Review Article

Platelet rich fibrin: a literature review of applications in oral and maxillofacial surgery

Timothy W. Neal^, Scott R. Sullivan, Scott Cannon, Wyatt Spresser, Thomas Schlieve

Department of Surgery, Division of Oral and Maxillofacial Surgery, UT Southwestern/Parkland Memorial Hospital, Dallas, TX, USA

Contributions: (I) Conception and design: All authors; (II) Administrative support: None; (III) Provision of study materials or patients: All authors; (IV) Collection and assembly of data: All authors; (V) Data analysis and interpretation: None; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Timothy W. Neal, DDS, MD. Department of Surgery, Division of Oral and Maxillofacial Surgery, UT Southwestern/Parkland Memorial Hospital, 5323 Harry Hines Boulevard MC 9109, Dallas, TX 75390, USA. Email: Timothy.Neal@UTSouthwestern.edu.

Background and Objective: Platelet-rich fibrin (PRF) is a second-generation autologous platelet concentrate with reported regenerative, angiogenic, antibacterial, and wound-healing capabilities. The purpose of this review was to examine the clinical applications of PRF in oral and maxillofacial surgery.

Methods: An online review of scientific articles was performed using the medical databases PubMed, the Cochrane Library, and clinicaltrials.gov. Databases were searched for articles in the English language from January 1st, 2001, to November 30th, 2023, using keywords dentoalveolar, orthognathic surgery, TMJ, temporomandibular, dental extraction, dental, dentistry, dental implant, craniofacial surgery, AND platelet-rich fibrin. MeSH terms were also used where available. Papers not written in the English language were excluded.

Key Content and Findings: The majority of literature investigating PRF in oral and maxillofacial surgery focuses on its utility in dentoalveolar procedures. Results are mixed in many areas of study; however, there is high-quality evidence to support the use of PRF for alveolar ridge preservation, as a bone graft adjunct, and for the treatment and prevention of alveolar osteitis.

Conclusions: PRF has potential utility in many different areas of oral and maxillofacial surgery. Future studies are needed to clinically justify and fully elucidate the utility of PRF in temporomandibular, craniofacial, orthognathic, osteonecrosis, and maxillofacial trauma surgery.

Keywords: Platelet-rich fibrin (PRF); autologous platelet concentrates; second-generation platelet concentrates

Received: 19 December 2023; Accepted: 11 March 2024; Published online: 26 March 2024.
doi: 10.21037/joma-23-35
View this article at: https://dx.doi.org/10.21037/joma-23-35

Introduction

The use of autologous platelet concentrates has been extensively studied in many specialties of surgery and medicine. Hematology and transfusion medicine pioneered the early development of platelet concentrates as a treatment for thrombocytopenia. Further advancements in technology and technique led to expanded uses as a hemostatic and adhesive agent in surgery. As clinical interest has continued to grow, much of the current literature investigating platelet concentrates focuses on regenerative applications. The multitude of protocols and categories of autologous platelet concentrates is a point of confusion for many clinicians and trainees. While this review focuses on platelet-rich fibrin (PRF), it is important to briefly discuss first-generation platelet concentrates.

In the long history of autologous platelet concentrates,

^ ORCID: 0000-0001-6168-9620.

the field of oral and maxillofacial surgery took an early interest. In 1982, Matras published a technique article and case series discussing the use of fibrin sealant in oral and maxillofacial surgery. The article describes the two-component fibrin sealant system obtained from human plasma. Component one is fibrinogen with associated factor XIII and fibronectin. Component two is made of thrombin and calcium chloride. Aprotinin solution is added to one of the two components as an antifibrinolytic. This fibrin sealant was used to anastomose the hypoglossal and facial nerves in a trauma patient, for hemostasis following the resection of a gingival tumor in a patient with anemia, and to secure a bone flap following the excision of maxillary polyps (1).

A disadvantage of fibrin sealant is the use of donor plasma and possible viral transmission, which resulted in commercial fibrin sealant products not receiving Food and Drug Administration (FDA) approval until 1998. Tayapongsak *et al.* introduced autologous fibrin adhesive to eliminate this disadvantage in 1994. The authors used autologous fibrin sealant combined with particulate cancellous bone grafts to reconstruct 33 mandibular continuity defects. Of the 33 included patients, 32 met the study success criteria, and the authors stated the addition of autologous fibrin sealant resulted in earlier bone remodeling and consolidation. The defect size was used to determine the protocol for producing the autologous fibrin sealant. Blood collection occurred at a preoperative visit when the defect was greater than 3 centimeters and at the time of surgery if less. The process of producing autologous fibrin sealant is lengthy and has a low yield compared to the amount of blood collected (2).

As an alternative, Whitman *et al.* proposed platelet gel in 1997, also known as platelet-rich plasma (PRP). Compared to autologous fibrin sealant, the protocol was simplified, with immediate preoperative blood collection and two centrifuge spin cycles. In their technique article, the authors reported success in reconstructing mandibular defects using PRP in combination with particulate bone graft (3). Marx *et al.* later performed histomorphometry studies utilizing PRP, which showed greater bone density in mandibular continuity defects grafted with PRP than those without (4). While the results of PRP were promising, the original protocol required a cell separator, central venous access, a large quantity of blood collection, two centrifugation cycles, and exogenous thrombin. These disadvantages led to the production of plasma rich in growth factors (PRGF). In 1999, Anitua investigated the use of PRGF for ridge preservation with positive soft and hard tissue healing outcomes (5). This protocol differed from PRP in that fractionation of the collected blood separated leukocytes from the platelet clot. Whether this exclusion is an advantage is debated in the literature. In addition, the PRGF protocol utilized a one-step centrifugation process, sodium citrate anticoagulant with calcium chloride activator, and no bovine thrombin. The simplification of protocol materials made this product easy to use in the ambulatory setting; however, the pipetting steps were tedious.

The first-generation platelet concentrates (fibrin glue, platelet gel, PRP, PRGF) shared common characteristics. All required some sort of additive as a coagulant, activator, or anticoagulant. Many of the first-generation protocols were tedious, time-consuming, required special equipment, or large volumes of blood collection. Regardless, many of these first-generation products are useful in many clinical scenarios. The development of PRP led to a shift towards protocol standardization, simplification, same-day blood collection, and utility in the ambulatory setting. With the introduction of second-generation platelet concentrates in 2000, many of the disadvantages of the first-generation were reduced (6). The purpose of this review is to examine the clinical applications of PRF in oral and maxillofacial surgery. We present this article in accordance with the Narrative Review reporting checklist (available at https://joma.amegroups.com/article/view/10.21037/joma-23-35/rc).

Methods

An online review of scientific articles was performed using the medical databases PubMed, Cochrane Library, and ClinicalTrials.gov. Databases were searched for articles in the English language from January 1st, 2001, to November 30th, 2023, using keywords dentoalveolar, orthognathic surgery, TMJ, temporomandibular, dental extraction, dental, dentistry, dental implant, craniofacial surgery, AND platelet-rich fibrin. MeSH terms were also used where available. Papers not written in the English language were excluded. A total of 1,656 articles were available. Studies that assessed the use of PRF in oral and maxillofacial surgery procedures were included. Titles and abstracts were screened for relevancy by the first four listed authors (T.W.N., S.R.S., S.C., W.S.), with disagreements reviewed and decided upon by the senior author (T.S.). *Table 1* outlines the review specifications.

Table 1 The search strategy summary

Items	Specification
Date of search	November 30th 2023
Databases and other sources searched	PubMed, Cochrane Library, ClinicalTrials.gov
Search terms used	Dentoalveolar, orthognathic surgery, TMJ, temporomandibular, dental extraction, dental, dentistry, dental implant, craniofacial surgery, AND platelet-rich fibrin
Timeframe	January 1st, 2001–November 30th 2023
Inclusion and exclusion criteria	Inclusion: studies that assessed the use of platelet-rich fibrin in oral and maxillofacial surgery procedures
	Exclusion: papers not written in the English language
Selection process	Titles and abstracts were screened for relevancy by the first four authors (T.W.N., S.R.S., S.C., W.S.) with disagreements reviewed and decided upon by the senior author (T.S.)

TMJ, temporomandibular joint.

Table 2 First and second-generation platelet concentrates

First-generation platelet concentrates
Fibrin glue
Platelet gel/PRP
PRGF
Second-generation platelet concentrates
L-PRF
A-PRF
A-PRF+
i-PRF

PRP, platelet-rich plasma; PRGF, plasma rich in growth factors; L-PRF, leukocyte and platelet-rich fibrin; A-PRF, advanced platelet-rich fibrin; A-PRF+, advanced platelet-rich fibrin+; i-PRF, injectable platelet-rich fibrin.

Narrative

Platelet function

Platelets play a fundamental role in primary hemostasis. They are small, anucleate, cytoplasmic fragments of megakaryocytes with a life span of 7–10 days. When endothelial damage occurs, Von Willebrand factor binds to exposed collagen. Platelets then bind to Von Willebrand factor by way of the receptor glycoprotein 1b (Gp1b). This binding stimulates the release of platelet alpha and dense granules. Alpha granules contain Von Willebrand factor, fibrinogen, fibronectin, growth factors, cytokines, and chemokines. Dense granules contain calcium, adenosine diphosphate (ADP), serotonin, and histamine, which increases platelet activation. This release induces GIIb/IIIa receptor expression on the surface of platelets, allowing fibrinogen to bind. This binding allows for the formation of a platelet plug. Platelets play a role in the hemostasis, inflammatory, proliferative, and remodeling phases of wound healing. Platelets release chemokines and cytokines that enhance the inflammatory phase. The release of fibroblast growth factor (FGF), platelet-derived growth factor (PDGF), transforming growth factor beta (TGF-β), and vascular endothelial growth factor (VEGF) stimulates angiogenesis and connective tissue healing in the proliferative and remodeling phases (7-9).

Types of PRF

Since the introduction of PRF by Choukroun *et al.* in 2000, many different protocols and subcategories have been reported in the literature (6). Like the first-generation platelet concentrates, the second generation has undergone many iterations (*Table 2*). Second-generation concentrates contain no added anticoagulants or activators; however, they have the disadvantage of a short working time. In a general sense, PRF is either solid form or liquid form. The form and distribution of cells and growth factors depend on the relative centrifugal force (RCF) and spin time (Eq. [1]).

$$RCF = 11.18 \times r \times \left(\frac{N}{1000}\right)^2 \quad [1]$$

The value N is the revolutions per minute (RPM) and r is the radius in centimeters.

Table 3 Original protocols for second-generation platelet concentrates

Second-generation platelet concentrate	Original protocol
L-PRF	3,000 RPM for 10 minutes
A-PRF	1,500 RPM for 14 minutes
A-PRF+	1,300 RPM for 8 minutes
i-PRF	700 RPM for 3 minutes

L-PRF, leukocyte and platelet-rich fibrin; A-PRF, advanced platelet-rich fibrin; A-PRF+, advanced platelet-rich fibrin+; i-PRF, injectable platelet-rich fibrin; RPM, revolutions per minute.

Since the original PRF protocol was introduced, termed leukocyte and PRF (L-PRF), protocols have decreased in RCF and spin time, with new subcategories, termed advanced PRF (A-PRF), advanced PRF+ (A-PRF+), and injectable PRF (i-PRF) (10-12). At high centrifugation forces, cells shift to the bottom of the tube, and because of this, protocols have progressively decreased in force and speed to distribute cells and growth factors evenly (*Table 3*). The end product is a PRF matrix concentrated with leukocytes and growth factors that slowly release over time.

Centrifuge and collection tubes

There is a significant commercial interest in the production of PRF. Several medical supply companies produce all-in-one kits with a centrifuge, collection tubes, and associated equipment to produce PRF clots, membranes, and i-PRF. Typically, these centrifuges are pre-programmed with the appropriate spin time and RCF to create the desired PRF form. This commercial interest may be partially to blame for the continuous development of new protocols and the associated confusing terminology. For research purposes, standardization of the centrifuge and tubes may enable investigators to reproduce and build upon previous works more efficiently. In clinical practice, most variable speed centrifuges may produce quality PRF products if the centrifuge radius is considered (13). In doing so, the speed may be adjusted to achieve the desired RCF for the chosen protocol (Eq. [1]). In a study comparing PRF produced by three different commercially available centrifuges, Miron *et al.* showed little variability in outcome when the appropriate protocol and collection tubes were utilized (14). Another important characteristic of the centrifuge is the angulation of the tube. Several studies have shown that horizontal centrifugation, compared to fixed angle, produces superior separation and distribution of leukocytes and platelets within the PRF matrix (15,16).

The ideal collection tube is dependent on the protocol and PRF form desired. In general, additive-free glass tubes should be utilized when producing solid-form PRF. When producing liquid PRF, additive-free plastic tubes should be utilized. Glass stimulates the clotting cascade, producing larger solid-form PRF matrices. Some studies have utilized silica-coated plastic tubes for the production of PRF. However, Tsujino *et al.* found silica microparticles incorporated into PRF matrices prepared with silica-coated plastic tubes. These silica microparticles negatively impacted cell survival and proliferation (17,18).

Dentoalveolar applications

When focusing on PRF applications in oral and maxillofacial surgery, the topic is dominated by studies investigating applications for dentoalveolar procedures. Of the articles identified for this review, nearly 90% were related to dentoalveolar procedures. Historically, research investigating the use of PRF in dentoalveolar procedures has produced mixed results, which is likely to blame for the lack of widespread adoption of PRF by oral and maxillofacial surgeons.

Several studies have reported promising results using PRF in extraction sockets following dental extraction for site preservation. In a split-mouth study by Temmerman *et al.*, the authors compared alveolar ridge width in 22 patients who received PRF versus control (natural healing) after dental extractions of bilateral and closely symmetrical teeth in the maxilla or mandible. At 3 months post-procedure, there was a statistically significant difference in alveolar ridge width, with less bone loss in extraction sites treated with PRF (19). Hauser *et al.* evaluated the effect of PRF on extraction site healing in a randomized control trial of 23 patients. Patients were randomly assigned to 3 treatment groups: simple extraction and PRF, extraction with mucosal flap and PRF, or simple extraction without socket filling before implant placement. The group that received simple extraction and PRF in the socket showed significantly better bone healing and microarchitecture when compared to the other treatment groups (20). Further studies investigated PRF as an adjunct to demineralized free-dried bone allograft (DFDBA) for socket preservation. In a randomized controlled trial by Thakkar *et al.*, the authors compared patients who received DFDBA combined

with PRF for socket preservation to those who received DFDBA only. There was a significant difference in the alveolar ridge width, with better ridge preservation in the group that received DFDBA combined with PRF (21). While many studies have reported promising results using PRF for ridge preservation, some have shown no significant difference in treatment outcomes (22,23). In addition, several systematic reviews have evaluated the use of PRF for alveolar ridge preservation with inconclusive results (24-29). With this in mind, the study by Hauser *et al.* may be the simplest to draw conclusions from. PRF may improve bone healing after dental extraction; however, other surgical factors may have a significant impact, such as a loss of blood supply to the alveolus during flap elevation.

As an adjunct to bone grafts in sinus lift procedures, multiple randomized clinical trials have shown no difference in bone formation with the addition of PRF (30-33). However, when PRF was used as the sole grafting material for sinus augmentation, multiple studies showed substantial regeneration of bone for implant placement (34,35). It is worth noting that the latter two studies used radiographic evaluations without a control group. When PRF was used as a barrier membrane at the lateral osteotomy site in sinus augmentation, there was no difference in bone regeneration compared to collagen membranes (36). While the literature is mixed, there is clinical utility in using PRF to improve the workability of bone graft materials.

Another widely studied topic is the use of PRF following third molar extractions to promote wound healing, pain and swelling reduction, and for prevention of alveolar osteitis. Multiple systematic reviews have reported decreased rates of alveolar osteitis and postoperative pain scores in patients who received PRF following third molar extractions (37-39). Methodological heterogeneity among studies included in these systematic reviews made it difficult to evaluate outcomes related to swelling and wound healing, although positive results were reported. PRF has also shown promise as a treatment for established alveolar osteitis. In a single-blinded prospective study by Reeshma *et al.*, the authors measured pain scores on days 1, 3, 5, and 7 following treatments with either PRF or zinc oxide eugenol (ZOE) for mandibular alveolar osteitis. There was a significant difference between the groups at all study time points, with greater pain relief experienced by the group that received PRF (40). In a similar study by Hussain *et al.*, the authors concluded that PRF is as effective as ZOE in managing alveolar osteitis pain and is superior in socket healing (41). The appropriate treatment of alveolar osteitis is debated in the literature, with many topical dressings advocated. While dressings like ZOE effectively relieve pain, several studies have reported a possible increase in infection risk, anaphylaxis, and delay in wound healing from these treatment modalities (42,43). With this in mind, PRF is an attractive option for the treatment and prevention of alveolar osteitis.

Adequate soft and hard tissue healing is paramount for dental implant success and stability. Compared to grafting and site preservation, fewer studies have investigated the effect of PRF on implant success and stability. Tabrizi *et al.* performed a split-mouth randomized clinical trial of 20 patients receiving bilateral maxillary molar implants with and without PRF in the implant site prior to placement. The study assessed implant stability with resonance frequency analysis at 2, 4, and 6 weeks post-procedure. At all study intervals, implants placed in sites treated with PRF had higher stability scores (44). Similar results were reported in studies by Pirpir *et al.* and Öncü and Alaaddinoğlu (45,46). Boora *et al.* evaluated the effect of PRF on peri-implant healing in 20 patients who received dental extraction and immediate dental implant placement. One group received a PRF membrane around the implant before soft tissue closure, while the control group received no membrane. At 3 months post-procedure, the PRF group had less marginal bone loss (47). However, a randomized clinical trial that evaluated dental implants coated with i-PRF before placement found no difference in implant stability over the 1-year study period compared to the control (48). It is challenging to draw practical conclusions from the available literature, and future studies investigating the effect of PRF on implant stability are needed.

Craniofacial surgery

Few studies have evaluated the utility of PRF in craniofacial and orthognathic surgery procedures. Shawky and Seifeldin investigated PRF as an adjunct to autogenous anterior iliac crest bone graft in a randomized clinical trial of 24 patients with unilateral alveolar clefts. New bone formation was evaluated at 6 months postoperatively, and patients who received PRF in combination with autogenous bone graft had a significant increase in the percentage of newly formed bone compared to the control group (49). In a similar study by Saruhan and Ertas, there was an increase in the percentage of newly formed bone in alveolar cleft patients who received PRF with autogenous anterior iliac crest bone graft compared to control; however, there

was no statistically significant difference (50). Given the results of PRF in combination with grafting materials for dentoalveolar procedures, more studies are needed in the cleft patient population. In addition, several applications still need to be investigated, such as the impact of PRF on hardware stability, bone healing, infection rate, and wound healing following orthognathic surgery.

Temporomandibular joint (TMJ)

Temporomandibular disorders are common conditions characterized by pain related to the TMJ, the muscles of mastication, or both. For disorders of the joint, many studies have investigated various products for use following joint arthrocentesis and as intra-articular injections. With the introduction of i-PRF, there has been a clinical interest in applications for conditions of the TMJ. PRF's biocompatibility, analgesic, and regenerative properties make it an attractive option. A recent scoping review by Sielski *et al.* analyzed the available literature investigating the use of i-PRF as a complement to arthrocentesis and found that i-PRF reduces articular pain and increases joint mobility (51). Manafikhi *et al.* reported decreased joint noise at 6 months in a cohort of 20 patients treated with two intra-articular i-PRF injections (52). In a retrospective study of 54 patients, Torul *et al.* reported improvement in maximal incisal opening and pain scores following intra-articular injections of i-PRF (53). Yuce and Komerik retrospectively compared i-PRF to hyaluronic acid following arthrocentesis in a cohort of 47 patients. The i-PRF group had a significant decrease in pain and improvement in maximum incisal opening at 12 months post-procedure compared to hyaluronic acid (54). In a prospective study by Vingender *et al.* comparing intra-articular injections of hyaluronic acid, PRP, and i-PRF, the authors found similar post-procedure effects on maximal opening and pain. The authors concluded that because the effects are similar, autologous products should be preferred to reduce the risk of possible adverse reactions. Of note, no adverse reactions were reported in the hyaluronic acid group in this study (55). Several randomized clinical trials have compared i-PRF combined with arthrocentesis versus arthrocentesis alone. In a study of 40 patients receiving arthrocentesis combined with i-PRF versus arthrocentesis alone, Ghoneim *et al.* reported a significant difference between the two groups at all study time points, with greater improvement in maximum incisal opening, pain, and lateral movement in the i-PRF group (56). Similar findings were reported by Işık *et al.* and Karadayi and Gursoytrak (57,58). The superiority of one injectable over another is a widely debated topic in the literature. It is important to note that arthrocentesis alone is an effective treatment for patients whose primary symptoms originate within the TMJ. While i-PRF has distinct regenerative advantages, further studies are needed to justify its routine clinical use over established effective products that are more simple-to-use such as hyaluronic acid and corticosteroids.

Osteonecrosis

Osteonecrosis of the jaws is a well-published side effect of certain medications and a complication of radiation therapy for head and neck cancer. The exact mechanism of medication-related osteonecrosis of the jaws (MRONJs) is unclear. Still, multiple factors have been shown to play a role in development, including inhibition of bone remodeling, inflammation or infection, inhibition of angiogenesis, and immune dysfunction (59). The likely mechanism for the development of osteoradionecrosis (ORN) is the dysregulation of fibroblastic activity that results in radiation-induced fibrosis (60). In either case, there is chronically exposed bone with impairment of remodeling and healing.

Few studies have investigated the utility of PRF as an adjunct treatment for MRONJ. Much of the available literature is limited to case series and retrospective studies (61-63). Two prospective studies without control groups reported 93% and 77% disease resolution for patients treated with surgery and PRF (64,65). Giudice *et al.* performed one of the few randomized clinical trials investigating PRF in MRONJ patients. The study groups included 24 stage II/III MRONJ patients who received necrotic bone removal and PRF compared to 23 patients who received necrotic bone removal only. Patients were evaluated at 1 month, 6 months, and 1-year post-intervention, with a primary outcome of mucosal integrity at the 6-month follow-up. At all time points, there was a greater percentage of patients with mucosal integrity in the group that received PRF; however, the difference was only statistically significant at 1-month post-intervention. There were also lower pain scores and a greater percentage of patients without infection in the PRF group, with statistical differences seen at the 1-month follow-up only. Several studies have investigated the utility of PRF in preventing MRONJ (66-69). MRONJ, while well-documented in the literature, is a rare complication. Because of this, it

is challenging to draw definitive conclusions from the available literature and evaluate the preventative potential of PRF.

Literature investigating the use of PRF in patients with ORN is limited to case reports. Compared to PRF studies in MRONJ patients, the lack of literature is surprising, considering ORN was described nearly 80 years before MRONJ. The available case reports describe treatment with PRF in combination with sequestrectomy with postoperative mucosal coverage and disease resolution (70-72). ORN is classically challenging to treat, and any modality that may benefit these patients should be investigated. Given the angiogenic, antibacterial, and regenerative properties, it is plausible that PRF may be beneficial as an adjunct treatment for ORN.

Conclusions

The purpose of this review was to examine the clinical applications of PRF in oral and maxillofacial surgery. While not comprehensive, this article aimed to provide a simple and concise review of a topic that may be a source of confusion to trainees and surgeons alike. Autologous platelet concentrates have a lengthy history intertwined with the fields of dentistry and oral and maxillofacial surgery, both of which have been drivers of advancement in first- and second-generation autologous platelet concentrates. The introduction of PRF and the simplification of equipment and protocols has expanded clinical utility in the operating room and ambulatory settings. While the literature investigating PRF for oral and maxillofacial surgery procedures is mixed, there are applications with promising results that may be clinically beneficial. In addition, many applications have not yet been investigated, such as the use of PRF in orthognathic surgery and the treatment of facial bony trauma. Future studies in patients with MRONJ and ORN are also needed.

Acknowledgments

Funding: None.

Footnote

Reporting Checklist: The authors have completed the Narrative Review reporting checklist. Available at https://joma.amegroups.com/article/view/10.21037/joma-23-35/rc

Peer Review File: Available at https://joma.amegroups.com/article/view/10.21037/joma-23-35/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://joma.amegroups.com/article/view/10.21037/joma-23-35/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

1. Matras H. The use of fibrin sealant in oral and maxillofacial surgery. J Oral Maxillofac Surg 1982;40:617-22.
2. Tayapongsak P, O'Brien DA, Monteiro CB, et al. Autologous fibrin adhesive in mandibular reconstruction with particulate cancellous bone and marrow. J Oral Maxillofac Surg 1994;52:161-5; discussion 166.
3. Whitman DH, Berry RL, Green DM. Platelet gel: an autologous alternative to fibrin glue with applications in oral and maxillofacial surgery. J Oral Maxillofac Surg 1997;55:1294-9.
4. Marx RE, Carlson ER, Eichstaedt RM, et al. Platelet-rich plasma: Growth factor enhancement for bone grafts. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1998;85:638-46.
5. Anitua E. Plasma rich in growth factors: preliminary results of use in the preparation of future sites for implants. Int J Oral Maxillofac Implants 1999;14:529-35.
6. Choukroun J, Adda F, Schoeffer C, et al. PRF: an opportunity in perio-implantology. Implantodontie 2000;42:55-62.
7. Doucet C, Ernou I, Zhang Y, et al. Platelet lysates promote

mesenchymal stem cell expansion: a safety substitute for animal serum in cell-based therapy applications. J Cell Physiol 2005;205:228-36.
8. Eisinger F, Patzelt J, Langer HF. The Platelet Response to Tissue Injury. Front Med (Lausanne) 2018;5:317.
9. van der Meijden PEJ, Heemskerk JWM. Platelet biology and functions: new concepts and clinical perspectives. Nat Rev Cardiol 2019;16:166-79.
10. Ghanaati S, Booms P, Orlowska A, et al. Advanced platelet-rich fibrin: a new concept for cell-based tissue engineering by means of inflammatory cells. J Oral Implantol 2014;40:679-89.
11. Fujioka-Kobayashi M, Miron RJ, Hernandez M, et al. Optimized Platelet-Rich Fibrin With the Low-Speed Concept: Growth Factor Release, Biocompatibility, and Cellular Response. J Periodontol 2017;88:112-21.
12. Miron RJ, Fujioka-Kobayashi M, Hernandez M, et al. Injectable platelet rich fibrin (i-PRF): opportunities in regenerative dentistry? Clin Oral Investig 2017;21:2619-27.
13. Neal TW, Schlieve T. Autologous platelet concentrates in oral surgery: a problem of reporting. Oral Surg Oral Med Oral Pathol Oral Radiol 2022;134:407.
14. Miron RJ, Xu H, Chai J, et al. Comparison of platelet-rich fibrin (PRF) produced using 3 commercially available centrifuges at both high (~700 g) and low (~200 g) relative centrifugation forces. Clin Oral Investig 2020;24:1171-82.
15. Fujioka-Kobayashi M, Kono M, Katagiri H, et al. Histological comparison of Platelet rich fibrin clots prepared by fixed-angle versus horizontal centrifugation. Platelets 2021;32:413-9.
16. Miron RJ, Chai J, Zheng S, et al. A novel method for evaluating and quantifying cell types in platelet rich fibrin and an introduction to horizontal centrifugation. J Biomed Mater Res A 2019;107:2257-71.
17. Tsujino T, Takahashi A, Yamaguchi S, et al. Evidence for Contamination of Silica Microparticles in Advanced Platelet-Rich Fibrin Matrices Prepared Using Silica-Coated Plastic Tubes. Biomedicines 2019;7:45.
18. Miron RJ, Kawase T, Dham A, et al. A technical note on contamination from PRF tubes containing silica and silicone. BMC Oral Health 2021;21:135.
19. Temmerman A, Vandessel J, Castro A, et al. The use of leucocyte and platelet-rich fibrin in socket management and ridge preservation: a split-mouth, randomized, controlled clinical trial. J Clin Periodontol 2016;43:990-9.
20. Hauser F, Gaydarov N, Badoud I, et al. Clinical and histological evaluation of postextraction platelet-rich fibrin socket filling: a prospective randomized controlled study. Implant Dent 2013;22:295-303.
21. Thakkar DJ, Deshpande NC, Dave DH, et al. A comparative evaluation of extraction socket preservation with demineralized freeze-dried bone allograft alone and along with platelet-rich fibrin: A clinical and radiographic study. Contemp Clin Dent 2016;7:371-6.
22. Abad CE, Sanz-Sanchez I, Serrano V, et al. Efficacy of the application of leukocyte and platelet-rich fibrin (L-PRF) on alveolar ridge preservation. A randomized controlled clinical trial. Clin Implant Dent Relat Res 2023;25:592-604.
23. Suttapreyasri S, Leepong N. Influence of platelet-rich fibrin on alveolar ridge preservation. J Craniofac Surg 2013;24:1088-94.
24. Stumbras A, Kuliesius P, Januzis G, et al. Alveolar Ridge Preservation after Tooth Extraction Using Different Bone Graft Materials and Autologous Platelet Concentrates: a Systematic Review. J Oral Maxillofac Res 2019;10:e2.
25. Al-Maawi S, Becker K, Schwarz F, et al. Efficacy of platelet-rich fibrin in promoting the healing of extraction sockets: a systematic review. Int J Implant Dent 2021;7:117.
26. Castro AB, Meschi N, Temmerman A, et al. Regenerative potential of leucocyte- and platelet-rich fibrin. Part B: sinus floor elevation, alveolar ridge preservation and implant therapy. A systematic review. J Clin Periodontol 2017;44:225-34.
27. Lin CY, Chen Z, Pan WL, et al. Effect of Platelet-Rich Fibrin on Ridge Preservation in Perspective of Bone Healing: A Systematic Review and Meta-analysis. Int J Oral Maxillofac Implants 2019;34:845–854.
28. Niu W, Wang P, Ge S, et al. Effects of Platelet Concentrates Used in Alveolar Ridge Preservation: A Systematic Review. Implant Dent 2018;27:498-506.
29. Del Fabbro M, Corbella S, Taschieri S, et al. Autologous platelet concentrate for post-extraction socket healing: a systematic review. Eur J Oral Implantol 2014;7:333-44.
30. Zhang Y, Tangl S, Huber CD, et al. Effects of Choukroun's platelet-rich fibrin on bone regeneration in combination with deproteinized bovine bone mineral in maxillary sinus augmentation: a histological and histomorphometric study. J Craniomaxillofac Surg 2012;40:321-8.
31. Cömert Kılıç S, Güngörmüş M, Parlak SN. Histologic and histomorphometric assessment of sinus-floor augmentation with beta-tricalcium phosphate alone or in combination with pure-platelet-rich plasma or platelet-rich fibrin: A randomized clinical trial. Clin Implant Dent Relat Res

2017;19:959-67.
32. Inchingolo F, Tatullo M, Marrelli M, et al. Trial with Platelet-Rich Fibrin and Bio-Oss used as grafting materials in the treatment of the severe maxillar bone atrophy: clinical and radiological evaluations. Eur Rev Med Pharmacol Sci 2010;14:1075-84.
33. Tatullo M, Marrelli M, Cassetta M, et al. Platelet Rich Fibrin (P.R.F.) in reconstructive surgery of atrophied maxillary bones: clinical and histological evaluations. Int J Med Sci 2012;9:872-80.
34. Mazor Z, Horowitz RA, Del Corso M, et al. Sinus floor augmentation with simultaneous implant placement using Choukroun's platelet-rich fibrin as the sole grafting material: a radiologic and histologic study at 6 months. J Periodontol 2009;80:2056-64.
35. Simonpieri A, Choukroun J, Del Corso M, et al. Simultaneous sinus-lift and implantation using microthreaded implants and leukocyte- and platelet-rich fibrin as sole grafting material: a six-year experience. Implant Dent 2011;20:2-12.
36. Gassling V, Purcz N, Braesen JH, et al. Comparison of two different absorbable membranes for the coverage of lateral osteotomy sites in maxillary sinus augmentation: a preliminary study. J Craniomaxillofac Surg 2013;41:76-82.
37. Canellas JVDS, Ritto FG, Medeiros PJD. Evaluation of postoperative complications after mandibular third molar surgery with the use of platelet-rich fibrin: a systematic review and meta-analysis. Int J Oral Maxillofac Surg 2017;46:1138-46.
38. Xiang X, Shi P, Zhang P, et al. Impact of platelet-rich fibrin on mandibular third molar surgery recovery: a systematic review and meta-analysis. BMC Oral Health 2019;19:163.
39. Zhu J, Zhang S, Yuan X, et al. Effect of platelet-rich fibrin on the control of alveolar osteitis, pain, trismus, soft tissue healing, and swelling following mandibular third molar surgery: an updated systematic review and meta-analysis. Int J Oral Maxillofac Surg 2021;50:398-406.
40. Reeshma S, Dain CP. Comparison of platelet-rich fibrin with zinc oxide eugenol in the relief of pain in alveolar osteitis. Health Sci Rep 2021;4:e354.
41. Hussain I, Singh S, Jain H, et al. A prospective randomized clinical study on evaluation of platelet-rich fibrin versus zinc oxide eugenol in the management of alveolar osteitis. Oral Surgery 2018;11:41-9.
42. Sarrami N, Pemberton MN, Thornhill MH, et al. Adverse reactions associated with the use of eugenol in dentistry. Br Dent J 2002;193:257-9.
43. Mainous EG. Foreign body reaction after zinc oxide-eugenol packing in localized osteitis. J Oral Surg 1974;32:207-8.
44. Tabrizi R, Arabion H, Karagah T. Does platelet-rich fibrin increase the stability of implants in the posterior of the maxilla? A split-mouth randomized clinical trial. Int J Oral Maxillofac Surg 2018;47:672-5.
45. Öncü E, Alaaddinoğlu EE. The effect of platelet-rich fibrin on implant stability. Int J Oral Maxillofac Implants 2015;30:578-82.
46. Pirpir C, Yilmaz O, Candirli C, et al. Evaluation of effectiveness of concentrated growth factor on osseointegration. Int J Implant Dent 2017;3:7.
47. Boora P, Rathee M, Bhoria M. Effect of Platelet Rich Fibrin (PRF) on Peri-implant Soft Tissue and Crestal Bone in One-Stage Implant Placement: A Randomized Controlled Trial. J Clin Diagn Res 2015;9:ZC18-21.
48. de Oliveira Fernandes GV, Malta Santos NB, Correia de Sousa MF, et al. Liquid Platelet-Rich Fibrin Coating Implant Surface to Enhance Osseointegration: A Double-Blinded, Randomized Split-Mouth Trial with 1-Year Follow-up. Int J Oral Maxillofac Implants 2022;37:159-70.
49. Shawky H, Seifeldin SA. Does Platelet-Rich Fibrin Enhance Bone Quality and Quantity of Alveolar Cleft Reconstruction? Cleft Palate Craniofac J 2016;53:597-606.
50. Saruhan N, Ertas U. Evaluating of Platelet-Rich Fibrin in the Treatment of Alveolar Cleft With Iliac Bone Graft By Means of Volumetric Analysis. J Craniofac Surg 2018;29:322-6.
51. Sielski M, Chęcińska K, Chęciński M, et al. Injectable Platelet-Rich Fibrin (I-PRF) Administered to Temporomandibular Joint Cavities: A Scoping Review. J Clin Med 2023;12:3326.
52. Manafikhi M, Ataya J, Heshmeh O. Evaluation of the efficacy of platelet rich fibrin (I-PRF) intra-articular injections in the management of internal derangements of temporomandibular joints - a controlled preliminary prospective clinical study. BMC Musculoskelet Disord 2022;23:454.
53. Torul D, Cezairli B, Kahveci K. The efficacy of intra-articular injectable platelet-rich fibrin application in the management of Wilkes stage III temporomandibular joint internal derangement. Int J Oral Maxillofac Surg 2021;50:1485-90.
54. Yuce E, Komerik N. Comparison of the Efficiacy of Intra-Articular Injection of Liquid Platelet-Rich Fibrin and Hyaluronic Acid After in Conjunction With Arthrocentesis for the Treatment of Internal Temporomandibular Joint

Derangements. J Craniofac Surg 2020;31:1870-4.
55. Vingender S, Dőri F, Schmidt P, et al. Evaluation of the efficiency of hyaluronic acid, PRP and I-PRF intra-articular injections in the treatment of internal derangement of the temporomandibular joint: A prospective study. J Craniomaxillofac Surg 2023;51:1-6.
56. Ghoneim NI, Mansour NA, Elmaghraby SA, et al. Treatment of temporomandibular joint disc displacement using arthrocentesis combined with injectable platelet rich fibrin versus arthrocentesis alone. J Dent Sci 2022;17:468-75.
57. Işık G, Kenç S, Özveri Koyuncu B, et al. Injectable platelet-rich fibrin as treatment for temporomandibular joint osteoarthritis: A randomized controlled clinical trial. J Craniomaxillofac Surg 2022;50:576-82.
58. Karadayi U, Gursoytrak B. Randomised controlled trial of arthrocentesis with or without PRF for internal derangement of the TMJ. J Craniomaxillofac Surg 2021;49:362-7.
59. Neal TW, Schlieve T. Medication-Related Osteonecrosis of the Jaws in the Pediatric Population. J Oral Maxillofac Surg 2022;80:1686-90.
60. Lyons A, Ghazali N. Osteoradionecrosis of the jaws: current understanding of its pathophysiology and treatment. Br J Oral Maxillofac Surg 2008;46:653-60.
61. George S, Neal TW, Schlieve T. Does the Addition of Platelet-Rich Fibrin in the Surgical Treatment of Medication-Related Osteonecrosis of the Jaws Impact Postoperative Disease Resolution? J Oral Maxillofac Surg 2022;80:S88-S89.
62. Szentpeteri S, Schmidt L, Restar L, et al. The Effect of Platelet-Rich Fibrin Membrane in Surgical Therapy of Medication-Related Osteonecrosis of the Jaw. J Oral Maxillofac Surg 2020;78:738-48.
63. Valente NA, Chatelain S, Alfonsi F, et al. Medication-Related Osteonecrosis of the Jaw: The Use of Leukocyte-Platelet-Rich Fibrin as an Adjunct in the Treatment. J Craniofac Surg 2019;30:1095-101.
64. Nørholt SE, Hartlev J. Surgical treatment of osteonecrosis of the jaw with the use of platelet-rich fibrin: a prospective study of 15 patients. Int J Oral Maxillofac Surg 2016;45:1256-60.
65. Kim JW, Kim SJ, Kim MR. Leucocyte-rich and platelet-rich fibrin for the treatment of bisphosphonate-related osteonecrosis of the jaw: a prospective feasibility study. Br J Oral Maxillofac Surg 2014;52:854-9.
66. Giudice A, Barone S, Giudice C, et al. Can platelet-rich fibrin improve healing after surgical treatment of medication-related osteonecrosis of the jaw? A pilot study. Oral Surg Oral Med Oral Pathol Oral Radiol 2018;126:390-403.
67. Stresser FA, Parise GK, Macedo FJ, et al. Use of Leukocyte- and Platelet-Rich Fibrin to Prevent Osteonecrosis of the Jaws Associated with the Use of Bisphosphonate Therapy: A Case Series. J Maxillofac Oral Surg 2023;22:1159-65.
68. Şahin O, Tatar B, Ekmekcioğlu C, et al. Prevention of medication related osteonecrosis of the jaw after dentoalveolar surgery: An institution's experience. J Clin Exp Dent 2020;12:e771-e776.
69. Asaka T, Ohga N, Yamazaki Y, et al. Platelet-rich fibrin may reduce the risk of delayed recovery in tooth-extracted patients undergoing oral bisphosphonate therapy: a trial study. Clin Oral Investig 2017;21:2165-72.
70. Chen YT, Chang YC. Use of platelet-rich fibrin and surgical approach for combined treatment of osteoradionecrosis: a case report. J Int Med Res 2019;47:3998-4003.
71. Law B, Mohd Yunus SS, Ramli R. Autogenous free fat graft combined with platelet-rich fibrin heals a refractory mandibular osteoradionecrosis. Clin Ter 2020;171:e110-3.
72. Baliga M, Chakraborty S, Kumari T, et al. Is there a role for PRF with simvastatin in stage I osteoradionecrosis? Oral Oncol 2018;87:177-8.

doi: 10.21037/joma-23-35
Cite this article as: Neal TW, Sullivan SR, Cannon S, Spresser W, Schlieve T. Platelet rich fibrin: a literature review of applications in oral and maxillofacial surgery. J Oral Maxillofac Anesth 2024;3:6.