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**REVIEW ARTICLE**

# PRP and PRF- A promising future aid in healing

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**ABSTRACT**

**With the wide spread use of implants as a routine treatment modality ,operators are on a constant look out to achieve more predictable results on the clinical outcome, vis a vis the quantity and quality of bone deposition in the graft sites and the subsequent stability and longevity of the concurrent implants placed. A recent Innovation in dentistry is the preparation and use of Platelet Concentrates (PRP, PRF), a concentrated suspension of growth factors found in platelets which accelerate wound healing and are postulated as promoters of tissue regeneration. The present paper describes the preparation and uses of two commonly used platelet concentrates: Platelet-rich plasma (PRP) and Platelet rich Fibrin (PRF).**

## Introduction

Ever since the introduction of the concept of Osseointegration, implants have gained significant ground in the field of dentistry. Osseointegration is the main stay in implant dentistry. It is the ultimate goal for Implantologists. One of the pre-requisites for this to happen is that the immediate milieu around the dental implant must be conducive for the proper healing and regeneration of the tissues.

Implant dentistry entails surgical reconstruction of the localized alveolar defects[1]. One of the revolutionary last achievements has been the use of platelet concentrates for the improvement of reparation & regeneration of the soft & hard tissues. The platelet concentrates accelerate and enhance the body's natural wound healing mechanisms. A natural blood clot contains mainly red blood cells, approximately 5% platelets and less than 1% white blood cells. It is now well known that platelets have many functions beyond that of simple homeostasis.

Platelets consists of certain growth factors, which when secreted, increasing cell mitosis, plays a role in increasing the collagen production, helps in recruiting other cells to the

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site of injury, helps in initiating the vascular in-growth and induces cell differentiation[2,3].

**Platelet concentrate evolution**

In general, platelet concentrates are blood derived products used for the prevention and treatment of hemorrhages due to serious thrombopenia of the central origin. The development of platelet concentrates as bioactive surgical additives that are applied locally to promote wound healing stems from the use of fibrin adhesives. Since 1990, medical science has recognized several components in blood, which are a part of the natural healing process; when added to wounded tissues or surgical sites, they have the potential to accelerate healing.

Fibrin glue was originally described in 1970 which is formed by polymerizing fibrinogen with thrombin and calcium. It was originally prepared using donor plasma; however, because of the low concentration of fibrinogen in plasma, the stability and quality of fibrin glue were low.

Further studies led to the development of an autologus platelet gel – platelet rich plasma (PRP) – which was used in various surgical fields[4].

Whitman et al have called PRP an "autologus alternative to fibrin glue". The main difference in PRP and fibrin glue is the presence of a high concentration of platelets and native concentration of fibrinogen in PRP[5].

Further, the second generation platelet concentrate known as Platelet rich fibrin (PRF) was developed in France by Choukroun *et al.* It has been shown to have several advantages over traditionally prepared PRP. Its chief advantages include ease of preparation and lack of biochemical handling of blood, which makes this preparation strictly autologus[2]

**Platelet Rich Plasma (PRP)**

By definition Platelet rich plasma (PRP) is an autologus concentrate of human platelets in a small volume of plasma. PRP can be prepared by 2 techniques:

1. **General-purpose cell separators**
2. **Platelet-concentrating cell separators**

*General-purpose cell separators*[2]

It requires large quantities of blood (450 ml) and generally requires to be operated in a hospital setting. Blood is drawn into a collection bag containing citrate-phosphate-dextrose adenosine anticoagulant. It is first centrifuged at 5,600 rpm to separate RBCs from platelet-poor plasma (PPP) and PRP. The centrifugation speed is then reduced to 2,400 rpm to get a final separation of about 30 ml of PRP from the RBCs. With this technique, the

remaining PPP and RBCs can be returned to the patient's circulation or can be discarded.

*Platelet-concentrating cell separators*[2]

It requires small quantity of blood and can be prepared in a dental clinic set up.

1. Venous blood is drawn into a tube containing an anticoagulant to avoid platelet activation and degranulation.

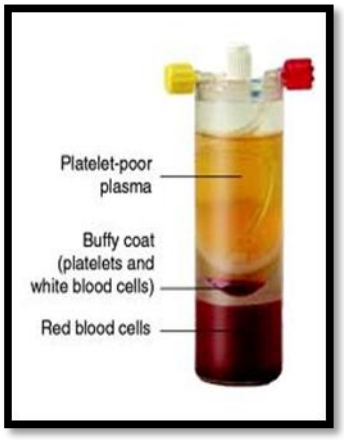
2. The first centrifugation is called "soft spin", which allows blood separation into three layers, namely bottom-most RBC layer (55% of total volume), topmost acellular plasma layer called PPP (40% of total volume), and an intermediate PRP layer (5% of total volume) called the "Buffy coat".

3. Using a sterile syringe, the operator transfers PPP, PRP and some RBCs into another tube without an anticoagulant.

4. This tube will now undergo a second centrifugation, which is longer and faster than the first, called "hard spin". This allows the platelets (PRP) to settle at the bottom of the tube with a very few RBCs, which explains the red tinge of the final PRP preparation. The acellular plasma, PPP (80% of the volume), is found at the top.

5. Most of the PPP is removed with a syringe and discarded, and the remaining PRP is shaken well.

6. This PRP is then mixed with bovine thrombin and calcium chloride at the time of application. This results in gelling of the platelet concentrate. Calcium chloride nullifies the effect of the citrate anticoagulant used, and thrombin helps in activating the fibrinogen, which is converted to fibrin and cross-linked.




PRP works via the degranulation of the α granules in platelets, which contain the synthesized and pre-packed growth factors. The growth factors which are released from activated platelets are:

1. Platelet derived growth factor (PDGF)
3. Transforming growth factors beta 1 and beta 2 (TGF β 1 & 2)
4. Vascular Endothelial Growth Factor (VEGF)

5. Platelet derived endothelial cell growth factor
6. Interleukin – 1 (IL-1)
7. Basic fibroblast growth factor (bFGF)
8. Platelet activating factor -4 (PAF-4)

The active secretion of these growth factors is initiated by the clotting process of blood and it begins within 10 minutes after clotting. More than 95% of the presynthesized growth factors are secreted within 1 hour. Hence, PRP should be used on the graft, flap, or wound, within 10 minutes of clot initiation. The growth factors immediately bind to the external surface of the cell membranes of the cells in the graft, flap, or wound via transmembrane receptors. These transmembrane receptors induce the activation of an endogenous internal signal protein, which in turn causes the expression of a normal gene sequence such as cellular proliferation, matrix formation, osteoid production, collagen synthesis etc[2].

*Thus PRP growth factors act through the stimulation of normal healing, just much faster.*

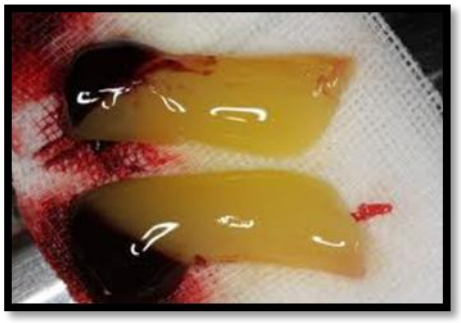
Its clinical applications include continuity defects, sinus lift augmentation grafting, horizontal and vertical ridge augmentations, ridge preservation grafting, periodontal/peri-implant defects, Cyst enucleations/Periapical surgeries, healing of Extraction wounds, endodontic surgeries and retrograde procedures, ablative surgeries of the Maxillo-Facial region and blepharoplasties[6,7,8].

**Platelet rich fibrin (PRF)**

Platelet rich fibrin (PRF) was developed in France by Choukroun *et al.* The preparation of PRF is very simple. Blood is drawn into 10 ml test tubes without any anticoagulant and centrifuged immediately. Centrifugation is done for 12 minutes at 2,700 rpm[2].

The resultant product consists of the following three layers:

• Topmost layer consisting of acellular PPP
• PRF clot in the middle
• RBCs at the bottom



PRF is in the form of a platelet gel can be used in conjunction with bone grafts. Its clinical applications include promoting wound healing, bone growth and maturation, graft stabilization, wound sealing and hemostasis, improving the handling properties of graft materials and use of PRF as a membrane.

**Use of PRF to enhance clinical outcomes in implant therapy**

Choukroun *et al*[9,10]. attempted to evaluate the potential of PRF in combination with freeze-dried bone allograft (FDBA) (Phoenix; TBF, France) to enhance bone regeneration in sinus floor elevation and nine sinus floor augmentations were performed; in 6 sites, PRF was added to FDBA particles (test group), and in 3 sites FDBA without PRF was used (control group). Four months later for the test group and 8 months later for the control group, bone specimens were harvested from the augmented region during the implant insertion procedure. After 4 months of healing time, histologic maturation of the test group appears to be identical to that of the control group which was for a period of 8 months. Moreover, the quantities of newly formed bone were equivalent between the 2 protocols[9,10].

Jang *et al*[9,11] determined the capability of silk fibroin powder as biomaterial template for the restoration of peri-implant defects when mixed with Chaukroun's PRF in ten New Zealand White rabbits. Histomorphometric analysis show greater bone formation and removal torque force shows significant higher values for experimental (silk fibroin and PRF) than in control (unfilled) group[9,11].

Lee *et al*[9, 12]. further suggested that because silk is cheap and readily available material, acid digested silk fibroin combined with Chaukroun's PRF could provide a possible new bone substitute for the reconstruction of various bone defects[9, 12].

Mazor *et al*[9]. Assessed the relevance of autologous leukocyte- and platelet-rich fibrin (PRF) concentrate and membranes as the sole filling material during a lateral sinus lift with immediate implantation in a case series. From a radiologic and histologic point of view at 6 months after surgery, the use of PRF as the sole filling material during a simultaneous sinus lift

and implantation stabilized a high volume of natural regenerated bone in the subsinus cavity up to the tip of the implants. Further, they advocated that Choukroun's PRF is a simple and inexpensive biomaterial, and its systematic use during a sinus lift seems a relevant option, particularly for the protection of the Schneiderian membrane[9].

Simonpieri *et al*.9 reported maxillary reconstruction using FDBA, PRF membranes and 0.5% metronidazole solution in twenty patients who were treated using this new technique and followed up during 2.1 years (1-5 years). Finally, 184 dental implants were placed, and they found no implant or graft loss in a case series, thus confirming the validity of this reconstructive protocol. Small quantities of 0.5% metronidazole solution (10 mg) provide a proficient protection of the bone graft against unavoidable bacteial contamination. PRF membranes protect the surgical site and promote soft tissue healing and cut few milimeters PRF fragments mixed with graft material functioned as a "biological connector" between the different graft elements, and as a matrix that supports neo-angiogenesis, capture of stem cells and migration of osteoprogenitor cells to the center of the graft.

Toffler advocated osteotome-mediated sinus floor elevation (OMSFE) or crestal core elevtion (CCE) with simultaneous implant placement using PRF plugs, prepared by placing PRF clot into the cylinder in the PRF box and slowly compressing with piston. Thick PRF plugs or small disks of 1 cm diameter can also be easily inserted into the residual extraction sockets[9].

**Use of PRP to enhance clinical outcomes in implant therapy**[13]

Role of PRP in implant therapy to provide adhesion and tensile strength for wound stabilization and sealing is of critical importance to osseointegration itself. Attachment & stabilization of the blood clot to the surface of the dental implant facilitates the migration of bone cells to the implant surface. This results in contact osteogenesis, a process that completely determines the percentage of bone implant contact (BIC).

***Enhancing osseointegration***

When an implant is to be placed with an immediate or delayed approach, the activated PRP solution is delivered into the socket or osteotomy preparation and then the implant is delivered to sink its full depth. The growth factors enriched blood clot fills the spaces in between the implant & the osteotomy walls.

Direct application of PRP to the implant surface may disrupt or pull away the clot from the implant surface when the fixture is placed.

***Alveolar ridge preservation***

For an immediate placement, particulate bone graft can be mixed with PRP. This facilitates graft material delivery to the site. After the condensation to the site, few drops of activated PRP are added additionally, to ensure the saturation of the implant body, the graft material and the socket walls, to reestablish the fibrin network within the graft that is disrupted during graft delivery & condensation.

**Safety concerns**

Because it is an autogenous preparation, PRP and PRF are inherently safe and therefore free from concerns over transmissible diseases such as HIV, Hepatitis etc.

However, Sanchez *et al* have elaborated on the potential risks associated with the use of PRP. The preparation of PRP involves the isolation of PRP after which gel formation is accelerated using calcium chloride and bovine thrombin. It has been discovered that the use of bovine thrombin may be associated with the development of antibodies to the factors V, XI and thrombin, resulting in the risk of lifethreatening coagulopathies. Bovine thrombin preparations have been shown to contain factor V, which could result in the stimulation of the immune system when challenged with a foreign protein. Marx et al in their article stated that the second set of bleeding episodes in the patients who developed coagulopathies were not due to antibodies against bovine thrombin or human thrombin but instead due to antibodies that developed to bovine factor Va that was a contaminant in certain bovine thrombin commercial preparations. Other methods for safer preparation of PRP include the utilization of recombinant human thrombin, autologous thrombin or perhaps extra-purified thrombin. Landesberg *et al* have suggested that alternative methods of activating PRP need to be studied and made available to the dental community[2].

**Summary**

Histological samples have revealed the enhanced rate of maturation showing increased density & greater quantities of viable bone than expected with the use of PRP and PRF. There have been clinical trials for the use of combination of bone grafts and growth factors in PRP and PRF and have shown to enhance the bone density. Also, the affinity of osteoblasts to the PRF membrane appeared to be superior. Choukran's PRF has revolutionsied the field of regenerative

dentistry and motivated the researchers and clinicians further to apply this procedure along with tissue engineerging protocol. Although earlier clinical observations are positive, additional studies must be conducted in order to scientifically document the benefit of using PRP & PRF in implant therapy & to guide the clinician in case selection.

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