# Platelet-Rich Fibrin application in interdental papilla reconstruction: A systematic scoping review

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# Platelet-Rich Fibrin application in interdental papilla reconstruction: A systematic scoping review

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## ABSTRACT

**Background and Objectives.** Interdental papilla (IDP) loss presents a dual challenge in contemporary dentistry. It is related to the esthetics and functionality of both natural teeth and dental implants. Although Platelet-rich Fibrin (PRF) is commonly used for papilla reconstruction, the result is inconclusive. No standard procedure to apply PRF in IDP reconstruction. This review was to map, summarize, and rate the use of PRF in IDP reconstruction by looking at how it was prepared, how it was applied, the types of cases, how the treatment worked, and what suggestions should be made for the future.

**Materials and Methods.** A systematic electronic search was performed following the standard JBI systematic review. All case reports, case series, and clinical trials that meet the criteria were selected.

**Results.** Each selected article highlighted the advantages of PRF for IDP regeneration. In IDP surgery, connective tissue graft (CTG) has a higher papilla reduction than PRF.

However, the PRF membrane applied with the tunneling technique showed complete fill in Class I and Class II Norland and Tarnow classifications, equivalent to CTG, if the black triangle height is ≤3 mm, or the bone crest-papilla tip is ≤5mm. Liquid PRF injected non-surgically provides complete and partial fill, but the literature is still limited.

**Conclusions.** IDP reconstruction necessitates the use of appropriate materials, case selections, and application techniques. PRF is a viable substitute material for IDP reconstruction, both surgical and non-surgical. Further investigation is necessary to prepare the PRF and to optimize its positive impacts on IDP reconstruction.

**Keywords:** Platelet-rich fibrin, papilla loss, esthetics, gingiva, regeneration

## INTRODUCTION

The interdental papilla (IDP) loss has become a substantial concern and obstacle in the field of oral reconstruction surgery. IDP loss affects 38% of adults (119 cases) and 41.9% of adolescents (129 cases), according to the prevalence rates. In addition to esthetics concerns, the absence of IDP can lead to food impaction, inflammation, and phonetic complications in natural teeth, dentures, restorations, and implants. It is important to maintain an appropriate balance between hard tissue and IDP to protect the teeth against plaque-related problems, such as periodontal disease and dental caries [1].

The procedure to rebuild the inadequate IDP is commonly known as IDP reconstruction. It may be accomplished through surgical, non-surgical, or a combination of both approaches. This treatment aimed to increase the dimension or volume of IDP tissue [2]. The gold standard for IDP reconstruction is a surgically placed connective tissue graft (CTG); nevertheless, this approach induces patient discomfort due to the necessity of inflicting additional injury to harvest the graft. Platelet-rich fibrin (PRF) is frequently employed as a therapeutic intermediary for this complication.

PRF is a second-generation blood concentrate that comprises cells and growth factors. Clinical investigations and case reports showed that PRF has been used surgically and non-surgically to regenerate IDP, but the result is inconclusive. There is no standard procedure for the use of PRF for IDP reconstruction [3]. It may be caused by variations in insufficient papilla characteristics, PRF preparation and application techniques, observed parameters, and observation period. The current review examines the practical application of PRF in IDP reconstruction and discusses the potential of the most recent PRF to facilitate papilla regeneration. The results are expected to provide a guide for further comprehensive study and standards for the implementation of PRF in IDP reconstruction.

## MATERIALS AND METHODS

### The Review Protocol

The scoping review implemented the methodology outlined by the Joana Briggs Institute. This review focuses on mapping, summarizing, and evaluating all articles that use PRF to reconstruct the IDP loss surgically and non-surgically. The review questions are stated below.

a) What is the characteristic of IDP treated with PRF, in terms of Norland and Tarnow classification and clinical parameters?
b) What is the characteristic of the PRF used, in terms of the type of centrifuge machine, centrifugation speed, and time?
c) What is the result of IDP reconstruction treatment after PRF application, in terms of clinical parameters and patient discomfort score?

### Database and Search Strategy

A literature search is conducted using the Scopus, PubMed, Cochrane, and Google Scholar databases. To maintain transparency and objectivity throughout this process, study selection is conducted independently by two independent investigators. The Boolean Operator AND/OR was applied to the following keywords: interdental papilla, papilla loss, black triangle, and platelet-rich fibrin. Scopus-indexed case reports, case series, and clinical trials published January 2013 – December 2023 were included. Due to the linguistic proficiency of the team, studies composed in languages other than English were excluded from our evaluation. Selected literature that met the predetermined criteria were subsequently chosen for data extraction and analysis. The PRISMA 2020 flowchart is presented in Figure 1.

## RESULTS

The initial search strategies produced a total of 7709 articles. After eliminating duplicates, 6537 articles remained for evaluation of their titles and abstracts. A disparity with our criteria resulted in the exclusion of 6522 papers, while 15 articles were selected for the final full-text review. In the end, eight clinical investigations, six case reports, and one case series that had previously assessed the impact of PRF on the reconstruction of IDP loss were selected (Figure 1). The selected studies were classified under the following subheadings: PRF for surgical and non-surgical interdental papilla reconstruction in terms of case descriptions, PRF preparation methods, and PRF application techniques as well as treatment outcomes. The schematic mapping of the current scoping review is presented in Figure 2.

## DISCUSSION

### PRF Application as a Standalone Material in Surgical IDP Reconstruction

Surgical interventions employed to repair the papilla deficit consist of periodic interproximal curettages and gingival grafts. Nevertheless, the positive impacts of this treatment remain constrained in their efficacy [4]. At present, no specific technique for IDP restoration has been proposed [5].

Eight studies utilized PRF membranes for the treatment of Class I and II Norland and Tarnow classification (5 case reports, 1 case series, and 2 clinical trials) [6 - 10]. In the surgical procedure of IDP reconstruction, PRF membrane is frequently employed due to its stable and robust physical properties as well as simple application in the surgical site [6-12]. It is produced by fixed-angle centrifugation of venous blood at 2700 rpm for 12 minutes [7,12], 3000 rpm for 10 minutes [6,8,10,11] or 1500 rpm for 14 minutes [2]. The fibrin layer, located in the central layer, is hypothesized to comprise a profusion of platelets and leukocytes [8,13]. Therefore, this layer is separated with a tweezer and is compressed using a PRF box [6,9,10] or sterile gauze [7,8,11,12]. Although the theory suggests that centrifugation processes affect the composition and physical properties of membranes, there is currently a lack of literature comparing the outcomes of interdental papilla regeneration treatment using PRF membranes derived through different centrifugation methods.

To rebuild the insufficient papillae, the PRF membrane is inserted surgically below the flap. It requires skill and mandates precision of techniques. Various surgery techniques are frequently implemented including the Han and Takei technique [14-16], the micro technique [11,14,17], a single media interincisal incision followed by an inter-crevicular incision [17], and two vertical incisions connected by a horizontal and crevicular incision [5,18]. Some modifications are performed such as the Han and Takei microsurgery approach [6,7,11] and the formation of pouches/tunnels through semilunar incisions [12]. The pouch/tunnel procedure involves incisions of approximately 1 mm split-thickness flap at the coronal mucogingival junction to transfer the PRF membrane into the interdental space. Tunnel blades may also be utilized to create tunnels through the creation of 3–4 mm semilunar incisions at 2 mm coronal mucogingival junctions [10]. An alternative approach is the Modified Beagle's technique which employs an ophthalmic crescent scalpel to assess the interdental line angles of the IDP. To maintain the integrity of the surgical site, a Coe-pack periodontal dressing was applied and removed two weeks after the procedure [9]. In addition to surgical techniques, outcomes of IDP reconstruction surgery are affected by case-specific factors.

Postoperative evaluations were conducted to assess the efficacy of the treatment within two weeks [9], one month [18,19], three months [9,10,12,18], and six months [10,17]. The complete fill of IDP deficiency by PRF membranes is contingent upon the contact point-bone crest (CP-BC) distance being less than or equal to 5 mm [7,9,10]. Nonetheless, the PRF membrane produces partial fill results when CP-BC is greater than 5 mm [8,12]. This result supports the previous hypothesis that complete IDP filling is demonstrated when the distance between the CP and BC is no more than 5 mm. It was further explained that the potential for complete filling is substantially decreased when the deficit is higher than 5 mm. Fifty percent less complete filling occurs for every 1 mm of additional IDP deficiency [9]. Additionally, the distance between the contact points and the tip of the papilla (CP-TP) is employed as a clinical indicator. When the CP-TP is equal to or less than 4 mm, the PRF membrane can reconstruct the IDP deficiency area in its entirety [11]. Clinical trials, on the other hand, suggest that closure is only partial when the CP-TP surpasses 4 mm [7]. Unfortunately, certain articles fail to provide information regarding the CP-BC and CP-TP distances. This complicates the process of comparing the treatment outcomes with previous theories.

In conjunction with the clinical indicators, the patient's distress was assessed. PRF provides an exceptional color match, minimal irritation, and seamless recovery [8, 9, 20]. Therefore, PRF is suggested as a papilla reconstruction material due to its user-friendly application process, ability to augment papilla height, and positive impact on patient satisfaction.

**PRF vs CTG in Surgical IDP Reconstruction: Application and Evaluation**

Connective tissue graft (CTG) is the gold standard in IDP reconstruction surgery, particularly for long-term outcome stabilization. However, the application of CTG for the reconstruction of papilla leads to patient distress and an undetermined prognosis [9]. To alleviate patient distress, PRF is employed as an alternative to connective tissue transplantation [21,22].

During IDP reconstruction, PRF is utilized instead of CTG to prevent the need for a second operation. Five randomized controlled clinical trials [19 - 24] comparing the efficacy of PRF and CTG in the treatment of papilla reconstruction were identified for this review. Moreover, an integration of PRF and CTG was elaborated upon in a case report [25]. Individuals who were presented with class I and/or II IDP loss and a bone crest distance of no more than 6 mm from the papilla apex [19–24] were the subjects of the study. It is critical to acknowledge, nevertheless, that certain sources were deficient in details about case classification [21,25].

Varying surgical techniques are utilized in the literature that compares the effects of PRF and CTG. Han and Takei [23], Azzi et al. [24], the pouch and tunnel techniques [19, 21, 22, 25], and other approaches are included among the techniques previously mentioned. A semilunar incision is required 6-10 mm apically from the gingival margin and is followed by an intrasulcular incision to establish a split-thickness chamber using the Han and Takei technique. Azzi et al. [24] described a procedure wherein the papilla is joined with the palatal membrane via a parallel incision to the CEJ. Concerning the tunnel technique, a horizontal incision is made two to three millimeters away from the apex of the papilla [19-22].

Postoperative assessments were conducted at specified time intervals following the IDP surgical procedure, specifically two weeks, one month, three months, and six months. While both PRF and CTG membranes demonstrated complete restoration of the IDP four weeks after treatment [24]. CTG membranes are generally favored over PRF membranes for the reasons listed below: they exhibit superior resistance to relapse in comparison to PRF membranes, increase the height of papilla, and decrease the height of black triangles/papilla loss [19-23]. Additionally, it has been stated that CTG yields more consistent results in comparison to PRF. Subsequently, CTG remains the "gold standard," while PRF is acknowledged as a supplementary or alternative treatment [22].

Interestingly, a trial suggested that there was no statistical difference between CTG and PRF for IDP reconstruction, and subjectively PRF was a preferable approach due to less pain compared to CTG [16]. According to a clinical study, PRF and CTG demonstrate similar efficacy in the reconstruction of IDP loss during the six months. The implementation of micro tunneling techniques, which preserve a greater quantity of micro blood vessels in the papilla and thus guarantee superior gingivopapillary integrity, may account for this sophisticated result. The primary benefit of employing microsurgical techniques is the prevention of inflammatory symptoms. Therefore, it inhibits the development and enlargement of papilla that would arise due to the inflammatory process. In contrast, the exclusion of anesthetic in the intrasulcular and transpapillary regions will mitigate the risk of needle injection-induced trauma and prevent vasoconstrictive effects on the papilla. A clinical trial indicated that patients report a relatively lower distress score following PRF administration in comparison to CTG [7]. However, to attain maximum visibility in the surgical site, a magnifying loupe is still necessary for this technique [21]. Additional study is required to ascertain the impact of microsurgical interventions on the regeneration of IDP throughout observation periods.

Surgically reconstructing IDP loss is a complex and detailed procedure. It may be attributed to a restricted quantity of blood vessels. To guarantee the durability of treatment results, it is imperative to consider various parameters. These include anatomical considerations, the distance between the contact point and the bone crest, interdental and interradicular distances, the tooth's morphology, and the biotype of periodontal tissue. Case selections and surgical techniques are critical components to attain the most favorable results. Additionally, the treatment prognosis of papilla reconstruction surgery is significantly impacted by proper oral hygiene [15].

**PRF Application in Non-Surgical IDP Reconstruction**

Non-surgical papilla reconstruction refers to procedures in which the IDP is restored or augmented using non-invasive methods. While there is presently no universally accepted treatment for this condition, clinical evidence indicates that it may be possible to regenerate IDP using minimally invasive non-surgical methods [1]. By administering hyaluronic acid (AH) injections, it is possible to augment the height of the interdental papilla, particularly when treating IDP loss of Class I and/or Class II [26,27]. However, the lack of commercially accessible gingiva-specific AH preparations presents a possible risk of allergic reactions, which are distinguished by erythema and localized inflammation. It can be affected by a variety of factors, including viscosity, hygroscopic properties, host response, and ethnicity. To overcome this allergic reaction, liquid PRF is administered via injection [28].

Liquid PRF is capable of being administered to the interdental papilla. This injectable PRF (I – PRF) was derived from 10 ml of patient blood that had been centrifuged using a fixed-angle centrifugation machine for three minutes at 700 rpm. Using an insulin syringe, the uppermost layer, which is yellow orange in color, is extracted and administered at a 45° angle to the tooth axis, 2-3 mm apical to the papilla tip followed by a gentle incisal massage after the injection. It is critical to perform the injection promptly due to the rapid conversion of fibrinogen to solid fibrin within a time frame of 10 to 15 minutes [18].

As an evaluation, the area of the black triangle decreased considerably after 1, 3, and 6 months, as measured by its height. Even six months after injection, three sites continued to exhibit 100 percent papillary fill upon clinical evaluation. In one location, papillary fill was 75%, whereas in the other two, it was 66.6%. The clinical examination and the reduction in the black triangles observed during the photographic evaluation were highly consistent. Nevertheless, injectable PRF remains restricted in terms of quantity obtained. Since 10-13 ml of blood yields only 1-2 ml of I-PRF, additional blood is required if papilla loss occurs in numerous teeth [18]. However, no clinical trials examining the injectable effect of PRF for the reconstruction of IDP have been evaluated in this review. Only one case series showed that three cases resulted in partial fill, and three cases resulted in complete fill

**PRF Role in IDP Reconstruction: Proposed Mechanism**

PRF is commonly used to enhance bone regeneration and promote soft tissue healing. It is an endogenous biological compound that is extracted from the blood of a patient and subsequently centrifuged for a specified duration. Although research explaining the mechanism of PRF for IDP reconstruction is still very limited, this mechanism is hypothesized to be related to the role of PRF in increasing volume and inducing regeneration of periodontal tissue, particularly gingiva [2].

Fibrin is the physiologically active form of the platelet aggregating agent fibrinogen, which is involved in hemostasis. Blood clot microporous fibrin filaments may facilitate cell migration, proliferation, and differentiation in three dimensions [29]. The autologous fibrin matrix of PRF is composed of platelets, leukocytes, and cytokines derived from platelet-derived growth factors. Platelets are important in hemostasis and have properties such as anti-inflammatory, reservoir of growth factors and cytokines. Therefore, it is defined as the key to the regeneration and maturation of soft tissues and bones. In addition to platelets, leukocytes contained in PRF play a role in preventing infection, chemotaxis, and cytokine release (IL-1, IL-4, IL-6, TNF-α). Therefore, leukocytes are considered important in immune system modulation, and matrix remodeling. The role of PRF in gingival regeneration is also closely related to the content of growth factors, namely Fibrin Transforming Growth Factor-β (TGF-β), Platelet-Derived Growth Factor (PDGF), Vascular Endothelial Growth Factor (VEGF), Insulin Growth Factor-1 (IGF-1), Fibroblast Growth Factor (FGF), and Epidermal Growth Factor (EGF) [20, 30 - 33]. PRF membrane facilitates the release of growth factors for extended periods, exceeding 7 days [34], and potentially as long as 14 days [35,36]. As the second generation of platelet concentrates, PRF's effectiveness is contingent on several critical variables. These consist of blood handling, tube type, centrifugation speed, and duration [37].

**Future Recommendations**

To enhance the effectiveness of treatments, it is critical to refine the procedures used to generate and apply PRF for IDP reconstruction [22]. The leucocyte PRF (L-PRF) procedure is in a constant state of evolution and modification. It was initially generated through the centrifugation of 10 ml of blood at a fixed-angle centrifugation machine with a speed of 2700 rpm for 12 minutes. It is believed that the L-PRF fibrin layer comprises platelets and leukocytes in a high concentration resulting in the slicing of the fibrin layer in the second layer. This fibrin layer is compressed to produce a membrane and liquid exudate as compression by-product is not fully utilized whereas it still contains growth factors that promote the proliferation of periodontal ligament cells [37]. In addition to liquid exudate, the buffy coat layer directly underneath the fibrin layer is not fully used.

Interestingly, a recent investigation utilized the pipetting technique to separate the layers of PRF centrifugation. The findings revealed that the Concentrated PRF (C-PRF), comprising 0.3-0.5 ml of buffy coat, contained the greatest concentration of leukocytes and platelets, in contrast to the fibrin level. In addition, the C-PRF layer is specified to be precisely 1 ml beneath the fibrin layer and above the red blood cell layer. This layer contains leukocytes and platelets greater than the concentration of whole blood. Platelets and leukocytes are greater in C-PRF compared to PRF derived from other liquid formulations, such as Injectable PRF [42].

As with other liquid PRF formulations, C-PRF is supposed to be administered non-surgically in interdental papilla to reduce surgical risks and improve patient comfort. However, the restricted quantity limits the application of this liquid C-PRF. To address this issue, liquid L-PRF exudate may be utilized to overcome this limitation. Further comprehensive research is needed to explore the potency of injectable C-PRF and L-PRF exudate as regenerative material in non-surgical IDP reconstruction procedures, in terms of its effect on stimulating fibroblasts, epithelium, collagen, and new blood vessels.

Recent research has presented evidence that horizontal centrifugation can be employed to generate PRF membranes and PRF liquid, in addition to fixed-angle centrifugation. Horizontal centrifugation maintains a consistent pressure on the blood throughout the entire centrifugation process. Horizontal centrifugation mitigates cell loss and injury during the production process by preventing blood cells from coming into contact with the distal wall of the tube. As a result, platelets and leukocytes are distributed more uniformly. The fibrin contained in a membrane produced by horizontal centrifugation is denser and more substantial than that produced by fixed-angle centrifugation [39 - 40]. Another additional benefit associated with horizontal centrifugation is its ability to generate a greater growth factor [40,41]. Thus, it is expected that this material can be utilized to achieve superior IDP reconstruction outcomes. A comprehensive investigation is required to ascertain the efficacy of H-PRF (PRF membrane and liquid PRF) in restoring IDP deficiency.

A novel drug delivery technique using microneedling has been developed to deliver injectable PRF (I-PRF). Previous research has demonstrated the ability of I-PRF microneedling to improve gingival tissue thickness and keratinized tissue width. It stimulates the generation of percutaneous collagen and enhances the tissue regeneration process [42,43]. It is expected that liquid PRF microneedling will be useful as an initial way to rebuild IDP loss before pursuing a surgical approach.

## CONCLUSION

Case selection and the application of suitable materials and techniques are essential components of the complex reconstruction of the IDP loss. IDP has been surgically reconstructed by inserting the PRF membrane produced by fixed-angle centrifugation. PRF liquid may also be administered non-surgically, although the literature on this subject remains limited. Interestingly, PRF produced via horizontal centrifugation has emerged in recent times and has demonstrated superior physical characteristics and growth factor content in comparison to PRF prepared at a fixed angle. It is predicted to improve treatment outcomes in IDP surgery. Further comprehensive research is necessary to validate this potential so the results could serve as a benchmark for enhancing the utilization of PRF in papilla reconstruction procedures.

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

## AUTHOR'S CONTRIBUTIONS

"Conceptualization, Rezmelia Sari; methodology, Rezmelia Sari, Heni Susilowati, Usi Sukorini, Suryono; writing—original draft preparation, Rezmelia Sari.; writing—review and editing, Heni Susilowati, Usi Sukorini, Suryono; visualization, Rezmelia Sari; supervision, Heni Susilowati, Usi Sukorini, Suryono.; All authors have read and agreed to the published version of the manuscript."

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Word Count – Words: 5067

## FIGURES

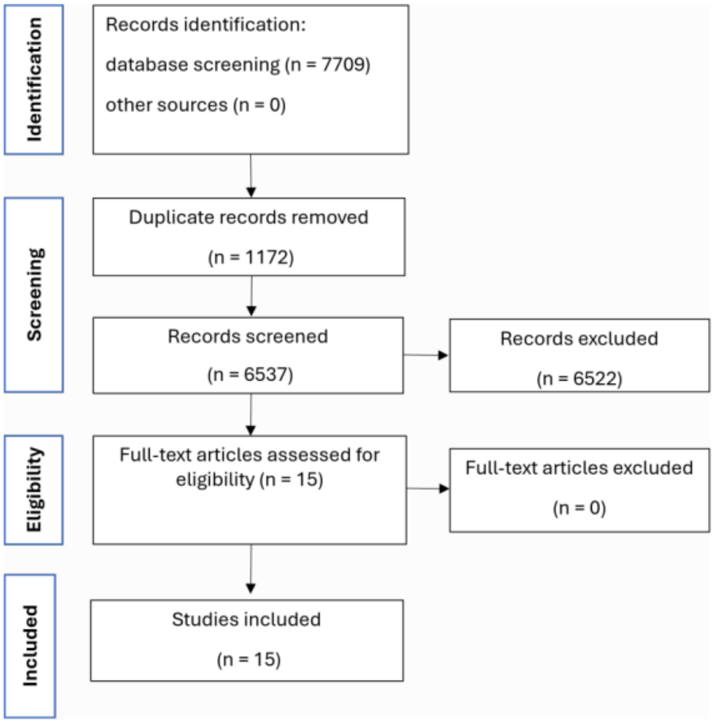


**Figure 1. PRISMA 2020 Flowchart**

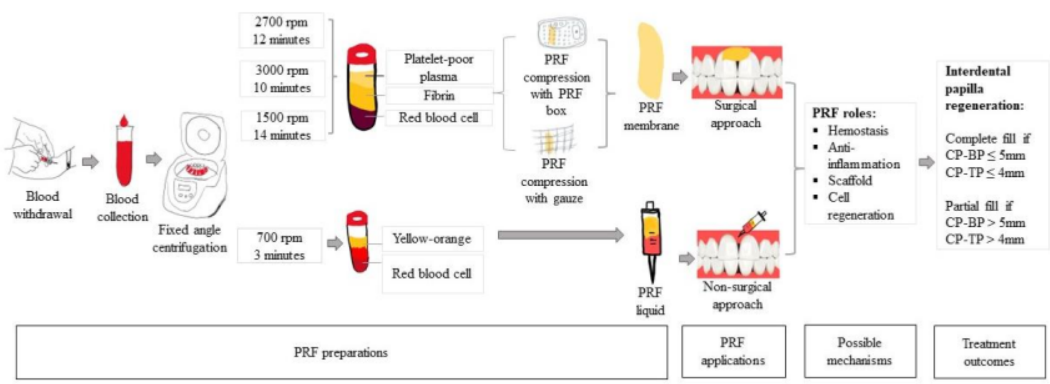


**Figure 2. The schematic figure of PRF application in IDP reconstruction**

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## CONFLICT OF INTEREST STATEMENT

"I undersign and certificate that I do not have any financial or personal relationships that might bias the content of this work."

Best regards,

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