Medical and Research Publications
International Open Access

Review Article **Journal of MAR Dental Sciences (Volume 5 Issue 4)**

Platelet Rich Fibrin – A Rising Tide in Implant Dentistry

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Received Date: April 27, 2022

Published Date: May 01, 2022

Introduction

Platelet-rich fibrin is a second-generation platelet concentrate which consists of growth factors and cytokines encapsulated in a fibrin matrix. It forms the perfect environment for tissue regeneration and wound healing by combining fibrant sealing properties and growth factors. (Agrawal and Agrawal, 2014), (Raaj, Gautam and Kumari, 2015)

Why PRF Over PRP?

I. The method of preparation is simple and inexpensive.

II. It reduces the rate of cross infection by eliminating usage of bovine thrombin and anticoagulants. The use of bovine thrombin has been linked to the formation of antibodies to factors V, XI, and thrombin, putting the patient at risk for life threatening coagulopathies.

III. PRF's fibrin matrix is more organised, making it more efficient in haemostasis, wound and bone healing, graft stabilisation and stem cell migration.

IV. It supports the immune system.

V. On contacting the glass particles of the test tube PRF demonstrates a slow natural polymerization which results in a physiologic thrombin concentration. However, in PRP fibrin polymerization occurs suddenly which is dependent on the presence of surgical additives. (Deeb, 2020),

Method of Preparation:

Dr Joseph Choukron invented the traditional procedure for the preparation of PRF in the year 2000. The process for the preparation of PRF is fairly easy, nevertheless, it must be prepared right before it is used. The main advantage in PRF preparation is the single stage centrifugation.

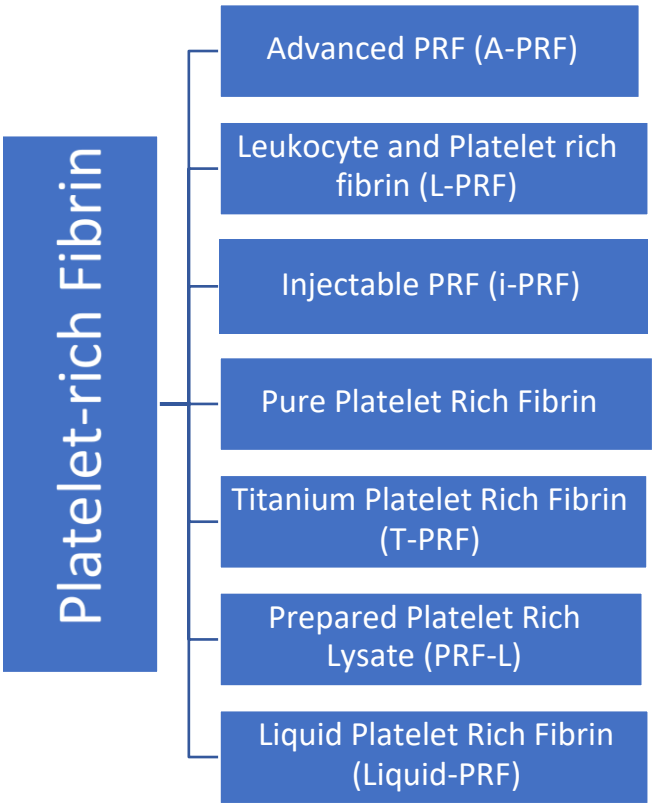
A butterfly needle and 10ml blood collection tubes are used to collect blood without anticoagulants from the patient intravenously. After the blood is drawn, it is immediately centrifuged at 3000 rpm for 10 minutes on a table top centrifuge.

After soft centrifugation, 3 levels form –

- Acellular plasma (platelet poor plasma)
- Platelet Rich Fibrin clot and
- Erythrocyte layer at the bottom, respectively.

The junction between the PRF and the RBC layer is rich in growth factors and therefore this region is also to be preserved.

Classification



The key differences in the PRF types would be the centrifugation protocols/speed. The difference in centrifugation protocols for each type of platelet aggregate influences the different cell populations and growth factors responsible for the variation of growth factors over time.

We can classify PRF as:

1. L-PRF (Leukocyte and Platelet Rich Fibrin)

2. A-PRF (Advanced PRF)

3. I-PRF (Injectable PRF)

4. T-PRF (Titanium PRF)

5. P-PRF (Pure PRF)

6. Liquid-PRF

7. PRF-L (Prepared platelet-rich lysate

1. L-PRF: Leukocyte and Platelet Rich Fibrin.

No anticoagulants are used to centrifuge blood samples at low speed. This variant is a high provider of leukocytes. It has a high-density fibrin network after activation, therefore having a strong fibrin scaffold. It exists only in an activated form and can only be of use in a gel form. We can also refer to this platelet concentrate as Choukroun's PRF. L-PRF has high antibacterial properties, wound healing and growth factor regulating properties such as TGF-β.

Studying the L-PRF matrix, stated that it dissolves slowly, allowing the progressive release of cytokines and platelet- derived growth factors, acting as an anti-infective agent with a key role in immune regulation.

It is considered as the most simple and cheap method to get PRF.

2. A-PRF: Advanced Platelet Rich Fibrin.

This platelet concentrate is got by modifying the RPM. It requires longer centrifugation time and lower rpm. This is done to reduce the loss of cells within the PRF matrix. More neutrophilic granulocytes appear in the distal region of the clot, and the cells are more dispersed throughout the clot. It is leukocyte rich and aids in fastening the healing process.

PRF clots formed with the A-PRF centrifugation protocol (1500 rpm, 14 minutes) show a porous structure with more interfibrous space, and more cells are counted in the fibrin-rich clot. Special glass tubes are used to enable faster clot formation.

The protocol of centrifugation followed for obtaining A-PRF improved the growth factor release. Overall, the regenerative capacity of PRF is improved.

A slight decrease in centrifugation period by maintaining the RCF range within 208 g resulted in an improved clot termed Advanced PRF plus (A-PRF+), showing supplemented characteristics.

3. T-PRF: Titanium Platelet Rich Fibrin.

It is a 3rd generation platelet concentrate. The primary aim of developing T-PRF was to avoid the health hazards associated with silica by using dry glass or glass-coated plastic tubes.

Titanium is known for its excellent biocompatibility.

It has better hemocompatibility compared to glass, which leads to the formation of a more polymerized fibrin. This could also be a reason T-PRF lasts longer in tissues.

T-PRF shows a more well-organized matrix and fibrin maturation compared to L-PRF. The fibrin network formed covers a larger area and demonstrates a much thicker fibrin clot.

Titanium as a material shows excellent biocompatibility and excellent osseointegration. It is commonly used in dental implantology, artificial heart valves and other medical devices.

The centrifugation protocol is 2,800 rpm for about 12 minutes. The concept of T-PRF was devised by Mustafa Tunali et al. in 2011.

4. Pure PRF: Leukocyte-Poor Platelet-Rich Fibrin.

Pure PRF demonstrates a lack of leukocytes and has a high-density fibrin network. It is used as a solid material–strongly activated gel form. Platelets are well preserved, and the concentration is high. The cost and the complex procedure make Pure PRF not readily obtainable.Centrifugation protocols include a specific separator gel due to which a tiny quantity of leukocytes is got.

The first centrifuge is of 6 minutes- high speed. This step transfers the buffy coat and the PPP (platelet poor plasma) to the second tube. The second tube contains CaCl2. The second centrifuge is then done for 15 minutes. After which a stable platelet-fibrin is formed.

5. Liquid PRF:

It is obtained at low-speed centrifugation. Fibrinogen and thrombin in a liquid-PRF formula are obtained. It does not form a fibrin matrix.

6. PRF-L: Prepared platelet-rich Lysate.

This is the newest application of PRF. Centrifugation protocols include incubation at 37 degrees Celsius in a humidified atmosphere of 5% CO2 and 95% air. PRF Lysate is referred to the exudate formed and collected after centrifugation.

It is said to be an excellent source of several growth factors. In a study, they found that PRF-L can significantly improve the proliferation index, collagen deposition and migration rates in chronically UVA-irradiated human dermal fibroblasts [13]. This is a new technique that requires further studies.

7. I-PRF: Injectable Platelet Rich Fibrin

I (Injectable) -PRF, is got by centrifuging for 3 minutes at 800 rpm in a plastic tube. This form of PRF may also contain stem cells which have high regenerative properties. It is basically a liquid form of PRF. PRF is in gel form, which makes its use limited. For this reason, the recent advancement of i-PRF, PRF in liquid formulation, makes it easier to be injected in areas of soft tissue or the mucous membrane.

Uses of I-PRF:

- Facial rejuvenation and hair growth, replacing the use of PRP
- Wide-open blunderbuss canals for apex closure
- GBR procedures where it is mixed with autogenous bone or bone substitutes (allografts)
- Root surface bio-modification on root coverage
- Periodontal therapy for thin gingival phenotypes, infrabony and furcation defects
- Local drug delivery
- Antimicrobial activity against Porphyromonas gingivalis and Aggregatibacter actinomycetemcomitans

Advantages of i-PRF have been of utmost help clinically. Shorter centrifugation times, increased number of regenerative cells and greater concentration of growth factors (vascular endothelial growth factor [VEGF] and transforming growth factor-β1) make i-PRF clinically useful as they are required for neovascularization and angiogenesis. i-PRF is shown to induce higher cell- migration, mRNA expression of TGF-ß, PDGF and COL1a2.

Compared to PRP, i-PRF induces a much higher fibroblast migration, whereas PRP was responsible for higher levels of cell proliferation. Over time, i-PRF continues to release additional growth factors. Revascularization and maturogenesis can be achieved with i-PRF.

A-PRF and i-PRF contain monocytes which play an essential role on bone growth, vascularization, and production of VEGF. The monocytes have BMP receptors and produce BMP-2.

An extracellular glycoprotein with a high molecular weight, Fibronectin; is found in i-PRF.

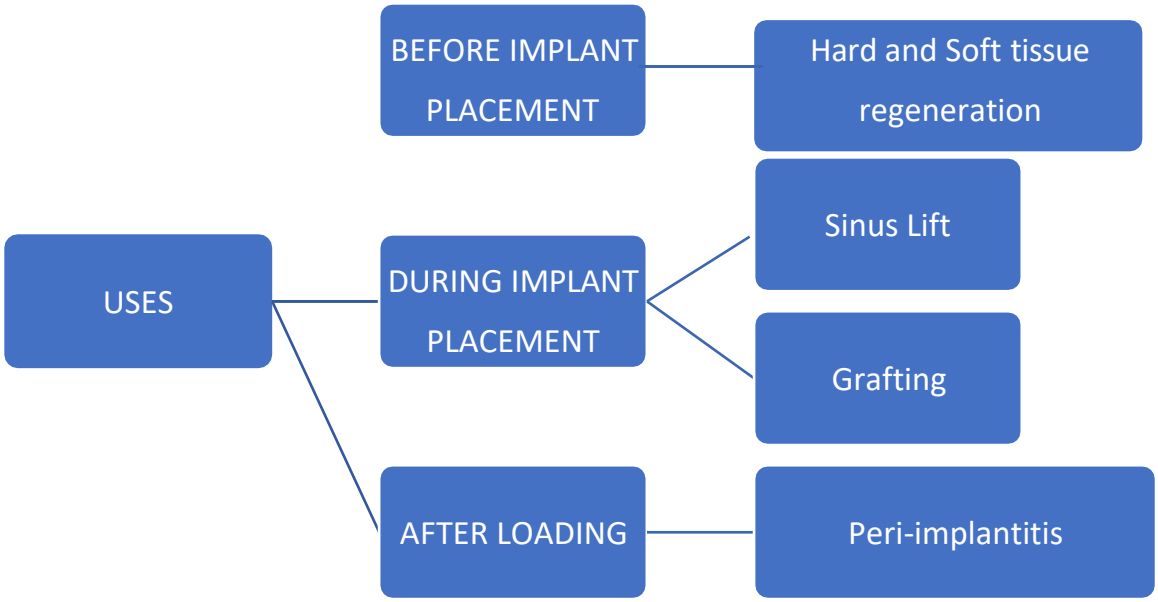
Application of i-PRF to root surface improves cellular proliferation from the periodontal ligaments towards the supracrestal parts because of the presence of fibronectin.

According to a study conducted by Mustafa Tunali, i-PRF is also found to be effective in lesions of erosive Lichen Planus. It can be considered a successful alternative to corticosteroids, which exhibit an array of local and systemic adverse effects.

Centrifugation Protocols

TYPE OF PRF	TEST TUBE USED	CYCLES PER MINUTE (RPM)
L-PRF	Sterile silicon coated interior glass tubes / Sterile glass coated plastic tubes – RED VACUTAINER TUBE	2,700 rpm for 12 minutes (700 g for 12 minutes)
A-PRF	Sterile plain glass-based vacuum tubes – RED VACUTAINER TUBE	1,500 rpm for 14 minutes
i-PRF	Plain plastic tube – PURPLE VACUTAINER TUBE Sticky bone – WHITE VACUTAINER TUBE	800 rpm for 3 minutes
T-PRF	Titanium tubes (Grade IV titanium)	2,800 rpm for 12 minutes
P-PRF		1st centrifuge – High speed for 6 minutes 2nd centrifuge – Done with CaCl2 for 15 minutes
Liquid-PRF		Low speed centrifugation (60g for 3 minutes)
PRF-L		Incubation at 37 degrees Celsius in a humidified atmosphere of 5% CO2 and 95% air

Uses In Implants



Before Implant Placement

Hard and Soft Tissue Regeneration:

Periodontal therapy aims to stop the advancement of periodontal disease while also regenerating structures that have been destroyed due to the disease. Regeneration is defined as reproduction or reconstruction of a lost or injured part in such a way that the architecture and function of the lost or injured tissues are completely restored. Periodontal regeneration is a multifaceted process that involves cell adhesion, migration, proliferation, and differentiation in an organised sequence.

Interaction between various cells, such as the epithelial cells, osteoblasts, periodontal ligament cells and gingival fibroblasts are required for periodontal wound healing.

Platelets can play an important role in periodontal regeneration, as they are reservoirs of cytokines and growth factors which are essential for soft tissue maturation and bone regeneration.

PRF is one such complex natural scaffold which is commonly used for tissue repair and regeneration. The combination of fibrins and cytokines within PRF becomes a powerful bio- scaffold with an integrated reservoir of growth factors for tissue regeneration. The physiologically available thrombin in PRF causes fibrinogen to polymerize slowly into fibrin, resulting in an architecture favourable to wound healing.

Use of PRF in periodontal regeneration has two major benefits:

1) The induction of new alveolar bone formation facilitated by the fibrin mediated effect of PRF on RUNX2 expression, osteoblast differentiation, and matrix mineralization, and also by the alkaline phosphatase activity-stimulating effect of fibrin.

2) The effect of PRF on progenitor proliferation and migration has been linked to soft tissue (Li et al., 2013), ('6 Indian Dental Congress', 2015), (Preeja and Arun, 2014)

During Implant Placement

Sinus Lift

A sinus lift, also referred to as a sinus augmentation procedure, is described as a surgical technique to increase the amount of bone in the posterior maxilla. It could be done for various reasons, such as placement of implants or treatment for perforation of the Schneiderian membrane.

PRFs have been widely used in sinus lift procedures owing to their various favorable properties.

PRF is used as the sole filling material or in combination with bone graft materials for the procedure.

The addition of a graft material with PRF makes it easier in terms of graft manipulation. PRF and bone grafts are combined for cases where one or more walls are missing or defective. PRF acts as a glue between the healing wound tissues and increasing the cohesion when used in combination with graft materials and speeding up graft maturation.

Bone graft materials such as xenografts, allograft and alloplast lack osteogenic and osteoinductive properties, along with other disadvantages such as prolonged healing time and host response. Autogenous bone graft, although it is osteogenic, osteoinductve and osteoconductive, still has the disadvantages of donor site morbidity and the need for additional surgical procedures.

PRF membranes can be used as the sole filling material overcoming such problems by being osteoinductive and accelerating healing time, besides also being inexpensive and easily attainable.

Another use of the PRF membranes, more specifically A-PRF, is the use of healing barriers in cases of perforated Schneiderian membranes. Subsequently, rapid healing takes place. The fibrin matrix of PRF leads to a sticky consistency, enabling the membrane to stay in place. A Schneiderian membrane perforation should ideally be covered with a double membrane layer given the short resorption period of 12-14 days, associated with a PRF membrane. This double layering technique enables the extension of the resorption period, giving adequate healing time.

Its fibrin matrix properties and ability of slowly releasing growth factors make it an ideal replacement biomaterial to replace xenogenic and expensive collagen membranes in some situations.

Various clinical case reports describe the lateral approach for sinus floor elevation using only PRF as the grafting material.

L-PRF can be used successfully as a "sole" filling material during sinus augmentation–but only if simultaneous with the placement of implants.

Alveolar Ridge Regeneration and GBR

After the extraction of a tooth, dimensional loss of bone height and width occurs naturally throughout the healing phase. Alveolar bone remodelling at the extraction site always reduces the ridge volumes and distorts the ridge configuration, making the correct placement of implants difficult. Hence, it is well acknowledged that ridge preservation techniques after tooth extraction are beneficial.

Guided bone regeneration (GBR) is an established treatment modality to achieve bone regeneration, especially in the maxillofacial region. It's a technique which involves covering an osseous defect using a barrier membrane. The idea behind GBR is that using a membrane prevents the non-osteogenic tissues from interfering with bone healing for effective bone formation.

A significant amount of bone volume in the vertical and horizontal dimensions of the alveolar ridge is required to support stable teeth and implants. It is important to create a space between the implants and the surrounding soft tissues during the process of GBR with simultaneous implant placement. The space created should be maintained for an appropriate period of time to prevent the non-osteogenic tissues from migrating into the affected area, hence ensuring proper osteogenesis.

The membrane can also be used for graft stabilization apart from being used in space maintenance and preventing the migration of non-osteogenic tissues.

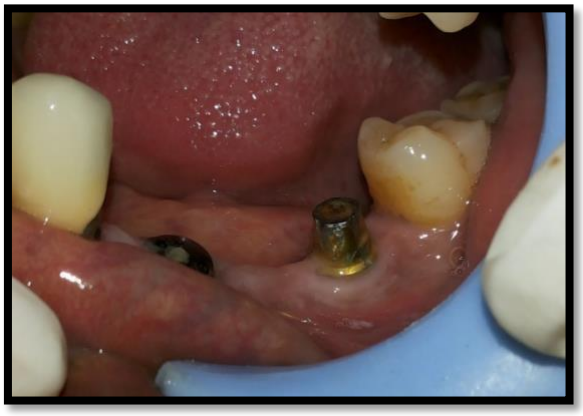
PRF membranes can be successfully used as a resorbable barrier membrane while performing GBR procedures. It is an inexpensive, and a naturally derived autologous source of growth factors. It can be used as barrier membrane for GBR by either cutting in into small pieces and mixing with a variety of bone biomaterials/grafting materials or by compressing it into flattened fibrin.

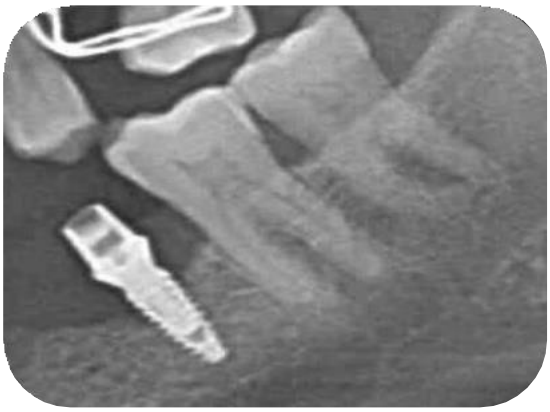
When compared to standard collagen membranes, it has various advantages because it contains autologous growth factors and living host immune leukocytes. Because these cells combat invading pathogens, the rate of infection gets reduced significantly.

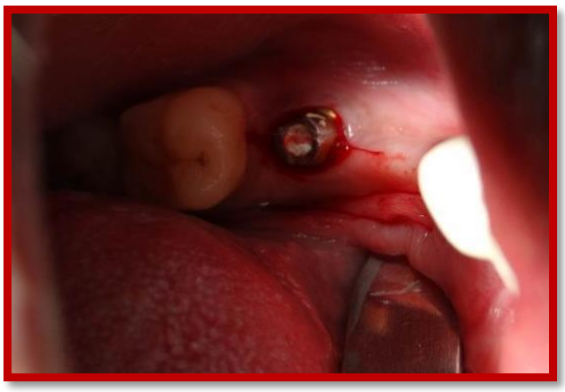
(Zhang et al., 2018),(Suttapreyasri and Leepong, 2013) ,(Hartshorne and Gluckman, 2016), (Soni et al., 2020), (Turri et al., 2016).

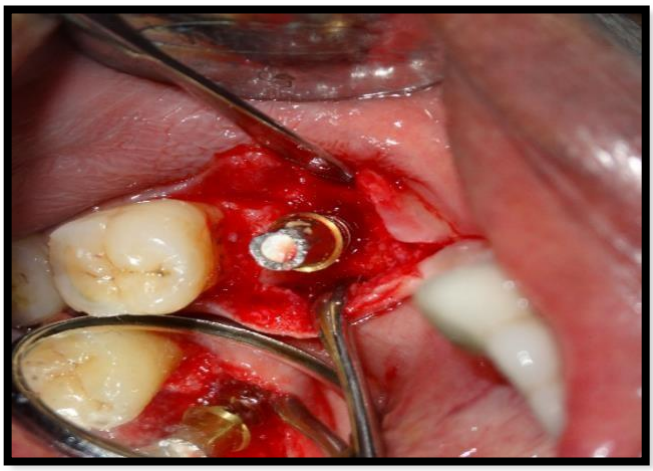
Pre-Operative

Incision



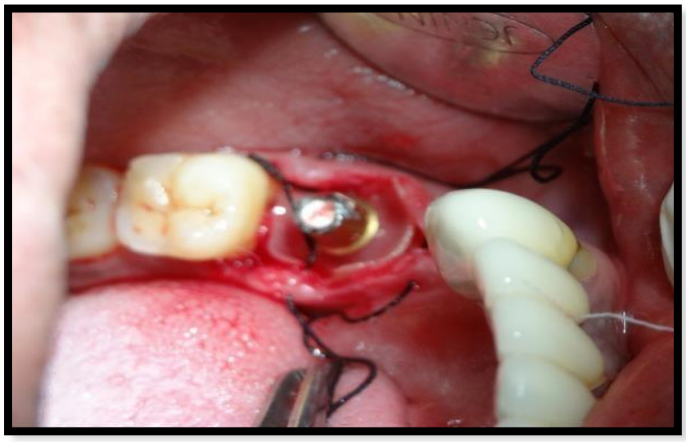




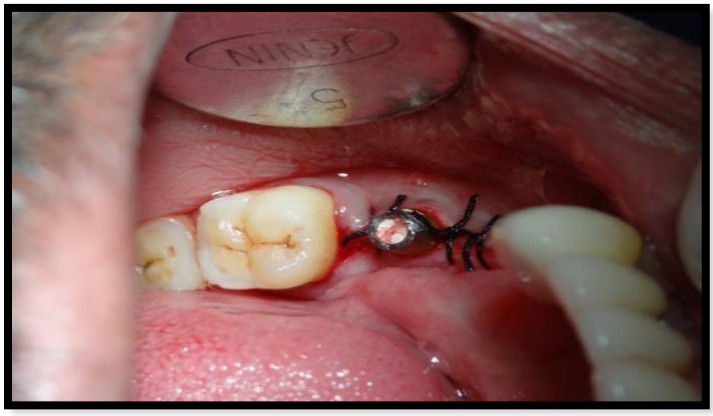


Flap Reflection

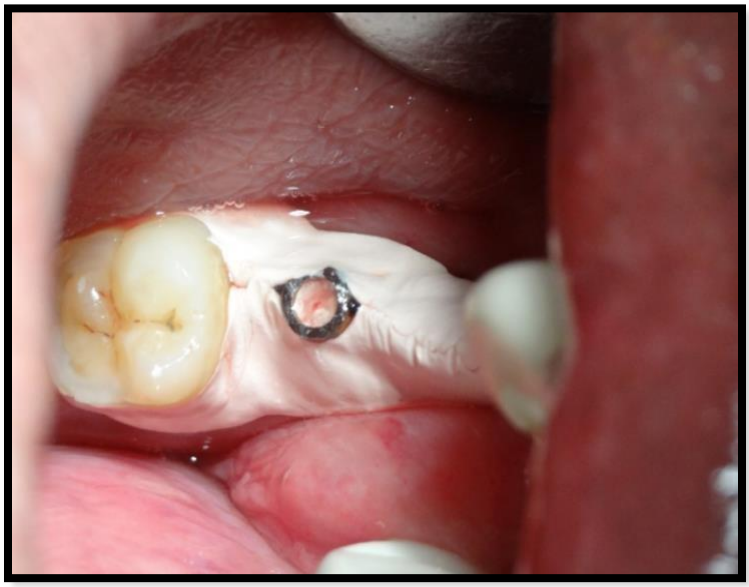
Membrane & Graft



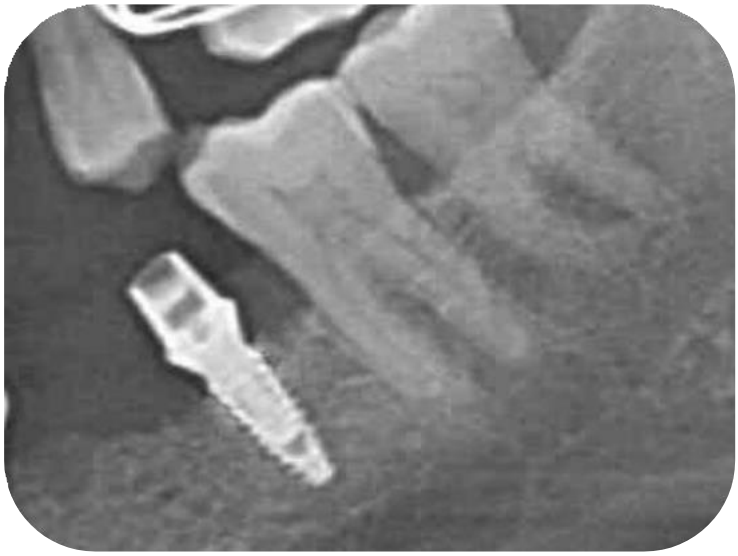
Graft and Membrane Placed



Suture Placed



Pack Placed



Post-Operative

After Implant Loading

Peri Implantitis

Peri-implantitis is an inflammatory and pathological disease accompanied by irreversible bone loss surrounding an implant with bleeding on probing and/or suppuration.

The primary goals of peri-implantitis treatment are:

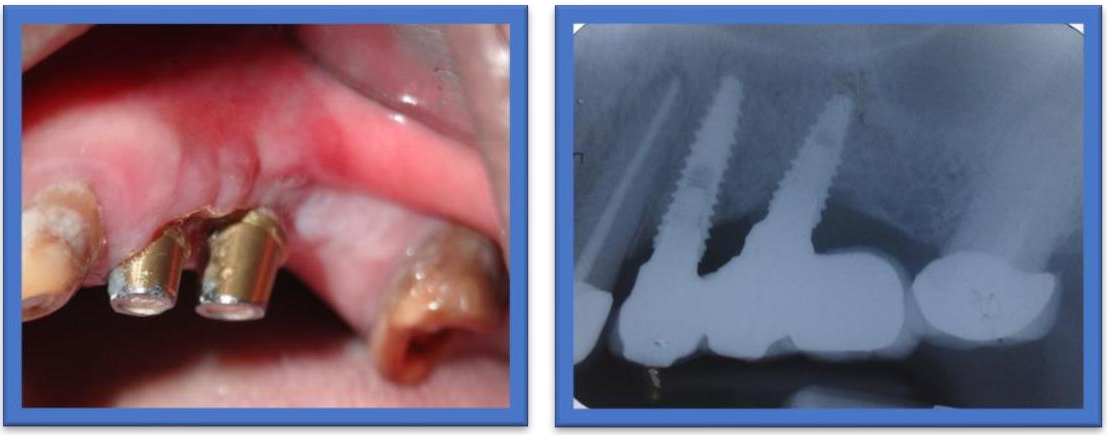
- Resseointegration of the contaminated implant surface,
- Preserving the implant supporting tissues and
- Increased bone fill within the implant defect.

PRF can be used as a therapeutic adjuvant with immediate implant placement and can be considered as a healing biomaterial with a favourable effect on peri implant tissue.

It helps in early bone regeneration because of the presence of concentrated bioactive molecules like insulin like growth factor (ITGF), platelet derived growth factor (PDGF), transforming growth factor (TGF)-beta. Growth factors are protected from proteolysis by the natural fibrin scaffolding, allowing them to remain active for longer periods of time. This results in successful neovascularization and faster wound closure, as well as a lower risk of infection after surgery.

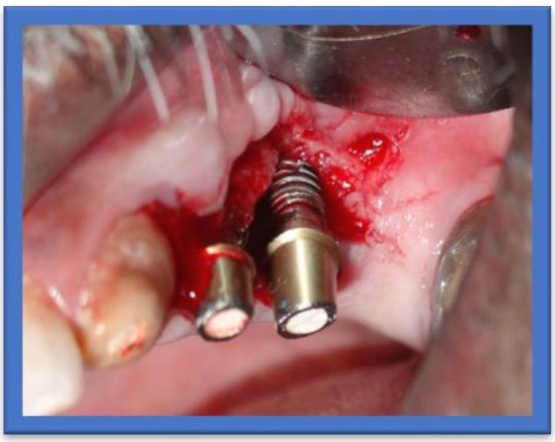
Coronal bone loss seen in peri-implantitis and the buccal gap with immediate implant placement are among the most popular peri-implant defect types.

PRF clot (A –PRF or L – PRF) or solution (I-PRF) mixed with the bone substitute can be used for the augmentation of the peri implant jump gap in immediate implant placement. The leukocytes, cytokines and growth factors present in PRF has appositive influence on the healing of the bony defect.(Hamzacebi, Oduncuoglu and Alaaddinoglu, 2015), (Hehn et al., 2016).

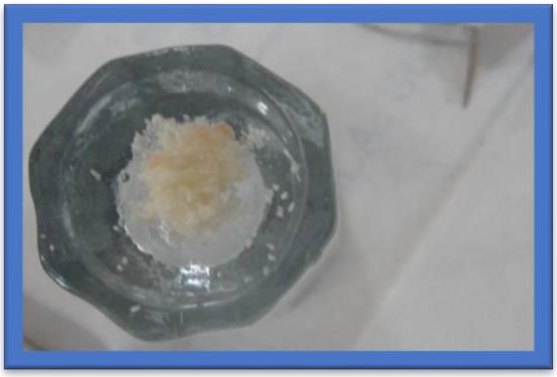


Pre-Operative

Probing Depth

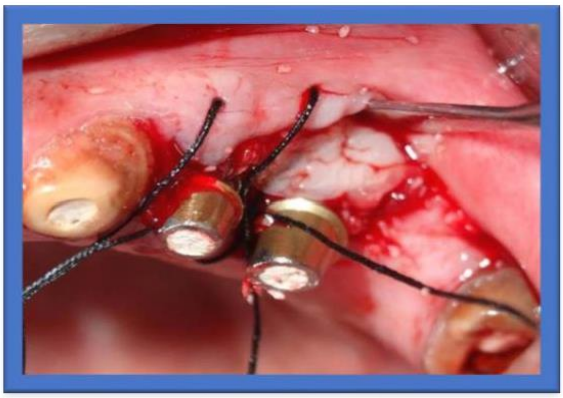


Flap Reflection

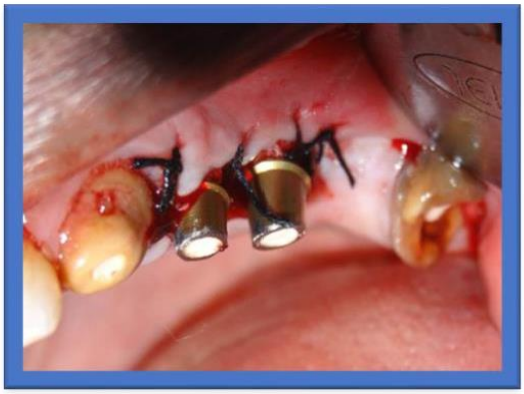


Graft & PRF

Graft Placed

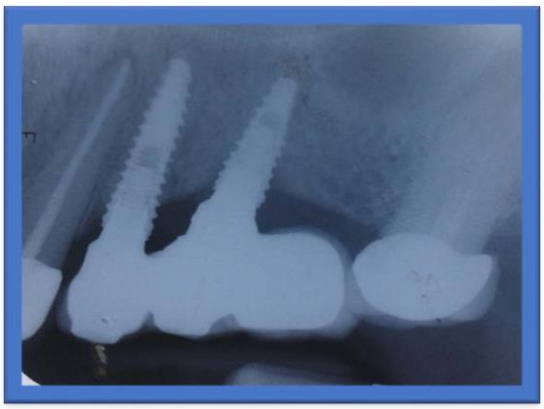


PRF Placed



Sutures

COE Pack



Post-Operative

Perioplastic Surgery

PRF is a biomaterial used for regeneration and soft tissue wound healing and is commonly used in periodontal plastic surgery.

Interdental Papilla

PRF can successfully be used In cases of loss of interdental papilla because of periodontal disease and papillary fill can be achieved with its use.

As a standard practice, connective tissue grafts are used for interdental papillary augmentation.

Platelet rich fibrin has mechanical adhesive properties and biological functions like fibrin glue, that enhances neo-angiogenesis, reduce the necrosis and shrinkage of flap.The dense fibrin matrix will be stable enough to fill the papillary space. The release of growth factors like fibroblast growth factor (FGF) and epidermal growth factor (EGF) etc. are favourable for regeneration. With PRF there is a consistent release of these growth factors for a minimum of 7 days.

The favorable properties of PRF help to maintain the flap in a stable position, allow less healing time, and do not require a second surgical site.

Root Coverage – Gingival Recession

Esthetics are not the only concern with gingival recession, but dentine hypersensitivity and increased chances of dental caries are also to be considered.

The type of PRF known distinctly to have a positive effect in periodontal therapy is L-PRF. Rich in leukocytes, not only does it release favorable growth factors, but it also has anti-bacterial properties, and faster healing with much fewer complications.

The gold standard in the treatment of Gingival Recession–The Sub-epithelial connective tissue graft, comes with several limitations. Hence, PRF can be considered a successful alternative in periodontal plastic surgery owing to its cellular contents.

Another approach to using PRF as treatment in gingival recession is the use of PRF membranes as a palatal wound bandage or a protective membrane over the placement of connective tissue grafts. This acts to speed up wound healing and exhibit anti-bacteria properties. The membranes are very thin and inhomogeneous and leucocytes and platelet aggregates are believed to be concentrated in end of the membrane. Therefore, two layers of membrane in opposite sense can prevent the resorption of the thin membrane and to allow the entire surgical area to be exposed to same components (leucocytes and platelet aggregates).

With mandibular anterior teeth recessions, treatment would depend mainly on the gingival biotype as the challenges this area faces. Other factors would also include the periodontal biotype and the thickness of the keratinized tissue. In the case of a thin gingival biotype, the gold standard would be the treatment of choice.

PRF Gel for Keratinization

According to a study by Temmerman A et al., it has been confirmed that L-PRF can increase the width of keratinized mucosa around implants. Regarding all its benefits, L-PRF can produce keratinized tissue with lesser patient complications and at a much lesser cost.

However, the stability of the keratinized mucosa in PRF is reportedly lesser when compared to connective tissue grafts. This can be considered a limitation in using PRF for keratinization, making it necessary to use CTG in combination with PRF or CTG as a sole material. This especially applies to patients who exhibit thin gingival biotype or Millers class III recessions.

Bioactivation With PRF Coating on Implants

The use of PRF to condition the implant surface provides contradictory results, from improving the process of osseointegration to no benefits achieved by coating the implant surface.

The coating of PRF on an implant also depends on its surface. Coating an implant with platelet concentrates is also known as bio-activation of the surface. The advantages of bio-activation is only limited to short-term improvement of osseointegration and early healing. Long-term effects were not that reliable.

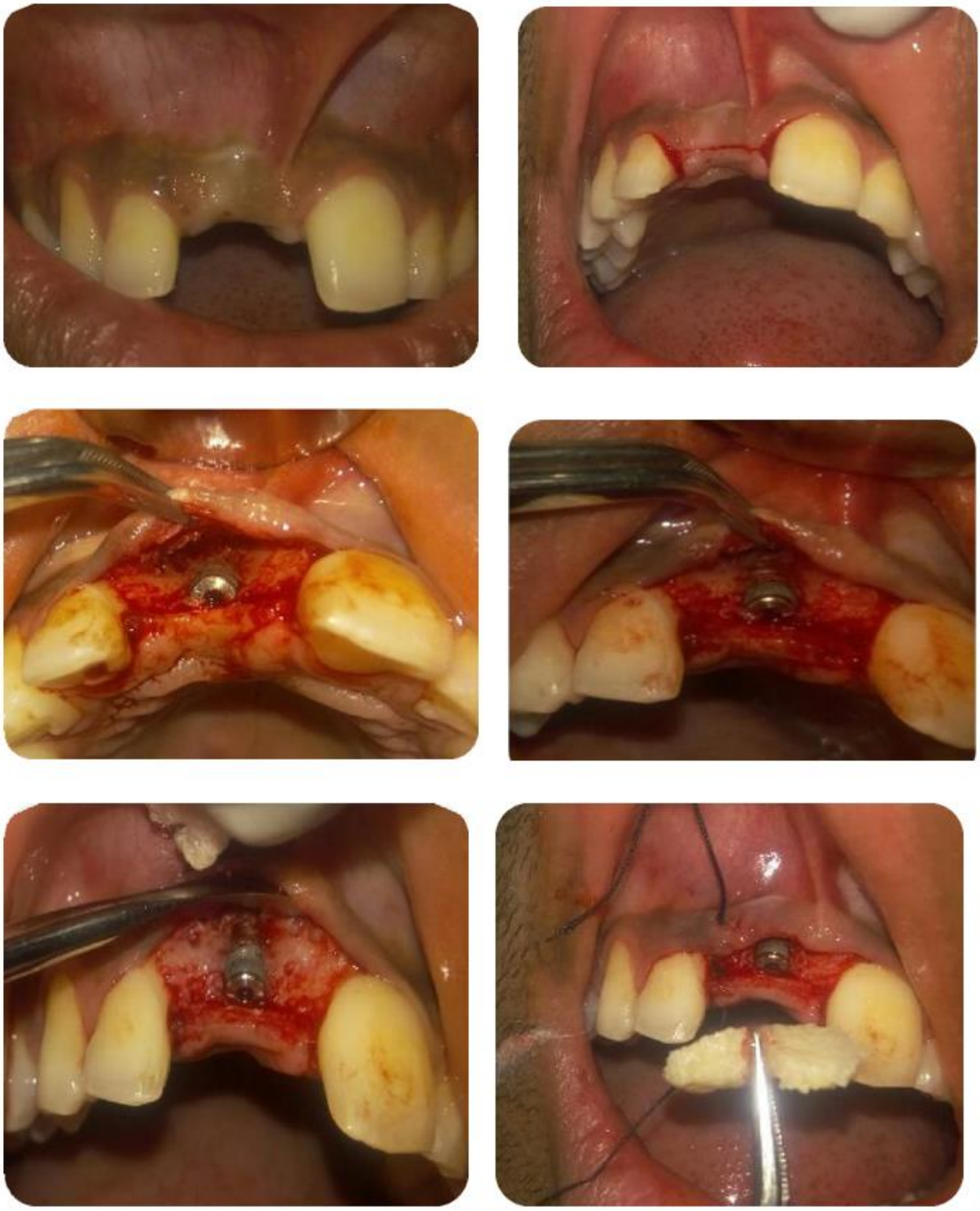
Long-term effects can only be worked on by altering the characteristics of the implant surface itself. Therefore, selection of a good implant system would be an efficient approach, rather than bio-activation of the surface with PRF.

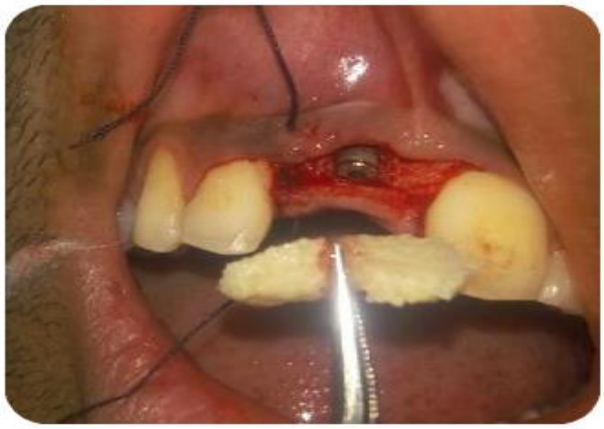
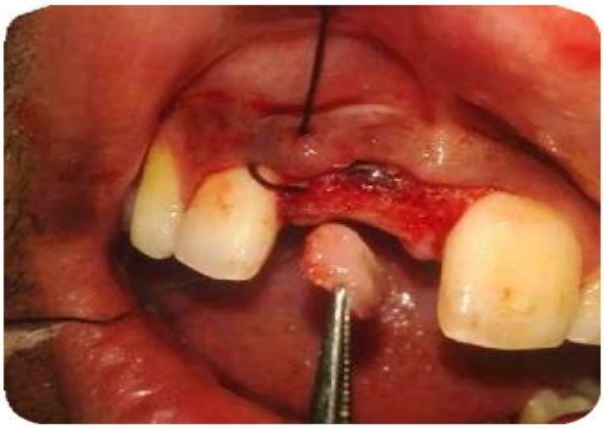
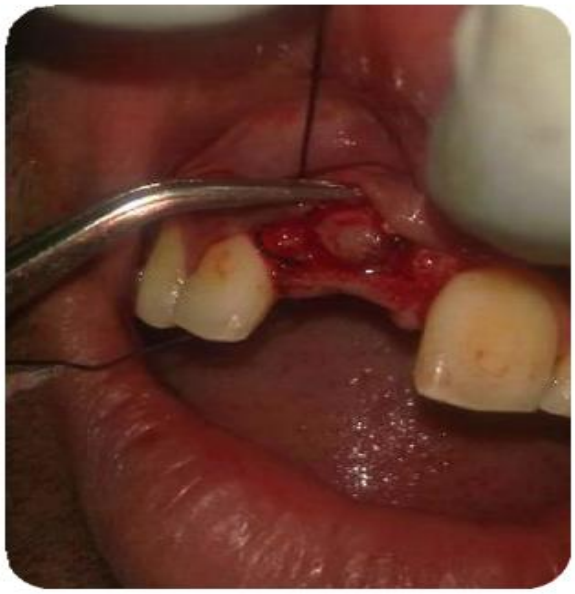
Sticky Bone (Autologous Fibrin Glue and Bone Graft)

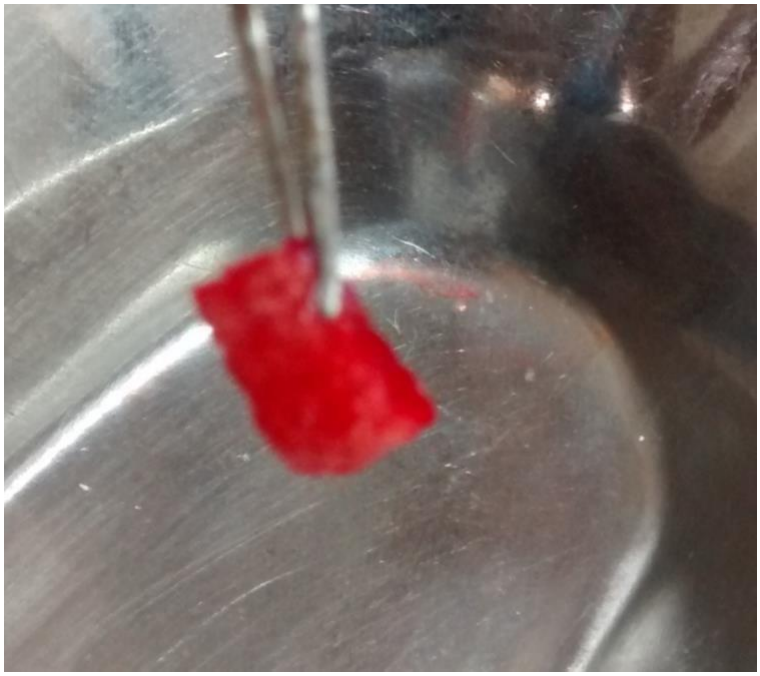
Mixing i-PRF with granules of bone graft is referred to as sticky bone. After centrifugation according to i-PRF protocols, the upper autologous fibrin glue layer was got and mixed with particulate bone powder. It is then made to sit for 5-10 minutes for polymerization. The end- product of which is yellow colored sticky bone.

Sticky bone is a stable fibrin bone graft. It's easy to handle, has less graft mobility and can be made into the desired shape as it has its own body. This combination helps in:

- Stabilization of the bone graft,
- Acceleration of tissue healing,
- Minimizing bone loss,
- Enhancing the rate of new bone formation and
- Increasing the quality (density) of newly formed bone.



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