A comprehensive clinical review of Platelet Rich Fibrin (PRF) and its role in promoting tissue healing and regeneration in dentistry. Part III: Clinical indications of PRF in implant dentistry, periodontology, oral surgery and regenerative endodontics

Johan Hartshorne¹ and Howard Gluckman²

Summary
The purpose of Part III of this review is to analyse the available literature and clinical-based evidence on PRF relating to its clinical indications in implant dentistry, periodontology, oral surgery and regenerative endodontics. An improved understanding of the clinical indications of PRF will facilitate the clinicians’ ability to enhance the therapeutic applications of PRF in these fields. PRF is increasingly being investigated and used worldwide by clinicians as an adjunctive autologous biomaterial to promote bone and soft tissue healing and regeneration. PRF has also grabbed the attention of clinicians worldwide because this biomaterial is derived from the patients’ own blood; is easy to make at chair-side, easy to use within the daily clinical routine; widely applicable in dentistry with virtually no risk of rejection; whilst being financially realistic for the patient and the practice. The 3D architecture of the fibrin matrix provides the PRF membrane with great density, elasticity, flexibility and strength that are excellently suited for handling, manipulation and suturing. The gold standard for in vivo tissue healing and regeneration requires the mutual interaction between a scaffold (fibrin matrix), platelets, growth factors, leukocytes, and stem cells. These key elements are all active components of PRF, and when combined and prepared properly, in whichever form, are involved in the key processes of tissue healing and regeneration. PRF is widely being used with promising results in various clinical applications with the primary aim of promoting wound healing, accelerating graft maturation, decreasing the healing period, protecting and promoting improved outcomes in soft tissue and bone healing, and tissue regeneration. PRF combined with GBR procedures offers several added and synergistic advantages including promoting wound healing in compromised wound healing situations, bone growth and maturation, graft stabilization, wound sealing and hemostasis, and improving the handling properties of graft materials. PRF added to, or combined with bone substitutes, offer an effective and easy way for managing and/or augmenting peri-implant osseous defects, sinus floor elevations, intrabony defects, fresh extraction sockets and alveolar ridges with deficient or atrophied alveolar bone. PRF membranes used as a protective or wound bandage on connective tissue harvesting sites (palate) or donor sites (vestibule), significantly accelerates wound healing and reduces post-operative pain and discomfort. The use of PRF in revitalization, revascularization, and regenerative pulpal therapies are currently attracting a lot of attention and several case studies in the field of regenerative endodontics are being reported.

One of the clinical limitations to note is the heterogeneity in the quality of platelets and blood components due to use of different PRF preparation protocols. Irrespective

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of the protocol used all studies have all reported successful outcomes with regards to soft and bone tissue healing and regeneration. It should also be noted that at this stage in time there is not a single RCT or CCT to compare the effectiveness of A-PRF or L-PRF protocols. The clinical effectiveness of different PRF preparation protocols in various clinical settings remains to be validated through independent robust RCT’s.

Introduction
The prospect of having new therapies, biomaterials and bioactive surgical additives available that will improve success and predictability of patient outcomes in soft and bone tissue healing and regeneration are key treatment objectives in dental implantology, periodontology and oral surgery.

Platelet Rich Fibrin (PRF), a patient blood-derived and autogenous living biomaterial, is increasingly being investigated and used worldwide by clinicians as an adjunctive autologous biomaterial to promote bone and soft tissue healing and regeneration. The gold standard for in vivo tissue healing and regeneration requires the mutual interaction between a scaffold (fibrin matrix), platelets, growth factors, leukocytes, and stem cells. These key elements are all active components of PRF, and when combined and prepared properly are involved in the key processes of tissue healing and regeneration, including cell proliferation and differentiation, extracellular matrix synthesis, chemotaxis and angiogenesis (neo-vascularization). An improved understanding of the development, biological and physiological properties and characteristics of PRF in tissue healing and regeneration over the last two decades, has led to more successful therapeutic applications, especially in the fields of dental implantology, periodontology and oral surgery.

The purpose of this comprehensive review is to analyse the available scientific literature on PRF regarding its: (Part I) definition and purpose in the clinical environment; (ii) development and classification of platelet concentrate biomaterials; (iii) biological characteristics and composition; (Part II) (iv) preparation technique; (v) optimizing quality; (vi) physical application and handling; and (vii) the benefits and limitations of PRF; and (Part III) (viii) its clinical indications in implant dentistry, periodontics, oral surgery and regenerative endodontics.

Methodology, Search strategy and inclusion criteria
An electronic MEDLINE (PubMed) and Google Scholar search was performed for all articles on Platelet Rich Fibrin (PRF) and Platelet concentrates up to May 2016. The search was complimented by an additional hand search of selected journals in oral implantology, oral surgery and periodontal, as well as grey literature. The reference lists and bibliographies of all included publications were also screened for relevant studies. The search was limited to the English language. Randomized controlled trials (RCT’s), controlled clinical trials (CCT’s), case reports, case series, prospective, retrospective and in-vitro/in vivo studies were included in the narrative review. Only RCT’s, CCT’s, and systematic reviews were used for evaluating evidence-based data (Tables 1, 2, 3). Animal studies were excluded from this review.

Where and how can I use PRF?
A general rule of guidance is to use PRF in surgical situations where protection and stimulation of healing and regeneration is critical and where the prognosis for tissue repair is poor or potentially compromised in the absence of a tissue regeneration scaffold and addition of growth factors.

Implant dentistry
Most of the PRF clinical research in implantology is currently focused in the fields of improving clinical outcomes with sinus floor elevations using PRF as sole grafting material, simultaneous with implant placement, or SFE using a combination of PRF and bone allograft (FDBA) prior to implant placement. Other focus areas of clinical implantology research are use of PRF in alveolar ridge preservation (socket augmentation), peri-implant tissue healing, and improving implant stability. (Table 1)

In-vitro studies have shown PRF-induced gene expression of the early and late markers of osteogenesis, stimulates bone and soft tissue healing. This finding suggests that PRF is indicated in numerous clinical applications, such as, socket augmentation, jump gap filling during immediate extraction and implant placement; and stimulation of bone and soft tissue healing during bone augmentations or during sinus elevation.

- Sinus floor elevation using PRF as sole or combination graft biomaterial

A systematic review showed that PRF used as a sole filling material in SFE with simultaneous implant placement is a simple technique with promising results. Various clinical case reports describe the lateral approach for sinus floor elevation using only PRF as the grafting material.
The PRF membrane is recommended as an inexpensive and easily handled substitution biomaterial during sinus elevation, to reduce the healing time before loading. It is a cheap and easily handled material with healing properties. Its fibrin matrix properties and ability of slowly releasing growth factors makes it an ideal replacement biomaterial to replace xenogenic and expensive collagen membranes in some situations. The review also suggests that PRF combined with a bone allograft or other bone substitutes, accelerates graft maturity.

Table 1. Evidence-based literature on the use of PRF in implant dentistry

<table>
<thead>
<tr>
<th>Application</th>
<th>Reference</th>
<th>Type of Study</th>
<th>Evidence / Conclusion†</th>
</tr>
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<tbody>
<tr>
<td>Sinus floor elevation</td>
<td>Ali S, Bakry SA, Abd-Elhakam, 2016</td>
<td>Systematic review</td>
<td>PRF as a sole filling material for sinus lift with simultaneous implant placement is a simple technique with promising results. Addition of PRF to DFDBA accelerates graft maturation and decreases the healing period before implant placement. PRF membranes represent an easy and successful method to cover sinus membrane or osteotomy window.</td>
</tr>
<tr>
<td>Socket Augmentation</td>
<td>Hauser F, Gaydarov N, Badaud I et al., 2013</td>
<td>RCT</td>
<td>Use of PRF membranes to fill the socket after tooth extraction led to improved alveolar bone healing and better preservation of the alveolar crest width. These results support the use of a minimally traumatic procedure for tooth extraction and socket filling with PRF to achieve preservation of hard tissue.</td>
</tr>
<tr>
<td>Peri-implant stability and healing</td>
<td>Oncio E, Alaaddinooglu E, 2015</td>
<td>CCT</td>
<td>Results of this study demonstrated that PRF application into the osteotomy site increases implant stability during the early healing period. Simple application of this material seems to provide faster osseointegration.</td>
</tr>
<tr>
<td>Peri-implantology sinus floor elevation</td>
<td>Boora P, Rathee M, Bhoria M., 2015</td>
<td>RCT</td>
<td>PRF can be considered as a healing biomaterial with potential beneficial effect on peri-implant tissue and can be used as a therapeutic adjuvant in the clinical scenario of one stage, single tooth implant placement procedure in maxillary anterior region.</td>
</tr>
<tr>
<td>Pre-implantology sinus floor elevation</td>
<td>Choukroun J, Diss A, Simonpieri A, et al (Part 5) 2006</td>
<td>CCT</td>
<td>Sinus floor augmentation with FDBA and PRF leads to a reduction of healing time prior to implant placement. From a histologic point of view, this healing time could be reduced to 4 months.</td>
</tr>
<tr>
<td>Pre-implantology sinus elevation</td>
<td>Tatullo M, Marraggi M, Cassetti M, et al, 2012</td>
<td>CCT</td>
<td>PRF together with deproteinized bovine bone (Bio-Oss) and piezosurgery favors optimal bone regeneration compared to bone graft material alone. At 106 days, it is already possible to achieve good primary stability of endosseous implants, though lacking of functional loading. PRF favors clot stability and the membranous shape allows creating a natural &quot;barrier effect&quot; on the bone breaches that were opened in the surgical areas.</td>
</tr>
</tbody>
</table>

† Within the limitations of the studies, and more and large samples rigorous clinical trials are required to validate the evidence.
A therapeutic alternative for implant site preparation. Alternatively, PRF can also be mixed with a bone substitute to fill the socket, and used as a protective cover over the graft. This is particularly important when gingival wound closure is impossible or difficult with the sutures. The purpose of the PRF membrane is to stimulate gingival healing, but also to protect the bone graft from the oral environment and to maintain it within the extraction socket, like a biological barrier. It is suggested that this technique negates the need for using more complex flaps and GBR protocols to close and augment extraction sockets.

Maturation and decreases the healing period before implant placement. The latter finding has also been confirmed by other clinical trials and case studies. Various case studies have demonstrated that PRF membranes can be used successfully as a protective barrier to cover the sinus membrane during grafting procedures. PRF membranes also represent an easy and successful method to cover sinus membrane or osteotomy window to protect the Schneiderian membrane, facilitate wound closure and to enhance healing. Cases have also been reported showing that A-PRF membrane can be used as a healing barrier when perforations or tears of the Schneiderian membrane occur.

- **Alveolar ridge preservation (socket augmentation) for early or late implant placement**

  Use of PRF membranes to fill the socket after tooth extraction has shown to improve alveolar bone healing and preservation of the alveolar crest width. PRF plugs or membranes can also be used to fill extraction sockets, even when associated with compromised extraction sockets, severe cystic destructions or after cyst enucleations, to allow early bone and gingival regeneration required for implant placement. Clinical and histological findings suggest that filling a fresh extraction socket with PRF provides a viable therapeutic alternative for implant site preparation. Alternatively, PRF can also be mixed with a bone substitute to fill the socket, and used as a protective cover over the grafted socket. This is particularly important when gingival wound closure is impossible or difficult with the sutures. The purpose of the PRF membrane is to stimulate gingival healing, but also to protect the bone graft from the oral environment and to maintain it within the extraction socket, like a biological barrier. It is suggested that this technique negates the need for using more complex flaps and GBR protocols to close and augment extraction sockets.
leukocyte-platelet rich fibrin (L-PRF or A-PRF) membranes for the stimulation of bone and gingival healing around the implant is particularly significant. 8,27 (Figure 6a - 6c) The elastic consistency of the PRF membrane allows the clinician to punch a hole in the membrane to facilitate draping the membrane over the healing abutment. (Figure 7a & 7b)

- **Augmentation of dehiscence and fenestration defects**

  Case reports indicate that PRF membrane cut in pieces or i-PRF combined with bone substitutes may offer an easy and simple method of handling and delivery a fibrin scaffold, growth factors and cells during the augmentation of dehiscence and fenestration defects, and at the same time reduce soft tissue and bone healing time. 20,28-29, 30

- **Immediate postextraction implant placement and jump-gap augmentation – Peri-implant healing**

  PRF can be considered as a healing biomaterial with potential beneficial effect on peri-implant tissue and can be used as a therapeutic adjuvant with immediate implant placement in the clinical scenario of one stage, single tooth implant placement procedure in maxillary anterior region. 8,119 With immediate implant placement the peri-implant jump gap can be augmented with PRF clot (A-PRF or L-PRF) or solution (i-PRF) mixed with a bone substitute. 26 (Figure 5a & 5b) In the latter case study it is suggested that the augmented jump gap is covered with cross-linked collagen membrane, overlayed by a double layer of PRF and the flap closed by sutures. Studies have demonstrated that the use of leukocyte-platelet rich fibrin (L-PRF or A-PRF) membranes for the stimulation of bone and gingival healing around the implant is particularly significant. 8,27 (Figure 6a - 6c) The elastic consistency of the PRF membrane allows the clinician to punch a hole in the membrane to facilitate draping the membrane over the healing abutment. (Figure 7a & 7b)
PRF has also been successfully used to treat fenestration defects around implants.\(^{31}\) PRF membrane cut in pieces (Figure 8), or platelet liquid (i-PRF) (Figure 9) can be mixed with bone graft material to cover the defect. The graft is covered with a resorbable collagen membrane to maintain form and shape and to confer graft stability and space maintenance on the bone particles. PRF membrane is then placed on top of the collagen membrane to prevent tissue dehiscence and aid in soft tissue healing. The application of PRF to GBR procedures offers several advantages including promoting wound healing, bone growth and maturation, graft stabilization, wound sealing and hemostasis and improving the handling properties of graft materials.

### Treatment of peri-implant osseous defects

One clinical study showed that treatment of peri-implant defects with PRF was clinically more effective than with conventional flap surgery alone, irrespective of the type of defect.\(^{32}\) In another study a successful treatment outcome was also reported after debridement and detoxification with a CR,CR:YCGG later, followed by filling the defect with a synthetic hydroxyapatite embedded in native blood and covered with a PRF membrane to prevent soft tissue infiltration into the grafted area. The authors concluded that the use of PRF added to the maintenance of the graft homeostasis due to release of growth factors, thus contributing to the successful outcome of treatment.\(^{33}\)

- **Augmentation of alveolar ridges (horizontal and vertical) and buccal bone defects (GBR)**

Several cases have been reported of successful augmentation of alveolar ridges where there is a buccal bone defect (GBR) using PRF combined with a bone substitute,\(^{6,29,34,35,36,37,38,39}\) and in cases of the severely resorbed posterior mandible.\(^{40}\) The latter authors suggest that three layers of L-PRF membranes used alone were adequate to use as competitive interposition barrier to protect and stimulate the bone compartment, and as healing membranes to stimulate the periosteum and gingival healing and remodeling. Periosteal incisions were done on the flaps to promote their tension-free closure.\(^{40}\) The concept of using PRF alone as a GBR barrier still raises many questions as well as limitations and needs to be investigated with robust RCTs to determine appropriate indications and relevant combinations.\(^{30}\) PRF liquid (i-PRF) can be injected, or PRF membrane placed above the GBR or GTR membrane to act as an interposition barrier to protect and stimulate the bone compartment, and as a healing membrane in order to

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**Figure 5a:** Residual root to be extracted for immediate implant placement.

**Figure 5b:** Jump gap between implant and socket defect grafted with xenograft mixed with PRF fragments and covered with a PRF membrane.

**Figure 6a:** Implant site ready to be draped with PRF membrane.

**Figure 6b:** PRF membrane draped around an implant to stimulate bone and gingival healing.

**Figure 6c:** Flap sutured.
improve the soft tissue healing and remodeling, and thus avoid soft tissue dehiscence.\textsuperscript{9,40}

**Guided bone regeneration**

Place harvested autogenous bone adjacent to the implant of defect that requires grafting. The next layer is made up of a mixture of bone grafting material with i-PRF or PRF membrane or clot cut in small pieces. The objective of this mixture is to help the rapid vascularization of the bone grafting material through the PRF fibrin matrix making the bridge between bone particles and allowing a quick new bone growth, while the xenograft material serves as space maintainer for the regenerative volume and supports the nucleation and accumulation of newly formed bone matrix. The bone/PRF mixture in the augmented site is covered with a cross-linked collagen membrane to maintain the bone compartment and to prevent ingrowth of soft tissue. The collagen membrane is overlaid with a double layer of PRF membranes. (Figure 10a - 10c) These membranes were used as competitive interposition barrier to protect and stimulate the bone compartment, and as healing membranes to stimulate the periosteum and gingival healing and remodeling. Periosteal releasing incisions are done on the flaps to promote their tension-free closure.\textsuperscript{40}

- **Increasing implant stability and osseointegration**

Case studies suggest that PRF application into the osteotomy site (Figure 11a -11c) increases implant stability during the early healing period, as evidenced by higher ISQ values. Simple application of this material also seems to provide faster osseointegration.\textsuperscript{9}

**Periodontal surgery**

Most of the clinical research in periodontology is currently...
Table 2. Clinical evidence on the use of PRF in periodontology

<table>
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<tr>
<th>Application</th>
<th>Reference</th>
<th>Type of Study</th>
<th>Evidence / Conclusion†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Furcation defects</td>
<td>Troiano G, Laino L, Dioguardi M, et al, 2016</td>
<td>Meta-analysis</td>
<td>The addition of autologous platelet concentrate (PRP and PRF) to open flap debridement (OFLD) may improve clinical parameters: horizontal and vertical clinical attachment level, probing depth and level of gingival margin in the treatment of mandibular class II furcation defects compared to OFLD alone.</td>
</tr>
<tr>
<td>Furcation defects</td>
<td>Sharma et al. 2011b</td>
<td>RCT</td>
<td>Significant improvement with PRF implies its role as a regenerative material in treatment of furcation defects.</td>
</tr>
<tr>
<td>Recession defects</td>
<td>Maraschini V, dos Santos E, Barboza P., 2015</td>
<td>Meta-analysis</td>
<td>The results suggest that the use of PRF membranes did not improve the root coverage, keratinized mucosa width, or clinical attachment level of Miller class I and II gingival recessions compared to the other treatment modalities.</td>
</tr>
<tr>
<td>Recession defects</td>
<td>Koceli H, Kamak G, Erdemir EO, et al , 2015</td>
<td>RCT</td>
<td>The addition of PRF did not further develop the outcomes of coronally advance flap combined with a connective tissue graft treatment except increasing the tissue thickness.</td>
</tr>
<tr>
<td>Intrabony defects</td>
<td>Shah M, Deshpande N, Bharwani A., 2014</td>
<td>Meta-analysis</td>
<td>The meta-analysis showed clinically significant improvements in periodontal parameters such as clinical attachment levels and intrabony defect reduction, and reduction in probing depth when IBDs were treated with PRF alone compared to OFD.</td>
</tr>
<tr>
<td>Intrabony defects</td>
<td>Gamal AY, Ghaffar KAA, Alghrezzy OA., 2016</td>
<td>RCT</td>
<td>PRF and PRGF platelet concentrate failed to augment the clinical effects achieved with the xenograft alone in treating intrabony defects. Periodontal defects could not retain extraphysiologic levels of GF suggested to be associated with platelet concentrate.</td>
</tr>
<tr>
<td>Intrabony defects</td>
<td>Shah M, Patel J, Dave D, Shah S., 2015</td>
<td>RCT</td>
<td>PRF has shown significant results after 6 months, which are comparable to DFDBA for periodontal regeneration in terms of clinical parameters. PRF has several advantages when used as a graft material for intrabony defects.</td>
</tr>
<tr>
<td>Intrabony defects</td>
<td>Sharma et al. 2011a</td>
<td>RCT</td>
<td>Greater pocket depth reduction and periodontal attachment level (PAL) gain, and bone fill at sites treated with PRF combined with conventional open-flap debridement compared to conventional open-flap debridement alone.</td>
</tr>
<tr>
<td>Intrabony defects</td>
<td>Pradeep AR, Rao NS, Agarwal P, et al, 2012</td>
<td>RCT</td>
<td>The use of autologous PRF or PRP was effective in the treatment of 3-wall IBDs with uneventful healing of sites. Treatment with autologous PRF or PRP stimulated a significant increase in the PD reduction, GML, and bone fill compared with OFD at 9 months.</td>
</tr>
<tr>
<td>Intrabony defects</td>
<td>Bansal C and Bharti V, 2013</td>
<td>CCT</td>
<td>PRF combined with demineralized freeze dried bone allograft (DFDBA) demonstrated better results in probing pocket depth reduction and clinical attachment level gain as compared to DFDBA alone in the treatment of periodontal intrabony defects.</td>
</tr>
<tr>
<td>Intrabony defects</td>
<td>Thorat MK, Pradeep AR, Pallavi B., 2011</td>
<td>RCT</td>
<td>Greater reduction in pocket depth, more clinical attachment level gain and greater intrabony defect fill at sites treated with PRF compared to open flap debridement alone.</td>
</tr>
<tr>
<td>Intrabony defects</td>
<td>Pradeep AR, Bajaj P, Rao NS,  et al, 2012</td>
<td>RCT</td>
<td>PRF when added to porous hydroxyapatite (HA) increases the regenerative effects observed with PRF in treatment of human three-wall intrabony defects.</td>
</tr>
<tr>
<td>Palatal bandage</td>
<td>Feminella B, Iaconi MC, DiTullio M, 2016</td>
<td>RCT</td>
<td>The PRF-enriched palatal bandage significantly accelerates palatal wound healing and reduces the patient’s morbidity.</td>
</tr>
</tbody>
</table>

† Within the limitations of the studies, and more and large samples rigorous clinical trials are required to validate the evidence.
induction of a strong and thick periosteum and gingiva. The boosted periosteum functions as a true barrier between the soft tissue and bone compartments, and constitutes probably the best protection and regenerative barrier for the intrabony defects. The NTR protocol is very simple and gives excellent results in most clinical situations, with no contraindication or risk of negative effects. However, in order to get the best results, the choice and the quantity of the adequate bone substitute has yet to be determined in various clinical configurations.

Theoretically, PRF can be used as a sole grafting material or in combination with bone substitutes can be used as a filling material in intrabony defects, following GTR principles. PRF membrane is a solid material with the advantage that it is easy to handle and to position in bony defects. PRF membranes can also be used as a protection membrane after the filling of the intrabony defect. In comparison to GTR membranes, PRF will undergo a quicker remodeling in situ than a resorbable collagen membrane, but will promote a strong induction on the periosteum and gingival tissue due to the slow release of growth factors and other matrix proteins. GTR membranes are cell-proof barriers, whereas a PRF membrane is a highly stimulating matrix, attracting cell migration and preferential differentiation allowing new blood vessel formation within the matrix, and also reinforcing the natural periosteal barrier. The hard and soft tissues migrate and interact within the PRF matrix. The PRF matrix becomes the interface between the tissues and therefore avoids the migration of the soft tissues deeper within the grafted defect or augmented site. This biological characteristic is referred to as a competitive barrier. These bioactive interactions are very important during tissue regeneration, since the periosteum covers the internal part of the gingival flap and is a key actor of bone healing and gingival maturation. While GTR membranes block the

Focus on the fields of improving clinical outcomes with treatment of intra-bony periodontal pockets, furcation defects, gingival recession defects, and healing of connective tissue graft sites in the palate. (Table 2)

**Intrabony and furcation periodontal defects**

The regenerative and wound healing effects have been very promising with PRF treating intrabony defects, and furcation lesions. Another study has also reported on using PRF successfully as a regenerative material in cases of aggressive periodontitis.

Surgical periodontal therapy accompanying the placement of PRF in angular defects of aggressive periodontitis patients showed decreased probing pocket depth, increased attachment level and radiographic bone fill when baseline and 9-month follow-up data was compared. Surgical reconstructive therapy with placement of PRF in angular defects can be suggested as an effective approach to enhance periodontal regeneration.

Platelet gel acts as a stabilized blood clot and therefore recommended as a perfect filling material for natural tissue regeneration and healing. Clinically, the general concept of “Natural Tissue Regeneration” (NTR) and Natural Bone Regeneration (NBR) requires to fill the periodontal intrabony defect with L-PRF, most times in association with a bone substitute used as a solid space maintainer, and then to cover the filled intrabony defect with L-PRF membranes, used for the protection of the grafted area and as a healing booster for the soft tissues above the defects. The objective of this cover is not only to protect the blood clot and/or the filling material, like in the GTR concept, but also to promote the induction of a strong and thick periosteum and gingiva. The boosted periosteum functions as a true barrier between the soft tissue and bone compartments, and constitutes probably the best protection and regenerative barrier for the intrabony defects. The NTR protocol is very simple and gives excellent results in most clinical situations, with no contraindication or risk of negative effects. However, in order to get the best results, the choice and the quantity of the adequate bone substitute has yet to be determined in various clinical configurations.

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Palatal bandage

PRF membranes can also be used as a palatal wound bandage or protection membranes after harvesting connective tissue grafts in the palate. Case studies show that PRF membrane used as a palatal bandage is an efficacious approach to protect the raw wound area of a palatal donor site and significantly accelerates palatal wound healing and reduces patient discomfort and healing time.

Inter-dental papilla augmentation

A case study reported that PRF combined with bone graft for regeneration of interdental bone may contribute towards improved clinical success with augmentation of lost dental papilla. The reconstructed papilla in the new position was stable when reviewed at 3 and 6 months postoperatively.

Recession defects and guided tissue regeneration (GTR)

The clinical evidence is less promising with the treatment of recession defects. Within the limitations of available clinical trials, the clinical evidence indicate that PRF does not improve root coverage or increases the width of keratinized mucosa in Miller’s Class I and II gingival recessions, compared to other treatment modalities. However, cases have been reported where PRF was successfully used for treating localized, and multiple gingival recessions. Another case study reported that the use of PRF membrane along with the VISTA technique allows clinicians to successfully treat multiple recession defects with optimal esthetic results and excellent soft tissue biotype.

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Oral Surgery

Most of the evidence-based research in the field of oral surgery is focused on the use of PRF membranes for healing potential and bone/gingival interactions. PRF membranes stimulate the periosteum’s regenerative properties. However, even if PRF membranes do not block the migration of the cells, no invagination of the soft tissues within the bone area were observed when PRF membranes covered a filled intrabony defect.
medication presenting a risk of osteonecrosis of the jaws, or patients receiving anticoagulants. 93

Delayed or compromised healing of extraction sockets is mostly related to an unstable blood clot within the socket. In such case a fibrin clot is simply placed in the socket, covered with a collagen plug or membrane and sutured. Placing PRF in a socket could amplify the natural coagulation process and enhance socket healing. 7, 24, 93, 83, 84, 88, 89, 90, 91, 92

• Prevention of periodontal complications in 3rd molar surgery
Complex third molar extractions frequently result in critical size bone defects and compromised healing impacting negatively on the outcome of periodontal tissues distal of the second molar. When bone defects after extraction are critical-sized (and often associated with cystic lesions), Using PRF as a filling material or mixing PRF with a bone substitute in order to use a significant volume of solid biomaterial for filling is considered as reliable option. These treatments are however no more simple dental extractions, and are often at the border of guided bone regeneration (GBR) or bone grafting. The use of a PRF as a filling material significantly promotes soft tissue healing and also faster regeneration of bone in these sites and neighboring periodontal tissues. 84, 94, 95

• Closing oro-antral fistulas
Oro-antral communications can complicate dental surgery, particularly during extraction of a posterior maxillary root. PRF clots can be used successfully for traumatic or minimal intervention closure of oro-antral communications, thus
Other oral surgical applications where PRF is used

- **Alveolar cleft grafting**
  The use of PRF has also been reported in other therapies including: alveolar cleft grafting. 106

- **Bisphosphonate related oral necrosis of the jaw**
  Recent case reports suggested that PRF might stimulate gingival healing and act as a barrier membrane between alveolar bone and the oral cavity, therefore offering a simple, though effective treatment for the closure of bone exposure in BRONJ. 107,108,109,120

- **Compromised wound healing situations (Diabetics)**
  PRF has also been used as an adjuvant in the management of problematic chronic wounds. 109 The authors have shown that growth factors in PRF are protected from proteolytic degradation. This may be advantageous in the treatment of chronic wounds characterized by high protease activity.

### Table 3. Evidence-based literature on the use of PRF in oral surgery

<table>
<thead>
<tr>
<th>Application</th>
<th>Reference</th>
<th>Type of Study</th>
<th>Evidence / Conclusion†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reducing complications in 3rd molar extractions</td>
<td>Reference Eshghpour et al, 201485</td>
<td>RCT</td>
<td>PRF application may decrease the risk of alveolar osteitis development after mandibular third molar surgery.</td>
</tr>
<tr>
<td>Enhance bone healing after 3rd molar extractions</td>
<td>Gürbüz B., Pikköken L, Tunali M, et al, 201083</td>
<td>CCT</td>
<td>PRF might not lead to enhanced bone healing in soft tissue impacted mandibular third molar extraction sockets 4 weeks after surgery.</td>
</tr>
<tr>
<td>Bone regeneration after 3rd molar extractions</td>
<td>Rao SG, Bhat P, K. S. Nagesh KS, et al, 201384</td>
<td>CCT</td>
<td>PRF accelerate regeneration of bone after third molar extraction surgery in cases treated with PRF as compared to the control group post operatively.</td>
</tr>
<tr>
<td>Bone healing and postoperative complications after 3rd molar surgery</td>
<td>Singh A, Kohli M, Gupta N, 201282</td>
<td>CCT</td>
<td>PRF is a valid method in promoting and accelerating soft and hard tissue wound healing and regeneration, and decreasing pain in mandibular 3rd molar extractions.</td>
</tr>
<tr>
<td>Postoperative complications following 3rd molar extractions</td>
<td>Uyanık LO, Bilgınaylar K, Ethikan I., 201586</td>
<td>CCT</td>
<td>PRF and combination use of PRF and piezosurgery have positive effects in reducing postoperative complications (pain and trismus) after impacted third molar surgery.</td>
</tr>
<tr>
<td>Rootend surgery / Healing of apico-marginal defects</td>
<td>Dhiman M, Kumar S, Duhan J, et al 2015102</td>
<td>RCT</td>
<td>A high success rate may be attained in apico-marginal defects with endodontic microsurgery, and addition of PRF may not necessarily improve the outcome.</td>
</tr>
</tbody>
</table>

† Within the limitations of the studies, more and large sample rigorous clinical trials are required to validate the evidence
Regenerative endodontic therapy

Regenerative endodontic procedures are widely being added to the current armamentarium of pulp therapy procedures. Recent case reports have shown that the combined use of platelet-rich fibrin (PRF), and mineral trioxide aggregate (MTA) as root filling material is beneficial for the endodontic management of an open apex. It is hypothesized that the combination of MTA and PRF may have a synergistic effect on the stimulation of odontoblastic differentiation of stem cells.

- **Management of open apex**

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- **Revascularization and revitalization**

  Revascularization is the most studied and successful approach of regenerative endodontics. Revitalization of necrotic infected immature teeth is possible under conditions of total canal disinfection combined with the additive effect of PRF. PRF is proposed as an ideal biomaterial for pulp-dentin complex regeneration because it is a potentially valid scaffold material containing leukocyte and growth factors to facilitate tissue healing and regeneration in immature necrotic teeth in children.

  Repair and regenerative potential of PRF, and enhanced cellular metabolism with laser bio stimulation, in combination with the sealing ability of MTA enhances the clinical success outcomes in pulpotomy and apexification procedures. Revitalization, revascularization, and regenerative pulp therapies still need to be validated with robust clinical trials.

**Conclusion**

PRF is increasingly being investigated and used by clinician’s worldwide as an adjunctive autologous biomaterial to promote bone and soft tissue healing and regeneration. PRF has also grabbed the attention of clinicians because this biomaterial is derived from the patients’ own blood; is easy to make at chair-side, easy to use within the daily clinical routine, widely applicable in dentistry with virtually no risk of rejection; whilst being financially realistic for the patient and the practice. The 3D architecture of the fibrin matrix provides the PRF membrane with great density, elasticity, flexibility and strength that are excellently suited for handling, manipulation and suturing. The gold standard for in vivo tissue healing and regeneration requires the mutual interaction between a scaffold (fibrin matrix), platelets, growth factors, leukocytes, and stem cells. These key elements are all active components of PRF in whichever form, and when combined and prepared properly are involved in the key processes of tissue healing and regeneration, whilst at the same time reducing adverse events. Clinicians are using PRF is extensively and successfully in various clinical applications in dental implantology, periodontology, maxilofacial and oral surgery, and lately in regenerative endodontics, to promote wound healing and tissue regeneration. The use of PRF in revitalization, revascularization, and regenerative pulp therapies are currently attracting a lot of attention and several case studies in the field of regenerative endodontics are being reported. These applications however still need to be validated with robust clinical trials.

One of the clinical limitations to note is the heterogeneity in the quality of platelets and blood components due to use of different PRF preparation protocols in the various studies reviewed. Irrespective of the protocol used all studies have all reported successful outcomes with regards to soft and bone tissue healing and regeneration. It should also be noted that at this stage in time there is not a single RCT or CCT to compare the effectiveness of A-PRF or L-PRF protocols. Furthermore, in vitro studies that claim superiority or inferiority of a specific PRF preparation have yet to be validated by independent clinical trials. The future of PRF and its applications in clinical dentistry, especially in the field of soft tissue and bone regeneration has enormous implications, but developing and strengthening its role in dentistry is dependent on its coherence and scientific clarity. The clinical effectevness of different PRF preparation protocols in various clinical settings remains to be validated with a greater number of independent and robust RCTs, preferably with a split mouth design, and larger sample sizes. Independent, coherent and scientific validation of PRF is needed to enhance the potential of this technology, thereby extending its therapeutic applications with improved successful and predictable outcomes for the benefit of the patient. PRF technology is in its infancy and will in future have a big impact in dentistry.

The benefits derived from the using PRF in various clinical applications for promoting wound healing and tissue regeneration, its antibacterial and anti-haemorrhagic effects, the low risks with its use, and the availability of easy and low cost preparation methods, should encourage more clinicians to adopt this technology in their practice for the benefit their patients.

**References**


25. Del Corso M, Vervelle A, Simonpieri A, Jimbo R,


70. Aroca S, Keglevich T, Barbieri B, Gera I, Etienne D.


of an oro-antral communication with platelet-rich fibrin. The British Association of Oral and Maxillofacial Surgeons. Accepted 30 September 2015 . http://dx.doi.org/10.1016/j.bjoms.2015.09.037


