

DENTAL TECHNIQUE

Biological activation of bone grafts using injectable platelet-rich fibrin



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Platelet-rich fibrin (PRF) is a platelet concentrate prepared by centrifuging autologous blood without additives.¹ The conventional protocol includes centrifuging freshly collected blood without any anticoagulant in glass-coated test tubes at 2700 rpm for 12 minutes. This treatment results in the formation of 3 distinct layers, the bottom layer contains red blood cells; the middle layer consists of a platelet-rich fibrin clot containing polymerized fibrin, platelets, white blood cells, and glycosaminoglycans (heparin, hyaluronic acid); and the top layer contains platelet-poor plasma. The middle layer can then be retrieved and used in its clot form or compressed to form a membrane. The rationale for using PRF as a surgical additive lies in its biological properties such as a sustained release of various growth factors including platelet-derived growth factor, transforming growth factor- β , and insulin-like growth factor, which make it conducive to healing.^{2,3} PRF finds wide applications in sinus lift procedures, socket preservation and augmentation, guided bone regeneration, gingival recession coverage with coronally advanced or lateral pedicle flap, filling of cystic cavities, combined periodontic-endodontic lesions, and furcation defects.¹⁻⁴ It has virtually replaced all other platelet concentrates, including platelet-rich plasma (PRP), in regenerative dentistry.³

ABSTRACT

Platelet-rich fibrin (PRF) is gaining acceptance as a bioactive surgical additive in regenerative dentistry. However, PRF has only been available in gel or membrane form and is not suitable for injection. Recently, however, a liquid, injectable PRF has been introduced. This paper introduces the concept of injectable PRF and discusses its applications for biologic activation of bone grafts. (*J Prosthet Dent* 2019;121:391-3)

The advantages of using PRF are that it is completely autologous, easy to prepare, inexpensive, and that it provides sustained release of growth factors over time.⁴ However, one of its drawbacks is that it is obtained in a gel form and cannot be easily injected.⁵ This limits its application in the management of acne, alopecia, back pain tendon/ligament injections, osteoarthritis, meniscal healing, and musculoskeletal regenerative procedures.^{6,7} A liquid form of PRF, such as the recently introduced injectable PRF, could be used to mix grafts cohesively and to spray over surgical sites. PRF has several additional advantages over PRP in that the total growth factors released by PRF are comparable to or higher in amounts and demonstrate a sustained slow release of up to 10 days.⁸ PRF is also devoid of the drawbacks related to bovine thrombin, including the development of antibodies to factors V, XI, and thrombin and chances of life-threatening coagulopathies.⁹ Because literature on injectable PRF is sparse, the purpose of this article was to demonstrate its preparation and applications.

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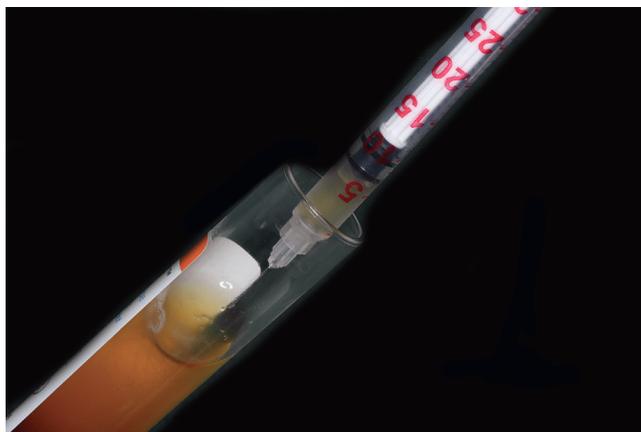


Figure 1. Injectable platelet rich fibrin aspirated from tube after centrifuging.

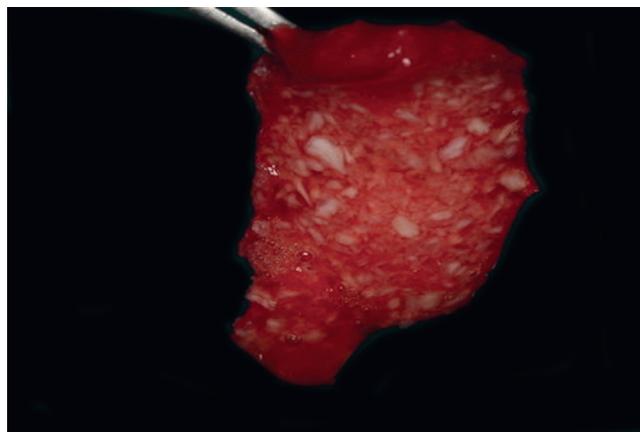


Figure 2. Injectable platelet rich fibrin mixed with particulate graft to form sticky bone.

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1. Draw 9 mL of blood without anticoagulant in plastic tube without any coatings.
2. Perform a quick centrifuge at 700 rpm for 3 minutes.
3. Retrieve the tube from the centrifuge and ensure that the blood has separated into 2 fractions. The bottom layer fraction consists of red blood cells, and the top layer consists of plasma, platelets, and coagulation factors still in uncoagulated form. The separated plasma and platelets form a light-yellow colored layer in liquid form as seen in [Figure 1](#).
4. Aspirate the top layer using a syringe. Place the tip of the syringe just above the junction of the 2 layers and carefully aspirate the top layer. The aspirate is a partially active injectable form of PRF.

Once the injectable PRF is obtained, it can be mixed with any particulate bone graft. After approximately 1 to 4 minutes, this aspirate becomes a cohesive mass with a putty-like consistency.

DISCUSSION

The rationale behind obtaining injectable PRF is that injectable PRF technically contains all components of PRF, including the platelets, white blood cells, and all the clotting factors comprising fibrinogen, in an uncoagulated form. The tubes used to prepare injectable PRF are made of plastic without any glass coatings. Unlike glass, plastic tubes have a hydrophobic surface and do not efficiently activate the coagulation process, thus retarding coagulation.¹⁰ The slower and shorter centrifugal speed increases the presence of regenerative cells with higher concentrations of growth factors, which are then collected in liquid form.⁵

When injectable PRF was compared with PRP in terms of cell proliferation, PRP was more effective than injectable PRF. However, concerning all the other criteria,

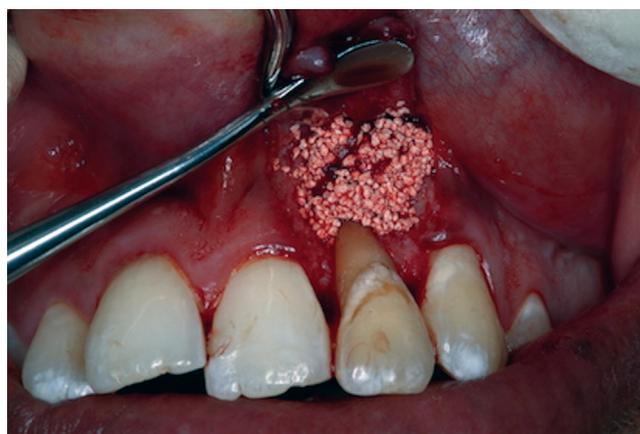


Figure 3. Ease of graft compaction with sticky bone.

injectable PRF demonstrated significantly better results than PRP did, including cell migration and messenger ribonucleic acid expression of transforming growth factor (TGF- β), platelet-derived growth factor (PDGF), and collagen type 1a2 at both 3- and 7-day intervals.⁵ Also, whereas PRP had completely dissolved over a period of 10 days, injectable PRF formed a small clot as a dynamic gel and maintained release of growth factor for over 10 days.⁵ The effect of the variable rotations per minute suggested by different authors on the structure and growth factors has yet to be assessed.^{1,11} Reports of injectable PRF are scarce, and the authors are unaware of a standardized protocol.

In dentistry, this liquid PRF/injectable PRF is being used for mixing with bone grafts. The aspirate is mixed with particulate bone graft, and, after approximately 3 to 4 minutes, on completion of the coagulation process, a gel or putty consistency graft is obtained as shown in [Figure 2](#). This is a PRF clot which coagulates in the presence of graft particles, which are incorporated into the clot. The graft thus formed has a good workable consistency, which reduces leaching of the graft as it is

tightly encapsulated in the fibrin matrix.^{3,11} This consistency is very conducive for grafting because it eliminates the need for presuturing and can easily be manipulated and condensed into the defect site (Fig. 3). It can also be sprayed into the site after placement of a bone graft to make it a cohesive mass and prevent leaching.

The major advantage of PRF is that it is a bioactive surgical additive. It brings with it a sustained release of growth factors, including TGF- β , PDGF, and vascular endothelial growth factor.² It induces local angiogenesis, entraps circulating stem cells, modulates the immune system of the wound site, and enhances the mitogenesis of epithelial cells.¹² In injectable PRF, the clot containing the platelets is found around the bone graft, incorporating the graft particles in its matrix. The platelets present in injectable PRF release their growth factors into the implant site, making it an inexpensive, straightforward chairside method of bioactivating a bone graft.² However, studies demonstrating the viability, number, and pattern of growth factor release are lacking.⁵ This also tends to enhance the volume of the graft as seen in Figure 3. The enhanced volume of the graft gives the clinician the opportunity to graft a wider area with a graft that is autologous, economical, and above all, bioactive. Based on previous studies, it appears that the quality of future bone would not be compromised.¹³ The possible applications of this includes, but is not limited to, grafting for intrabony defects, socket preservation, socket augmentation, ridge augmentation, sinus grafting, filling cystic cavities, or for guided tissue and bone regeneration.

The science of liquid PRFs in an injectable form is still in its infancy. By refining protocol and maximizing the bioactive properties of PRF, we may eventually move into an era when all platelet concentrates are completely autologous and free of external additives. The discovery of injectable PRF may lead to the discovery of an injectable and superior alternative of PRF to PRP for all kinds of medical and dental applications.

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