF PRF

PRF is also called Choukroun's PRF apart from other similar concentrates such as Vivostat PRF and fibrin PRF. The protocol for PRF preparation is very simple and simulates that of PRP. It includes collection of whole venous blood (around 5 ml) in each of the two sterile vacutainer tubes (6 ml) without anticoagulant and the vacutainer tubes are then placed in a centrifugal machine at 3,000 revolutions per minute (rpm) for 10 min, after which it settles into the following three layers: Upper straw-colored acellular plasma, red-colored lower fraction containing red blood cells (RBCs), and the middle fraction containing the fibrin clot. The upper straw-colored layer is then removed and middle fraction is collected, 2 mm below to the lower dividing line, which is the PRF [Figure 1].

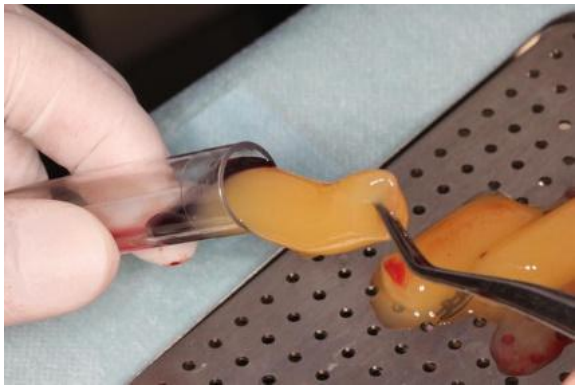

Figure 1- PRF Membrane Preparation

**ROLE IN MAXILLOFACIAL SURGERY**

The attention of maxillofacial surgery community was enhanced by a chain of scientific papers during the 1990s, which claimed that PRF could be valid for both hemostasis and bone grafting. Bone regenerative techniques include sinus lift for implant placement, which is considered to be one of the most common procedures for augmenting the maxilla. They are presently used to assess the importance of sinus lift and implantation with L-PRF (Choukroun's technique) as a sole sub-sinus filling material[9].

- ***PRF in post extraction socket-*** PRF have been shown to play an important role in tissue healing with the releasing growth factors from alpha granules, regulate cellular events such as cell adhesion, migration and proliferation [10,11]. PRF plugs can also be used in treating the residual extraction sockets [12]. Use of autologous PRF in extracted socket filling after immediate bone augmentation using titanium membranes applied to the socket walls and primary closure was found to be feasible and safe with adequate bone filling after 8 weeks or above for implant fixation [13].

- ***PRF in sinus lifting-***

In the literature there are some different application techniques for PRF in the sinus augmentation such as PRF as a sole grafting material, PRF with allografts or PRF with xenografts. All of these techniques have variable clinical, radiographic and histologic outcomes.

***Choukroun et al.,***[14] attempted to evaluate the potential of PRF in combination with freeze-dried bone allograft (FDBA) in sinus floor elevation to enhance bone regeneration and nine sinus floor augmentations were performed. Out of nine; in six sites, FDBA with PRF (test group), and in three sites FDBA without PRF (control group) was used. They found the rate of vital bone/inert bone%20 both in test and control group but with a reduced healing time at PRF group.

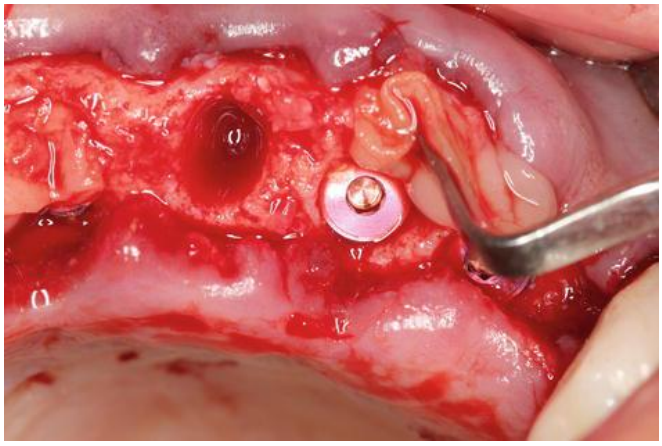

Figure 2- PRF membrane application in immediate implantation for filling the buccal gap.

***Mazor et al.***[15] ***and Simonpieri et al.*** [16] performed sinus lift by using lateral approach and PRF was used as a sole grafting material and implants were applied immediately. During the healing period there were no complications. A 100% survival rate was observed in total of 57 sinus lift procedures and 110 implants during the follow-up period (2 years). Radiographic examination was performed by CT scan or panoramic radiographs about 6 months after the sinus augmentation to examine the bone volume, where the average bone gain was 9.8 mm. Histologic examination accomplished by *Mazor et al*. showed dense collagen matrix, easily identified osteocytes and osteoblasts in the lacunae and well-organized and vital bone with structured trabeculae with more than %30 bone matrix.

***Zhang et al.*** [17] applied the PRF/xenograft mixture for the test group and xenograft as a sole graft material for the

control group. They found no statistically significant difference between the two groups.

- ***PRF for preserving bone around implants***

Marginal bone loss is an inevitable process which starts immediately following implant placement. Previous studies about preserving bone around implants, has focused on soft tissue thickness and it was hypothesized, adequate soft tissue volume around implants has a positive effect in preserving marginal bone and PRF is perfect material to augment soft tissue. PRF is a good autologous material to enhance soft tissue healing with its growth factors including VEGF, PRGF, etc.[18]

- ***PRF in rare clinical scenarios***

PRF could also be beneficial with growth factors including in rare clinical scenarios such as cyst treatment, sinus membrane perforations, oroantral fistulae closure and osteonecrosis.

***Oroantral fistula (OAF)*** is defined a pathological way between maxillary sinus and oral cavity. It can either come into existence spontaneously following a large maxillary cyst or tumor or as iatrogenic after tooth extraction or dental implant surgery. There are plenty of methods maintaining with OAF. PRF is one of them which is recently introduced (Figure 3). The technique is as following; PRF clots obtained by centrifugation should be isolated from PPP (Platelet Poor Plasma) and red blood cells, prepared as thin membranes and applied perforated area layer by layer. The researches about PRF in OAF closure conclude that, wound healing is faster and there was an increase in soft tissue thickness during healing. Due to its natural ingredients, there are no need to use additional materials, thus less donor site morbidity occurs.

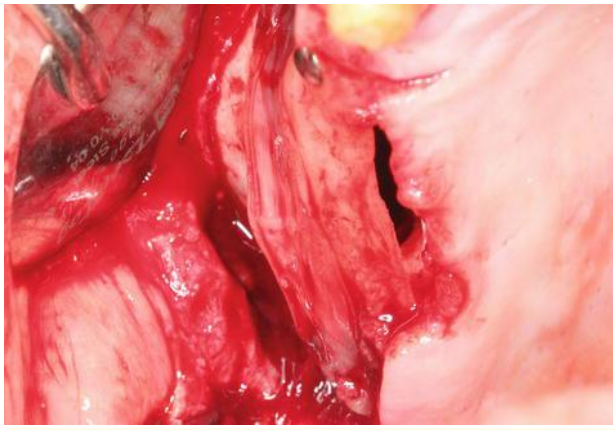

Figure 3- Sinus membrane perforation closure with PRF membrane.

The use of PRF in ***cyst*** depends on the same rationale with the enhancement of soft and hard tissue healing. Researches related to this topic conclude that using PRF as a graft material is beneficial for shortening healing time and increasing bone mineral density.

## DISCUSSION

PRF first described by Choukroun *et al*. is a new second generation of platelet concentrate. Simplified processing technique without any complex handling makes it superior to PRP. PRF can be used to promote wound healing, bone regeneration, graft stabilization, wound sealing, and hemostasis. Because the fibrin matrix is better organized, it is able to more efficiently direct stem cell migration and the healing program. Dohan *et al*.,[19] proved a slower release of growth factors from PRF than PRP and observed better healing properties with PRF. It was observed and shown that the cells are able to migrate from fibrin scaffold; while some authors demonstrated the PRF as a supportive matrix for bone morphogenetic protein as well.

## CONCLUSION

PRF utilizes the patient's own blood, thereby decreasing or eliminating the transmission of diseases. PRF membrane protects the surgical site and promotes soft tissue healing. It acts as a biological connector between different graft elements and as a matrix that supports neoangiogenesis, capturing stem cells and migration of

osteoprogenitor cells to the centre of the graft. Currently, PRF seems to be an accepted minimally invasive technique with minimal risks and good clinical results. For future perspectives, with the use of new generations of PRF with increased growth factor capacity, combined with graft materials, PRF will appear in more areas in oral surgery applications.

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