Acta Scientific DENTAL SCIENCES (ISSN: 2581-4893)

Volume 4 Issue 11 November 2020

Review Article

PRF from the Perspective of a Daily Practitioner: Where are the Limits?

Andreas Van Orten[1] and Hakan Bilhan[2]*

[1]*Private Dental Practice, Waltrop, Germany*

[2]*Witten/Herdecke University, School for Health Sciences, Department of Periodontology, Germany*

***Corresponding Author:** Bilhan, Witten/Herdecke University, School for Health Sciences, Department of Periodontology, Germany.

Received: September 23, 2020

Published: October 28, 2020

Abstract

Background: Platelet-rich fibrin (PRF) is being used in dentistry as an over physiological concentrate of autologous growth factors capable of stimulating tissue regeneration and being increasingly more popular in private practice. Since about 20 years platelet concentrates are being used in oral and maxillofacial surgery. With various modifications, mainly concerning the presence or absence of leukocytes and their concentration, as well as the presence and consistency of the fibrin matrix, the scope of application has continuously expanded.

Methods: The range of developments and studies on PRF is extensive. On the one hand, technical aspects such as centrifuge speed, forces and duration, on the other hand medical factors such as influence of the individual donor on fibrin product, or the hematocrit or the count of erythrocytes on the fibrin matrix or aspects of the further processing of the fibrin matrices, for example by heat application, to slow down degradation, so that the PRF membrane could become comparable to collagen membranes, are studied.

Primary Results: An international effort to extend the application diversity can be observed, as well. **Principal Conclusions:** In future, it can be expected that PRF will be a precious addition in maxillofacial surgery and also in the treatment of temporomandibular joint diseases, endodontics (pulp regeneration), the regeneration of peri-implant soft tissues around implants, the modification of the lip volume, to name a few.

Keywords: Platelet-rich Fibrin; Regeneration; Growth Factors; Improved Healing; Autologous

Abbreviations

PRF: Platelet-rich Fibrin; PRGF: Plasma-rich Growth Factors; L-PRF: Leucocyte Platelet-rich Fibrin; A-PRF+: Advanced Platelet-rich Fibrin; i-PRF: Injectable Platelet-rich Fibrin; PRP: Platelet-rich Plasma; P-PRP: Pure Platelet-rich Plasma; L-PRP: Leucocyte-and Platelet-Rich Plasma; P-PRF: Pure Platelet-rich Fibrin; GBR: Guided Bone Regeneration; CAF: Coronally Advanced Flap; CTG: Connective Tissue Graft.

Introduction

Platelet-rich fibrin (PRF) is being used in dentistry as a concentrate of autologous growth factors capable of stimulating tissue regeneration. First studies about modified bone grafts and the employment in the management of naso-/oro-antral fistulas and clefts with platelet-rich plasma were published in the 1990s [1].

Depending on the different parameters (e.g. centrifuge, platelet concentration, presence/condition of leukocytes, degree of polimerization) a classification can be made [2] (Table 1).

P-PRP (pure platelet-rich plasma)

The typical characteristic of this group is the absence of leukocytes and a lower degree of polymerization, usually associated with a fluid to gel-like consistency. The highest level of platelet concentration will be reached in this group by using cell separators. Due to the complicated equipment, the application in dental practices was limited.

	Time (min)	rpm	G-force	Vacuette color code	Main indication
i-PRF(female)	3	700	60 g	Yellow	For mixing with biomaterials
i-PRF (male)	4	700	60 g	Yellow	For mixing with biomaterials
a-PRF liquid	5	1300	208 g	Red	For individual membrabe moulding and sticky bone
a-PRF plus	8	1300	208 g	Red	For PRF membrane
s-PRF	8	1300	208 g	Green	For strong sticky bone

Table 1: Comprehensive information about typical use possibilities.

The PRGF technique (plasma-rich growth factors) was introduced nearly two decades ago [3]. Thanks to a modest investment in a lab centrifuge device and pipetting equipment, today this method can be used by many clinicians. After drawing venous blood (10-30 ml), which is centrifuged and processed in several pipetting steps, the reticulation of the plasma concentrates is activated optionally with a 10% calcium chloride solution and accelerated in a thermal device at 37°C. The production time is usually less than 30 minutes and therefore convenient for dental practices. The in average 30 pipetting steps are criticized by some authors, since the system is open and could result in errors in application with variance in platelet concentrations and also hygienic problems. Another subject of critics is the nearly complete absence of leukocytes [4].

L-PRP (leucocyte- and platelet-rich plasma):

The main difference of this group compared to the previous one is the presence of leukocytes.

P-PRF (Pure platelet-rich fibrin):

This group differs from the first group mainly my absence of leukocytes and with its high density, which provides slow release of growth factors.

L-PRF, A-PRF+, I-PRF (leukocyte- and platelet-rich fibrin):

The last group is characterized primarily by the following characteristics, which vary slightly depending on the type of preparation: Very simple, fast and inexpensive production without anticoagulants, a very high platelet concentration, as well as a high leucocyte concentration. An injectable to very highly networked consistency of the fibrin matrix which allows cutting and sewing.

The following fourth part presented in detail is particularly suitable for dental and oral surgery practice and is the most often found technique.

Choukroun's PRF

The concept of a highly polymerized and dense fibrin matrix containing leucocytes without anticoagulants, bases on the idea of a pain therapist from Nice, Dr. Choukroun. First attempts succeeded in form of fibrin membranes placed on leg ulcers and covered with plastic bandages with the aim of promoting the angiogenesis by supraphysiological growth factor doses and consecutively regenerate the skin surface integrity. A significant difference from the protocols practiced by then was the renunciation of anticoagulants during the production. The reduction or the renunciation of anticoagulant substances in preparation has been shown to lead to faster wound healing than with anticoagulants [5]. In recent years, the „low-speed Centrifugation Concept" was developed recently [6,7], where by reduction of G-forces in centrifuging, the number of leukocytes and the amount of growth factors could be increased.

In this manner following new preparations could be developed:

- **A-PRF+:** 1300 revolutions per minute, 8-minute centrifuge time, glass vacuettes. This creates a highly dense, highly networked fibrin matrix with a high proportion of leukocyte and growth factors, which after stripping off the erythrocyte clot is ready for use in an extraction socket, for example. Further processing is carried out for use as a membrane, to which a later analysis will be taken into detail.
- **A-PRF liquid:** 1300 revolutions per minute, 5-minute centrifuge time, glass vacuettes. This protocol allows the production of a not very densely polymerized fibrin matrix, which is in liquid consistency for a few minutes and allows big membranes being shaped in little bowls or mixed with bone grafts - „sticky bone" (Figure 1).
- **i-PRF:** 700 revolutions per minute, 3-minute centrifuge time in women and a 4-minute centrifuge time in men (based on gender-specific differences in particular hematocrit levels). The relative centrifugal force in this protocol are 60 grams. In contrast to the aforementioned methods, plastic instead of glass is used as vacuette material, in order to delay the polymerization in the vacuette, allowing a roughly 15-minute timespan to be able to further process, before it takes a more viscous consistency. Compared to the above described fibrin matrices L-PRF and A-PRF+, this one is more porous and contains more leukocytes and growth factors as shown by Ghanaati et al. in 2014 [8] and can be mixed with bone grafts and named "sticky bone" as well. A very recent systematic review concluded that there is limited evidence on the effects of L-PRF in intraoral bone grafting procedures and there is the need for further research to fully assess its clinical indications [9].

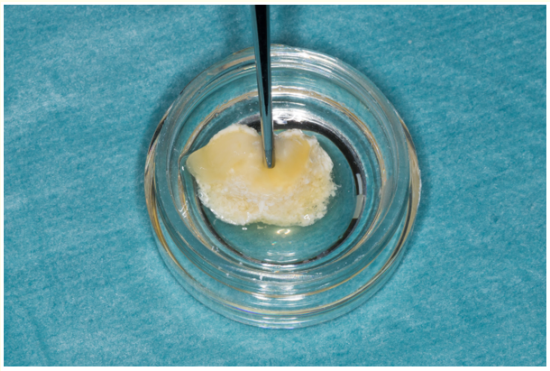

Figure 1

Review of Clinical Options

Most frequent indications can be listed as [10].

Management after extraction/socket preservation

The desire for a biomaterial that does not necessarily need to be covered plastically, that does not cause foreign body reactions and that may have a positive impact on wound healing has led to an increased use of PRF in extraction sockets. In terms of bone regeneration after tooth extraction however results of studies show various success levels. In part, when comparing a socket preservation with PRF where in control groups the wound healing was conventional via a blood clot, a significant advantage in the PRF group in terms of bone volume after wound healing and also bone density have been reported [11-13]. There are studies showing evidence of an advantages of PRF without statistical significance [12,14,15]. It's similar with detection of reduction in pain. In a study with visual analogue scales, it was possible to show a significant reduction in pain in the PRF group [14], while in another study, a tendency to statistically not significant pain reduction could be reported [15]. There is evidence that using PRF in extraction sockets in patients with hemorrhagic diathesis could reduce the complication rate [16] and additionally a significantly decreased osteomyelitis incidence after wisdom teeth extractions [17].

Bone augmentation and regeneration

There seems to be success of guided bone regeneration (GBR) with autologous as well as xenogenous bone grafts with a positive impact on bone formation. According to histological studies, this is justified by studies showing an improved angiogenesis. In the treatment of drug-induced jaw necrosis, for example, it seems that patients benefit mainly of faster reepithelialization of exposed bone surfaces when PRF is used. One of the most common applications of A-PRF+ membranes is the use as a barrier membrane in GBR, however, the drawback at this stage is the relatively rapid degradation within 7-9 days (Figure 2 and 3).

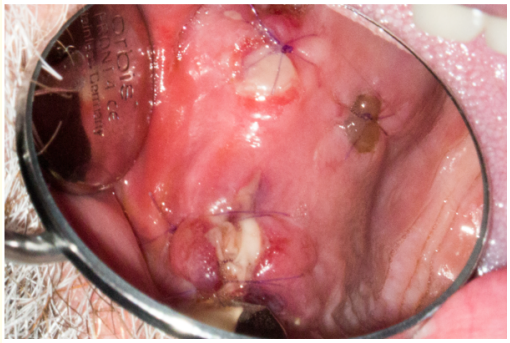

Figure 2

Sinus floor elevation

The following applications of PRF membranes in conjunction with sinus floor elevation procedures have been reported:

- As bone replacement material alone (Figure 3) or
- In conjunction with any bone graft materials (Figure 4),
- For the repair of defects of the Schneider's Membrane or
- To cover the lateral access windows of the sinuses in the external sinus lift technique.

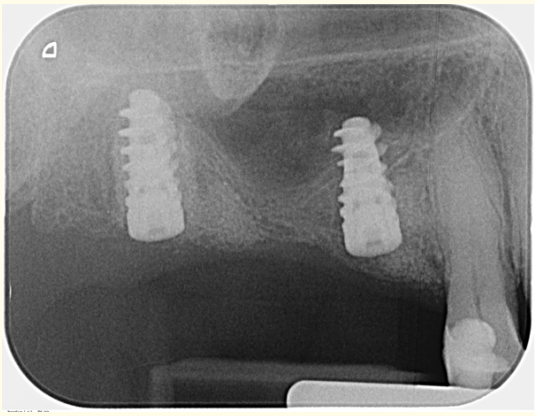

Figure 3

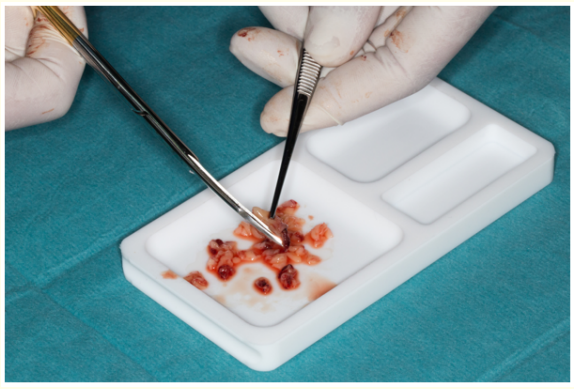

Figure 4

There are reasons to believe that with the simultaneous implantation and the use of A-PRF+-membranes as bone graft material alone could lead to bone formation in the space between the Schneider's Membrane and bony maxillary sinus floor [18]. In case of a two-stage procedure an augmentation with PRF alone seems to be not as efficient as in the simultaneous way, as premature collapse of the augmented volume should be expected, consecutively leading to insufficient bone volume. PRF could be used with xenogenous bone graft materials to aim a stronger regenerative capacity compared to the application without PRF, which may lead to a generally shortened healing time with these graft materials. A-PRF+ membranes to cover the lateral windows in external sinus lift procedures were evaluated in 2 RCT studies examining the use of A-PRF+ Membranes compared to collagen membranes from pork [19] and there were no significant differences in terms of undesired complications and new bone formation between both groups. There is little evidence on the use of A-PRF+-membranes for the closure of Schneider's Membrane perforations, however, there are case reports about successful results about the use of A-PRF+ membranes alone or in conjunction with collagen membranes [18].

Treatment of gingival recessions and periodontal bone defects

In the treatment of mucogingival recessions primarily two indications for the use of A-PRF+ membranes emerge. The harvesting site of connective tissue transplants are covered, where patients profit from less post-operative pain and an accelerated reepithelialization, and when recessions of Miller grades I and II defects are covered with A-PRF+ membranes, instead of coronally advanced flaps (CAF)/or tunnel techniques by utilization of connective tissue grafts (CTG) or xenogeneic grafts, the results are promising; whereas the Miller grade III defects can actually not be recommended (Figure 5 and 6). In the regeneration of periodontal bone or furcation associated grade II defects there is growing evidence that patients could benefit from combined or sole use (Figure 7 and 8).

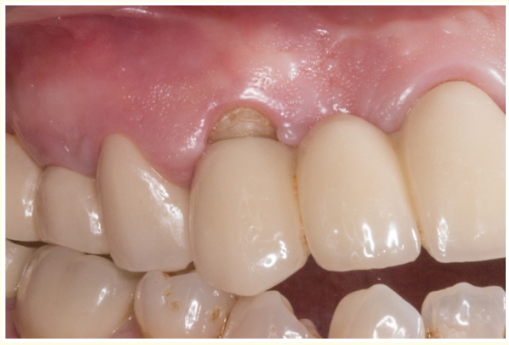

Figure 5

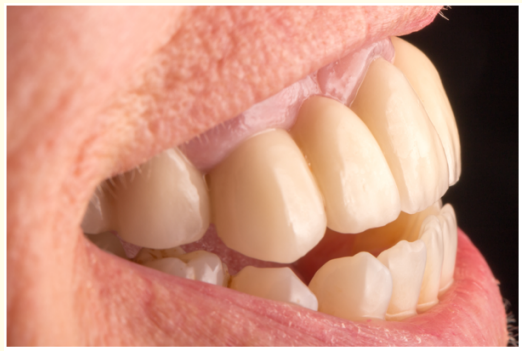

Figure 6

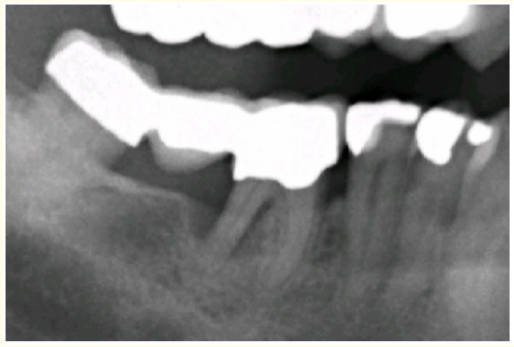

Figure 7

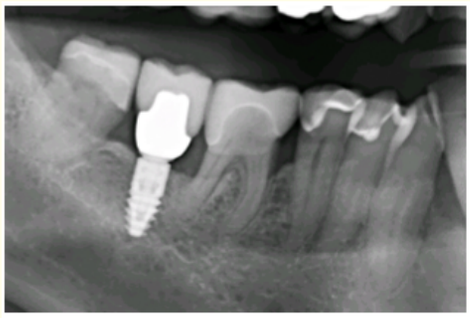

Figure 8

The technical prerequisites for the production of PRF are low; a suitable centrifuge is needed. The blood collection is not different than the routine. If finding the veins is problematic, for example, the Veinlite-LED+Device (TransLite, LLC, Sugar Land, TX, USA) can be a great help, since it can show veins very easily. The vacuettes where the blood is collected in, should be filled and centrifuged as quickly as possible. In order to prevent hemolysis, it is recommended to start centrifugation after filling a variety of vacuettes (about every 4-6 vacuettes) and add the next couple of vacuettes to the centrifuge after the final blood draw. It is reported that instead of waiting for all vacuettes to be filled, the longer centrifugation of the first group could be more advantageous than the danger of hemolysis. For the A-PRF+ membranes it is recommended to wait a couple of minutes after centrifugation in order to obtain a more stable fibrin clot, which is then also easier to separate from the erythrocyte clot.

Each fibrin clot then is processed into the desired form, for example into a membrane or a plug. In order to produce membranes, the metal riddle in the PRF box is used, while when making plugs a hollow stamp-like mold is used, whereby the pressing significantly reduces the volume (Figure 9). The serum collected in the box can be reused, for example, for wetting biomaterials. Since the i-PRF should normally be processed within 15 minutes, an additional blood collection intraoperatively can be necessary. The i-PRF is produced within a very short of time, about 3 minutes and is immediately ready for use.

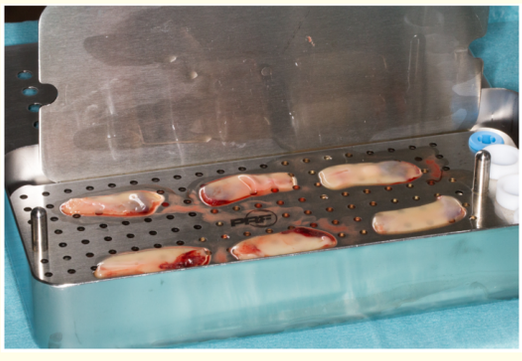

Figure 9

Discussion

Centrifugation protocols seem to be important for the end product. The findings from a very recent study demonstrated that a clinician has approximately 60–90 s on average between blood collection and the start of the centrifugation cycle to produce standard-sized PRF membranes. If this time window is missed, a significant reduction in size is reported to be observed. Additionally, females and older patients were found to produce larger PRF membranes, likely due to lower red blood cell counts [20]. More and more PRF is gaining acceptance as a bioactive surgical additive in regenerative dentistry. Until recently it has only been available in gel or membrane form and was not suitable for injection. Recently, however, a liquid, injectable PRF has been introduced [21].

Conclusion

PRF may be used in a broad variety of applications and may be a valuable help for the daily practical routine. Scientific evidence is more and more showing advantages of PRF use and clinically superior outcome..

Conflict of Interest

The authors declare that they have no conflict of interest with any product or method.

Acknowledgements

The authors would like to thank the clinical team of Do24 for the excellent support in succeeding the clinical goals which had been set.

Bibliography

1. Marx RE., *et al*. "Platelet-rich plasma: Growth factor enhancement for bone grafts". *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology* 85 (1998): 638-646.

2. Kawase T and Tanaka T. "An updated proposal for terminology and classification of platelet-rich fibrin". *Regenerative Therapy* 11.7 (2017): 80-81.

3. Anitua E. "The use of plasma-rich growth factors (PRGF) in oral surgery". *Practical Procedures and Aesthetic Dentistry* 13 (2001): 487-493.

4. Weibrich G., *et al*. "Collection efficiency and platelet counts of two different methods for the preparation of platelet-rich plasma". *Clinical Oral Implants Research* 13 (2002): 437-443.

5. Anitua E., *et al*. "Implementation of a more physiological plasma rich in growth factor (PRGF) protocol: Anticoagulant removal and reduction in activator concentration". *Platelets* 27 (2016): 459-466.

6. Choukroun J and Ghanaati S. "Reduction of relative centrifugation force within injectable platelet-rich-fibrin (PRF) concentrates advances patients' own inflammatory cells, platelets and growth factors: the first introduction to the low speed centrifugation concept". *European Journal of Trauma and Emergency Surgery* 44 (2018): 87-95.

7. Ghanaati S., *et al*. "A Proof of the Low Speed Centrifugation Concept in Rodents: New Perspectives for In Vivo Research". *Tissue Engineering Methods* 24 (2018): 659-670.

8. Ghanaati S., *et al*. "Advanced platelet-rich fibrin: a new concept for cell-based tissue engineering by means of inflammatory cells". *Journal of Oral Implantology* 40 (2014): 679-689.

9. Dragonas P., *et al*. "Effects of leukocyte–platelet-rich fibrin (L-PRF) in different intraoral bone grafting procedures: a systematic review". *International Journal of Oral and Maxillofacial Surgery* (2018): pii: S0901-5027 (18)30216-9.

10. Ghanaati S., *et al*. "Fifteen years of platelet rich fibrin (PRF) in dentistry and oromaxillofacial surgery: How high is the level of scientific evidence?" *Journal of Oral Implantology* (2018).

11. Anwandter A., *et al*. "Dimensional changes of the post extraction alveolar ridge, preserved with Leukocyte- and Platelet Rich Fibrin: A clinical pilot study". *Journal of Dentistry* 52 (2016): 23-29.

12. Kumar YR., *et al*. "Platelet-rich fibrin: the benefits". *British Journal of Oral and Maxillofacial Surgery* 54 (2016): 57-61.

13. Temmerman A., *et al*. "The use of leucocyte and platelet-rich fibrin in socket management and ridge preservation: a split-mouth, randomized, controlled clinical trial". *Journal of Clinical Periodontology* 43 (2016): 990-999.

14. Ruga E., *et al*. "Platelet-rich fibrin and piezoelectric surgery: a safe technique for the prevention of periodontal complications in third molar surgery". *Journal of Craniofacial Surgery* 22 (2011): 1951-1955.

15. Singh A., *et al*. "Platelet rich fibrin: a novel approach for osseous regeneration". *Journal of Maxillofacial Oral Surgery* 11 (2012): 430-434.

16. Sammartino G., *et al*. "Prevention of hemorrhagic complications after dental extractions into open heart surgery patients under anticoagulant therapy: the use of leukocyte- and platelet-rich fibrin". *Journal of Oral Implantology* 37 (2011): 681-690.

17. Hoaglin DR and Lines GK. "Prevention of localized osteitis in mandibular third-molar sites using platelet-rich fibrin". *International Journal of Dentistry* (2013): 875380.

18. Tajima N., *et al*. "Evaluation of sinus floor augmentation with simultaneous implant placement using platelet-rich fibrin as sole grafting material". *International Journal of Oral Maxillofacial Implants* 28 (2013): 77-83.

19. Bosshardt DD., *et al*. "Maxillary sinus grafting with a synthetic, nanocrystalline hydroxyapatite-silica gel in humans: histologic and histomorphometric results". *International Journal of Periodontics and Restorative Dentistry* 34 (2014): 259-267.

20. Miron RJ., *et al*. "The effect of age, gender, and time between blood draw and start of centrifugation on the size outcomes of platelet-rich fibrin (PRF) membranes". *Clinical Oral Investigation* (2018).

21. Shah R., *et al*. "Biological activation of bone grafts using injectable platelet-rich fibrin". *Journal of Prosthetic Dentistry* (2018): pii: S0022-3913 (18)30279-8.

22. Hegab AF., *et al*. "Platelet-Rich Plasma Injection as an Effective Treatment for Temporomandibular Joint Osteoarthritis". *Journal of Oral and Maxillofacial Surgery* 73 (2015): 1706-1713.

23. Lolato A., *et al*. "Platelet concentrates for revitalization of immature necrotic teeth: a systematic review of the clinical studies". *Platelets* 27 (2016): 383-392.