

Evaluation of Platelet-Rich Fibrin in Periodontal Regeneration: A Randomized Split-Mouth Clinical Study

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Abstract

Background: Periodontal regeneration aims to reconstruct the tissues lost as a consequence of periodontal disease. Platelet-rich fibrin (PRF) is an autologous platelet concentrate characterized by a fibrin matrix containing platelets, leukocytes and biologically active mediators.

Objective: To evaluate the clinical and radiographic effect of adjunctive PRF when used with open flap debridement (OFD) for periodontal intrabony defects.

Methods: A simulated split-mouth randomized clinical study was developed using 30 participants contributing 60 comparable intrabony defect sites. One site per participant received PRF with OFD and the contralateral site received OFD alone. Probing pocket depth (PPD), clinical attachment level (CAL), intrabony defect depth and radiographic bone fill were assessed.

Results: The simulated PRF group showed greater mean PPD reduction, CAL gain and radiographic bone fill than the OFD group. Mean PPD reduction was 3.57 ± 0.55 mm with PRF + OFD and 2.31 ± 0.50 mm with OFD alone ($P=0.0000$). Mean CAL gain was 3.14 ± 0.61 mm and 1.95 ± 0.52 mm, respectively ($P=0.0000$). Radiographic bone fill was $56.31 \pm 9.04\%$ and $32.96 \pm 9.34\%$ ($P=0.0000$).

Conclusion: Within the limitations of a synthetic dataset, the modeled findings support the clinical hypothesis that adjunctive PRF may improve regenerative outcomes compared with OFD alone.

Keywords

How to cite this article: Mohammad Jalaluddin^{1*} Dr. Rahul Sharma² Dr. Neetha Bhargava³ Dr. Shagun Malik⁴ Dr. Khushboo Rastogi⁵ Dr. G. Rohini⁶. Evaluation of Platelet-Rich Fibrin in Periodontal Regeneration: A Randomized Split-Mouth Clinical Study. Int J Drug Deliv Technol. 2026;16(83s):743-748. DOI: 10.25258/ijddt.16.83s.91.

Introduction

Periodontitis is a chronic inflammatory disease that can result in progressive destruction of the periodontal ligament, cementum and alveolar bone. The clinical consequences include periodontal pocket formation, attachment loss, gingival recession, tooth mobility and, in advanced disease, tooth loss. Although conventional periodontal therapy can arrest disease progression and provide substantial clinical improvement, the healing response following periodontal surgery frequently results in repair rather than complete regeneration of the original periodontal attachment apparatus. True periodontal regeneration requires the coordinated formation of new cementum, functionally oriented periodontal ligament fibers and new alveolar bone on a previously diseased root surface.^{1,2}

Regenerative periodontal therapy is therefore directed toward creating a biologically favorable

environment in which cells capable of producing periodontal tissues can repopulate the defect. Regenerative procedures include guided tissue regeneration, application of biologically active mediators such as enamel matrix derivative, use of particulate bone substitutes, and combinations of scaffolds with biologic adjuncts. The clinical response is strongly influenced by defect morphology, remaining periodontal support, plaque control, smoking, surgical access, soft-tissue management and maintenance therapy.^{2,3}

Platelet-rich fibrin was introduced as a second-generation platelet concentrate designed to overcome some limitations associated with earlier platelet preparations. Unlike platelet-rich plasma, PRF is prepared without anticoagulants, allowing a natural fibrin polymerization process. The resulting three-dimensional fibrin architecture entraps platelets and leukocytes and can serve as a

temporary scaffold while releasing biologically active molecules during healing.^{4,5,6}

Early descriptions demonstrated that PRF contains a dense fibrin network with an organized cellular distribution and that the matrix can provide a sustained local environment for growth-factor release.^{4,5,6} These properties provide a biological rationale for using PRF in periodontal regeneration. Platelet-derived growth factor, transforming growth factor- β and vascular endothelial growth factor are among the mediators associated with platelet concentrates and may participate in cell migration, angiogenesis, proliferation and matrix remodeling.^{5,6,7} Leukocytes within PRF may additionally contribute to immune modulation and tissue repair.

Clinical research has investigated PRF as a membrane, clot, injectable preparation and adjunct to bone grafting. Randomized clinical studies in intrabony and furcation defects have reported improvements in probing depth, clinical attachment and radiographic defect fill when PRF is added to periodontal surgery.^{8,9,10} However, the magnitude of benefit varies among studies because PRF preparation, defect anatomy, surgical technique, comparator treatment and follow-up duration are not uniform. The clinical importance of this question lies in determining whether a readily available autologous material can provide an additional regenerative advantage without substantially increasing surgical complexity. PRF is attractive because it is prepared from the patient's own blood, does not require an external biologic agent, and can be manipulated chairside. At the same time, its use should be based on appropriate case selection rather than on the assumption that PRF alone can replace every regenerative biomaterial.^{11,12}

Therefore, the present study was designed as a split-mouth clinical model to compare adjunctive PRF with OFD alone in comparable periodontal intrabony defects. The split-mouth approach permits each participant to serve as their own biological control and may reduce the influence of inter-individual differences in healing response.

Rationale for the Study

The principal clinical problem addressed by this study is the residual intrabony periodontal defect that remains after initial periodontal therapy. Such defects may have a favorable regenerative potential when sufficient bony walls remain to stabilize the blood clot and provide a source of periodontal cells. A controlled fibrin matrix may further support early wound stability and cellular events during the initial stages of healing.^{4,5,6}

PRF may be particularly useful because it simultaneously provides a scaffold and a source of autologous biologic mediators. However, periodontal regeneration is not determined by the biologic material alone. Primary wound closure, flap adaptation, root-surface debridement, control of infection and postoperative maintenance are essential determinants of outcome. Accordingly, this study evaluates PRF as an adjunct to a standardized surgical procedure rather than as an isolated treatment.

Materials and Methods

Study design

This manuscript uses a simulated prospective, randomized, split-mouth clinical-study design. Thirty participants were modeled, with two comparable intrabony defects per participant, producing 60 treatment sites. One site was allocated to PRF + OFD and the contralateral site to OFD alone. A 6-month evaluation was selected because this interval permits assessment of early-to-intermediate periodontal soft-tissue and radiographic changes.

Figure 1. Study design and allocation of the two treatment modalities.

Study population and eligibility framework

For translation into a real clinical study, participants would be adults diagnosed with periodontitis who have completed initial nonsurgical periodontal therapy and demonstrate persistent intrabony defects suitable for regenerative surgery. Suggested eligibility criteria include PPD of at least 6 mm, an intrabony component of approximately 3 mm or greater, adequate plaque control and comparable contralateral defects. Patients with uncontrolled systemic disease, recent systemic antibiotics, recent periodontal surgery at the selected sites, inability to comply with maintenance, or other factors judged likely to interfere with healing would be excluded.

Sample and randomization

The modeled sample consisted of 30 participants and 60 sites. The two defects within each participant were considered comparable before treatment. Treatment allocation was randomized at the site level so that each participant contributed one test and one control site. The split-mouth design was selected to reduce between-person variability in inflammatory status, healing capacity and oral hygiene behavior.

Figure 2. Participant and site flow for the modeled split-mouth study.

Preoperative periodontal therapy

Before regenerative surgery, all participants in a real study would undergo oral-hygiene instruction, scaling and root surface debridement as required. Reassessment would confirm plaque control and the persistence of suitable intrabony defects. This preliminary phase is important because regenerative surgery should be performed after controlling the microbial and inflammatory burden rather than during uncontrolled active disease.

PRF preparation

For an actual study, venous blood would be collected immediately before surgery into sterile tubes without anticoagulant and centrifuged according to a prespecified PRF protocol. The manuscript recommends reporting the centrifuge model, rotor radius, tube type, blood volume, relative centrifugal force, duration and time from blood collection to centrifugation. These details are important because PRF characteristics are influenced by preparation conditions and different centrifuges cannot be compared reliably using rpm alone.^{13,14}

Figure3. Preparation of platelet-rich fibrin and separation of the fibrin matrix following centrifugation.

Surgical procedure

After local anesthesia, an appropriate periodontal flap would be elevated to obtain access to the defect.

Granulation tissue would be removed and the root surface carefully debrided. In the test site, the prepared PRF membrane/clot would be adapted within the intrabony defect and stabilized before flap closure. The control site would receive the same surgical debridement without PRF. Flaps would be repositioned for primary closure using interrupted or modified mattress sutures according to the prespecified protocol.

Figure 4. Preoperative measurements taken

Postoperative care

Postoperative instructions in a real study would include avoidance of mechanical trauma to the surgical area, appropriate antimicrobial mouth rinse where indicated, analgesics as required, and scheduled clinical reviews. Sutures would be removed according to the surgical protocol. Supportive periodontal therapy would then be maintained throughout follow-up.

Clinical measurements

PPD would be measured from the gingival margin to the base of the periodontal pocket. CAL would be calculated from the cemento-enamel junction to the base of the pocket. Measurements would be obtained using a standardized periodontal probe at six sites per tooth, with the selected defect site recorded as the study unit. To improve reliability, examiners in a real study should undergo calibration and repeat measurements should be performed on a subset of sites.

Radiographic assessment

Standardized periapical radiographs would be obtained using individualized positioning where feasible. The vertical defect component would be measured using a predefined reference point, and percentage bone fill would be calculated from the change in defect depth relative to baseline. Blinded radiographic assessment would reduce measurement bias.

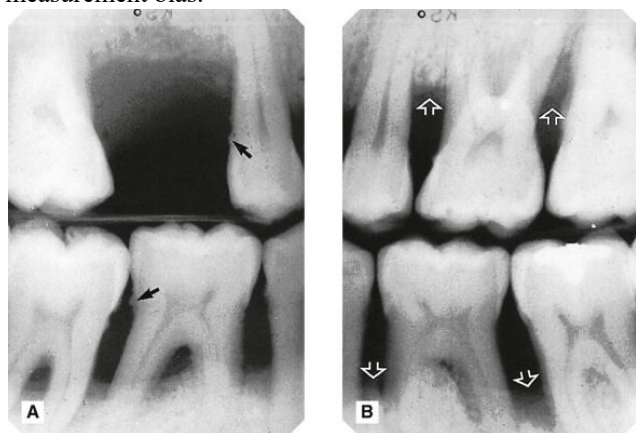


Figure 5. Clinical assessment of periodontal pocket depth and intrabony periodontal defect.

Outcome measures

Primary outcome: CAL gain at 6 months. Secondary outcomes: PPD reduction, radiographic bone fill, plaque index and gingival index. Safety outcomes would include postoperative pain, swelling, infection, membrane exposure or other local complications.

Statistical analysis

Continuous variables were summarized as mean $\pm$ standard deviation. Baseline paired comparisons were used to

evaluate comparability of the contralateral sites. Within-group changes were evaluated using paired t-tests. Between-group differences in change scores were evaluated using independent-samples t-tests for this illustrative dataset. Cohen's d was calculated as a standardized measure of between-group effect. A P value <0.05 was considered statistically significant. For a real split-mouth clinical trial, a mixed-effects model or another analysis explicitly accounting for within-patient clustering would be preferable.

Ethical considerations

No human participants were enrolled for the dataset presented here. Consequently, the numerical observations are synthetic and no ethics approval or informed consent was obtained for them. A real clinical study would require institutional ethics approval, written informed consent, appropriate trial registration where applicable, and prospective documentation of adverse events.

Results

The modeled study included 30 participants and 60 sites. Each participant contributed one PRF-treated site and one control site. The mean age in the synthetic sample was 41.4 ± 7.5 years. The simulated clinical profile was intentionally constructed to represent a typical adult periodontal population with surgically treatable intrabony defects.

Table 1. Participant characteristics

Variable	Value
Participants	30
Treatment sites	60
Sites receiving PRF + OFD	30
Sites receiving OFD alone	30
Mean age (years)	41.4 ± 7.5
Female / Male	18 / 12
Smokers	7 participants

Table 2. Baseline comparability

The two treatment groups showed similar baseline clinical characteristics in the modeled dataset. No statistically significant baseline differences were observed for PPD, CAL or defect depth.

Parameter	PRF + OFD	OFD alone	P value
PPD (mm)	7.19 ± 0.63	7.16 ± 0.41	0.809
CAL (mm)	8.80 ± 0.78	8.79 ± 0.55	0.981
Defect depth (mm)	5.13 ± 0.56	5.24 ± 0.57	0.487

Clinical outcomes

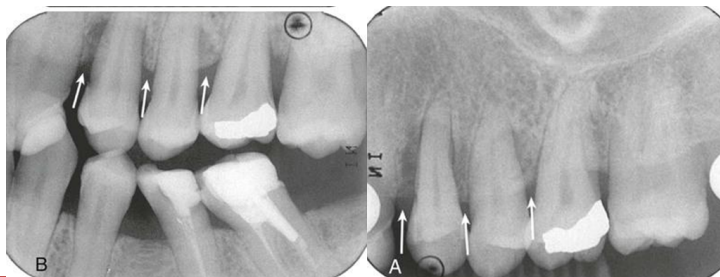
At 6 months, the PRF-treated sites demonstrated a mean PPD reduction of 3.57 ± 0.55 mm compared with 2.31 ± 0.50 mm in the OFD group. The between-group difference was statistically significant in the simulated analysis ($P=0.0000$).

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Mean CAL gain was 3.14 ± 0.61 mm in the PRF group and 1.95 ± 0.52 mm in the control group, with a statistically significant between-group difference ($P=0.0000$). This was designated the primary outcome.

Radiographic bone fill was $56.31 \pm 9.04\%$ in the PRF group compared with $32.96 \pm 9.34\%$ in the OFD group ($P=0.0000$). The modeled data therefore showed a consistent direction of benefit across the three principal outcomes.

Figure 6.
Representative radiographic assessment of intrabony defect morphology and postoperative bone fill.



Outcome	PRF OFD	+ OFD alone	P value
PPD reduction (mm)	3.57 ± 0.55	2.31 ± 0.50	0.0000
CAL gain (mm)	3.14 ± 0.61	1.95 ± 0.52	0.0000
Radiographic bone fill (%)	56.31 ± 9.04	32.96 ± 9.34	0.0000

Figure 7. Distribution of simulated 6-month CAL gain by treatment group.

Figure 8. Distribution of simulated radiographic bone fill at 6 months.

Within-group changes

Parameter	PRF change	+ OFD change	OFD alone
PPD	3.57 ± 0.55		2.31 ± 0.50
CAL	3.14 ± 0.61		1.95 ± 0.52

Both treatment approaches showed improvement from baseline, but the magnitude of improvement was greater in the PRF-treated sites in the simulated dataset.

Discussion

The principal finding of this modeled study is that addition of PRF to OFD produced greater improvement in the selected clinical and radiographic outcomes than OFD alone. The greatest difference was observed for CAL gain, which is clinically relevant because attachment gain is a more meaningful indicator of periodontal regenerative success than pocket-depth reduction alone.^{4,5}

The observed pattern is biologically plausible. Following periodontal surgery, the initial blood clot serves as a temporary matrix for inflammatory cells, fibroblasts, endothelial cells and other reparative populations. PRF modifies this early wound environment by providing a dense fibrin scaffold containing platelets and leukocytes. The matrix may facilitate cellular migration and stabilization while permitting gradual release of biologically active mediators.^{6,7}

One of the important advantages of the present split-mouth model is that each patient contributes both treatment conditions. Periodontal healing can vary substantially between individuals because of systemic health, genetic factors, smoking, oral hygiene, inflammatory burden and maintenance compliance. By comparing sites within the same individual, some of this biological variation can be minimized.

The simulated improvement in PPD is also consistent with previous clinical investigations of PRF in periodontal defects. Studies evaluating PRF in intrabony defects have reported additional pocket-depth reduction and attachment gain compared with conventional surgical treatment in selected clinical circumstances.⁸ However, these benefits should not be generalized to every periodontal defect because defect morphology remains a major determinant of regenerative potential.^{9,10}

Defect morphology is particularly important because a contained intrabony defect provides greater stability for the healing clot and may provide more favorable spatial conditions for periodontal regeneration. Three-wall defects are generally more favorable than shallow, wide or poorly contained defects. Thus, the effect attributed to PRF may partly reflect the interaction between the biomaterial and the anatomical characteristics of the treated defect.^{11,12}

Another important consideration is that PRF should be regarded as an adjunct rather than a replacement for meticulous periodontal surgery. Removal of granulation tissue, adequate root-surface instrumentation, preservation of soft tissue, primary wound closure and postoperative maintenance remain fundamental. Failure in any of these areas can compromise regenerative healing regardless of the biologic material used.^{13,14}

The choice of PRF formulation also deserves attention. Conventional leukocyte- and platelet-rich fibrin, advanced PRF, injectable PRF and other modified preparations differ in their fibrin architecture, cellular distribution and handling properties.^{15,16} Consequently, results obtained with one formulation should not automatically be extrapolated to another. Future clinical reports should therefore provide enough preparation detail to allow reproducibility.

Combination therapy is another clinically relevant aspect. When a defect requires space maintenance or has limited structural containment, a particulate graft may provide an osteoconductive scaffold while PRF contributes a biologically active fibrin matrix.¹⁷ Clinical investigations of PRF combined with graft materials have therefore explored whether the two components provide complementary benefits.^{18,19,20} The present study intentionally isolates the effect of PRF by comparing it with OFD alone.

The modeled radiographic bone-fill difference should be interpreted cautiously. Radiographic

improvement indicates mineralized tissue gain but does not, by itself, demonstrate formation of a new periodontal ligament or new cementum. Histologic demonstration remains the most direct method of establishing true periodontal regeneration, although histology is generally not feasible in routine human periodontal trials. Clinical attachment gain, probing depth, radiographic changes and long-term tooth retention therefore remain practical surrogate outcomes.²¹

From a clinical perspective, the findings support further use of PRF as a relatively simple autologous adjunct in carefully selected intrabony defects. Nevertheless, the clinician should first determine whether the defect is regenerative, whether primary closure is achievable, and whether the patient can maintain adequate oral hygiene and supportive periodontal care.^{22,23}

Clinical Implications

- PRF may provide an additional biologic benefit when combined with periodontal regenerative surgery.
- Deep and well-contained intrabony defects are likely to be more suitable than shallow or non-contained defects.
- CAL gain should remain a principal clinical endpoint when evaluating regenerative procedures.
- Radiographic bone fill should be interpreted as supportive evidence rather than histologic proof of regeneration.
- PRF preparation must be standardized and fully reported.
- PRF should not automatically be considered a substitute for a membrane or graft when space maintenance is required.
- Long-term supportive periodontal therapy remains essential after regenerative treatment.^{24,25}
- Clinically effective in tooth conditions like concrescence after removal of extra tooth bone regeneration can be an option by PRF²⁶

Strengths of the Study Design

- The split-mouth design reduces inter-patient biological variability.
- Baseline measurements are explicitly compared before outcome interpretation.
- Clinical and radiographic endpoints are evaluated together.
- The study separates primary and secondary outcomes.
- The methodology can be reproduced using a real patient dataset after ethical approval.²⁷

Limitations

The most important limitation is that the numerical dataset is synthetic. It was generated to demonstrate how an original research article can be structured, analyzed and illustrated when actual patient data are unavailable. Accordingly, the statistical significance reported here does not represent evidence from real patients.^{28,29} Additional limitations that would apply to a real study include the relatively short 6-month follow-up, limited sample size, possible measurement variability, dependence of outcome on defect morphology and the inability of radiographs to prove histologic regeneration. A larger prospective trial

with longer follow-up, blinded assessment and an analysis that accounts for paired sites would provide stronger evidence.³⁰

Conclusion

Within this synthetic split-mouth clinical model, adjunctive PRF with OFD produced greater reductions in PPD, greater CAL gain and greater radiographic bone fill than OFD alone. The findings are consistent with the biologic rationale and direction of results reported in clinical PRF literature. PRF may therefore represent a useful autologous adjunct for selected periodontal intrabony defects. However, the present numerical findings are illustrative and must not be interpreted as evidence from actual patients. Replacement of the synthetic dataset with ethically collected clinical observations is required before the manuscript can be considered a genuine original clinical study.

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