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# Platelet Rich Fibrin (PRF) Application in Oral Surgery

*Alper Saglanmak, Caglar Cinar and Alper Gultekin*

## Abstract

Platelet rich fibrin (PRF) is an autologous biological product which becomes popular day by day and available in a wide variety of fields in medicine. Platelet concentrates which are introduced at the early 90s have evolved over the years. The use such autologous materials have become trendy in recent years to encounter demanding expectations of patients, improve treatment success and maximize patient comfort. Despite its increasing use in dentistry and oral surgery, the most indications and effects are still being discussed. PRF is easily accepted by patients because of its low cost, easy to receive, low donor morbidity, low postoperative complication and infection rate. This biomaterial may be a solution for patients who have strong negative beliefs about the use of allografts and xenografts or who are afraid of complications during the grafting procedure. The objectives of these technologies are to use their synergistic effect to improve the hard and soft tissue regeneration. PRF in oral surgery are used for alveolar bone reconstruction, dental implant surgery, sinus augmentation, socket preservation, osteonecrosis, oroantral fistula closure, struggling with oral ulcers, preventing swelling and edema constitution. This chapter aims to review the clinical applications of platelets in oral surgery and the role of molecular components in tissue healing.

**Keywords:** platelet rich fibrin, oral surgery, tissue healing, dental implant

## 1. Introduction

In recent years, the question how to increase patient comfort after surgical interventions became the main topic of oral surgical applications. In addition to minimally invasive surgical techniques, extra procedures performed during or after surgery are aimed to reduce postoperative morbidity. As a result of various researches in recent years, the use of platelet concentrates give rise to improve patient comfort and enhance healing after the operation.

Surgical techniques to gain bone and soft tissue can be difficult and associated with higher morbidity. Although they are technique delicate, they just considered as gold-standard, because of their capacity in healing enhancement [1]. However, alternative autologous blood derivatives such as platelet rich fibrin (PRF) are becoming a current issue with its easy use and effectiveness.

PRF is an autologous product acquired from the patient's own blood and enters dental field as a second- generation platelet concentrate under the name PRF [Platelet Rich Fibrin] by Choukroun. Although they are known by different names according to the centrifugation time (A-PRF, L-PRF, I- PRF, P-PRF) their

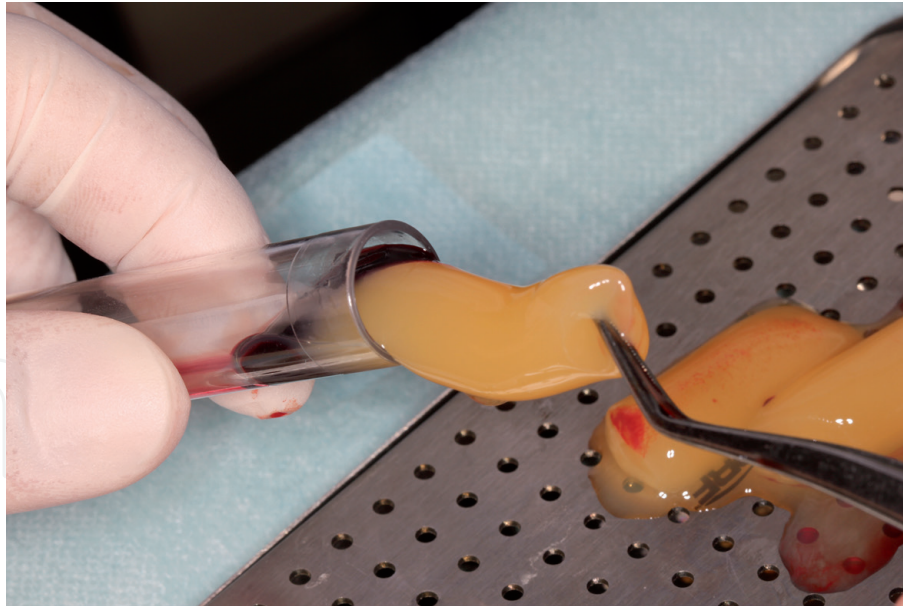
main rationale is the same. They are increasing the healing capability of the tissue by releasing growth factors from platelet granules. These factors are essential for inflammation process and they have positive effect on healing enhancing. Since it is an autologous product, it does not cause allergic reactions, it can be prepared rapidly and easily, there is no risk of disease transfer and no risk of donor site morbidity. The main advantages are controlling inflammation and suppressing infection by leukocyte and cytokine secretion [2] (**Figures 1 and 2**).

In order to get in depth information about the supportive effect of PRF one should know about the healing pattern of injured tissue. There are four sequential phases of wound healing: Hemostasis, inflammatory, proliferative and remodeling phase [3]. At hemostasis phase, platelets are essential for blood clot formation and PRF with rich platelet granules is promotive to accommodate a strong fibrin network. This blood clot serves as a reservoir which allows cell migration, adhesion and proliferation. The impact of this fibrin matrix proceeds throughout the whole healing process. Inflammatory phase starts with the injury and takes 5–7 days approximately. During this phase, platelets are releasing various growth factors to the injured site that migrate inflammatory cells (Lymphocytes, macrophages and neutrophils). These factors are PDGF (Platelet-derived growth factor), VEGF (Vascular endothelial growth factor), TGF B (Transforming growth factor) and pro-inflammatory cytokines such as interleukins (IL-1, IL-6, IL-8) and tumor necrosis factor alpha (TNF- $\alpha$ ), whose roles are enhancing angiogenesis and tissue healing. Within the comprising of new blood vessels with angiogenesis, acidic and hypoxic environment change. In the proliferative phase, MSCs (Mesenchymal stem cells) releasing from newly formed blood vessels, BMP's (Bone morphogenic protein) and TGF- $\beta$  are playing an important role in MSCs organism. MSC's role is inducing osteoblast differentiation. The last but not the least, remodeling phase is characterized as maturation process. Within this process, vascularity ratio and collagen deposition decreases and mineral deposition increases with the replacement of woven bone into lamellar one [4–6].

Fibrin forms a matrix for the migration of cells such as fibroblasts and endothelial cells, which are crucial in angiogenesis and new tissue formation. PRF is a strong fibrin matrix structure, platelets and leukocytes attach on it and activate degranulated growth factors with the consequence of releasing cytokines. It has been suggested that PRF, a natural fibrin network, can protect the growth factors containing in its own structure from proteolysis. Thus growth factors may maintain their activity for a long time and stimulate tissue regeneration [7].



**Figure 1.**  
*Bloodletting of a patient.*



**Figure 2.**  
*PRF membrane preparation.*

### 1.1 Types of PRF

The main purpose of using PRF is to release the rich content of alpha granules of platelets into the environment for therapeutic purposes. In addition to the basic functions of platelets, the contents of alpha and dense granules are very important for different processes such as inflammation and angiogenesis [8]. The main differences between PRF types are their centrifuge speed.

- **Advanced platelet rich fibrin (A-PRF):** It is obtained with longer centrifugation time and lower rpm. Thus, more neutrophilic granulocytes are present in the distal region of the clot. Neutrophilic granulocytes contribute to monocyte differentiation in macrophages (**Figure 3**).
- **Pure platelet rich fibrin (P-PRF):** After the first centrifuge (6 min high speed), transferring the buffy coat and PPP (Platelet poor plasma) to the second tube, which contains  $\text{CaCl}_2$ . After the second centrifuge starts and takes 15 min long, stable platelet-fibrin takes place. The authenticity of this method is the presence of separation gel at the first tube.
- **Leukocyte and platelet rich fibrin (L-PRF):** It is very simple and cheap method. Blood samples are taken into glass tubes without any anticoagulant and centrifuged immediately at low speed. It is formed three different layers with acellular plasma, platelet-rich fibrin and erythrocyte layer at the bottom, respectively. Thrombocyte rich fibrin matrix is very powerful and autologous biomaterial can be used in different fields in oral surgery.
- **Injectable platelet rich fibrin (I-PRF):** Blood involves high number of leukocytes. However coagulation occurs within few minutes after the centrifugation has finished. The use of I-PRF [Injectable] is at an early stage. But the results are very promising in terms of increasing vascularity and soft tissue healing.
- **Liquid platelet rich fibrin (Liquid-PRF):** Liquid-PRF was defined with low-speed centrifugation (LSC), which allows forming of a liquid-PRF formula of fibrinogen and thrombin rather than its conversion to fibrin [2].



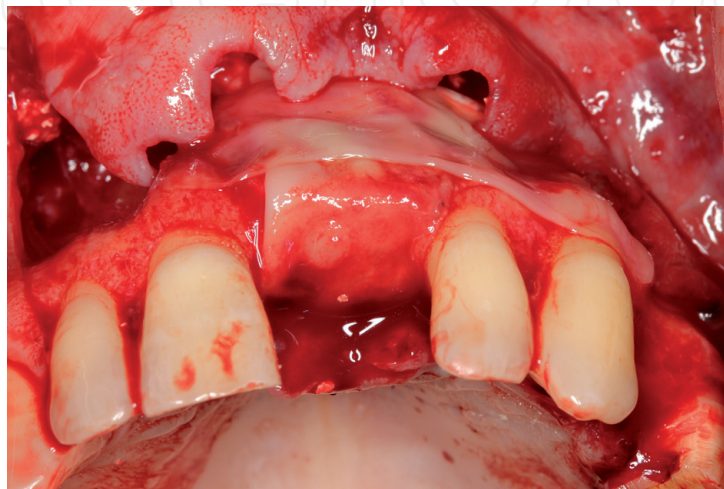
## 1.2 PRF in post extraction

Tooth extraction has various adverse effects such as pain, bleeding, swelling, infection etc. Wound healing in the tooth extraction is characterized by bone loss as a natural process. Furthermore; extraction will result recession around adjacent teeth and hinders the functional and esthetic prosthetic rehabilitation. PRF have been shown to play an important role in tissue healing with the releasing growth factors from alpha granules, regulate cellular events such as cell adhesion, migration, proliferation, differentiation and extracellular matrix deposition. Major changes occurred within the first year following extraction, but a major part of bone resorption takes place only within 3 months [9, 10].

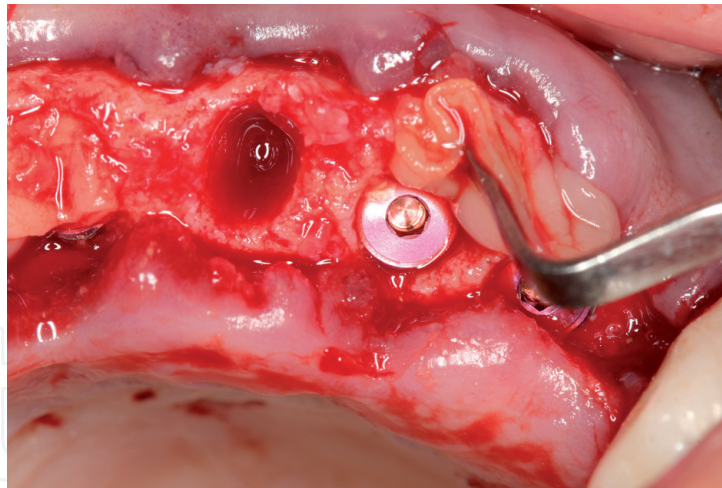
The rationale behind the enhancement of PRF in socket healing is very slowly polymerizing, cell migration and fibrin network capable of proliferation. During remodeling of the fibrin network many important growth factors from activated platelets and the release of the matrix glycoproteins. This biochemical structure gives rise to the tissue regeneration (**Figures 4 and 5**).



**Figure 3.**  
*A-PRF centrifuge device.*



**Figure 4.**  
*PRF membrane utilization in guided bone regeneration.*



**Figure 5.**  
*PRF membrane application in immediate implantation for filling the buccal gap.*

On the other hand the role of PRF in soft tissue healing has been shown at well-designed meta-analyses. In fact there are no significant differences in alveolar osteitis, acute inflammation or alveolar infection following tooth extraction. New bone gain and bone remodeling topic is also contradictory. However it was concluded that PRF is good at decreasing swelling, edema, pain and trismus following tooth extraction [9–11].

### **1.3 PRF for maintaining swelling, edema and pain**

Modern studies on clinical research showed that PRF aim to increase not only the success of the treatments but also the patient comfort. In this sense, the use of autologous products is advantageous such as high acceptability, low risk of disease transfer, low morbidity and low cost. PRF plays a crucial role in tissue repair. Their alpha granules include many substances, plenty of growth factors with significant effects on the inflammatory and proliferative resident cells at the site of injury, like mesenchymal stem cells, fibroblasts, chondrocytes and osteoblasts. This potential may be increased by the concentration of the platelets. Certain in-vitro and in-vivo studies have shown that the use of PRF is significantly advantageous in terms of cell migration. Most of clinical studies found the use of PRF positive at wound healing. According to the results of clinical studies, the use of PRF provides an advantage in soft tissue healing, reducing swelling and trismus and increasing patient comfort. However evidences on maintaining pain is scarce and pain usually adhere on early formation of soft tissue healing [12].

### **1.4 PRF in periodontal treatment**

PRF can also be used in regenerative periodontal therapy to enhance hard and soft tissue wound healing and promote periodontal tissue regeneration. Various studies have shown the favorable benefit of using PRF as an adjunct to traditional periodontal surgical techniques. These studies all exhibit improved clinical outcomes regarding key clinical parameters such as clinical attachment level and pocket depth with the use of PRF when compared to conventional techniques applied alone.

The rationale behind this benefit is believed to lie in the differentiation and proliferation inducing abilities of PRF. The rich source of bioactive cells within PRF itself stimulate the local environment and regulate the inflammation process,

thereby enhancing periodontal wound healing and reducing postoperative discomfort. In addition to these benefits the PRF sample also inherently supplies growth factors, releasing them slowly into the wound for 7–14 days. Other obvious benefits include graft stabilization. Furthermore, a possible antimicrobial effect of L-PRF is also present [13].

Another reason for PRF being favored in periodontal therapy is its multi-purpose nature. The centrifuged buffy coat can be used alone in defects, combined with particulate graft materials or as a thin membrane covering in regeneration techniques. Studies also show that PRF can be used as an alternative to connective tissue grafts (CTG) in periodontal plastic surgery owing to its cellular contents. Additionally, the many benefits of PRF use in periodontal therapy also include its graft stabilization, wound sealing and hemostatic abilities. Evidently, along with its favorable biologic outcomes and low-cost PRF seems to be almost ideally suited for various periodontal purposes [13, 14].

The performance of PRF in different periodontal surgery indications was measured and PRF was found to perform superiorly when compared to conventional perio-plastic surgeries applied alone. Its use in intra-bony defects and furcation defects have proved beneficial in reducing pocket depth values, clinical attachment level gains and bone fill percentages. Improved outcomes in intrabony defects were obtained when used alone or in conjunction with other biomaterials. In furcation defects also, traditional flap surgeries tended to perform better when complemented with PRF. Coronally Advanced Flap (CAF) procedures showed improved results when accompanied with either CTGs or PRF membranes. Compared to each other however, these two materials seemed to perform similarly. Therefore, it can only be said that PRF can be considered a suitable alternative to CTGs in periodontal plastic surgery [14, 15].

### 1.5 PRF in sinus lifting

Implant rehabilitation success is highly related with sufficient bone volume and density. The posterior maxilla represents a challenging and unique area for successful dental implant rehabilitation because of its relatively deficient bone volume and poor bone quality caused by alveolar bone resorption and maxillary sinus pneumatization. Rehabilitation of posterior maxillary bone volume has been successful by different procedures, such as Le Fort I osteotomies, onlay grafts and sinus lifts [16, 17]. Maxillary sinus floor elevation is considered one of the most successful procedures that can be performed using different grafting materials, such as autogenous, xenograft, allograft, alloplast and PRF [18, 19].

Autogenous bone with osteogenic, osteoinductive and osteoconductive properties is still considered to be the gold standard. However, grafting with autogenous bone is associated with donor site morbidity, extended duration of surgical procedures and the volume of bone graft harvested may be insufficient for the requirements. Biomaterials, thus, are promising substitutes for autogenous bone grafts in maxillary sinus augmentation. Osteoconductive properties of these biomaterials have been shown in clinical studies with satisfactory clinical outcomes.

On the other hand, these bone graft materials demonstrate lack of osteogenic and osteoinductive potential with distinct osteogenic capacity and bone formation. Moreover, some disadvantages, mainly related to a limited availability, prolonged healing time and impact on host responses can appear when using these bone substitutes. To overcome these problems, new substances with osteoinductive properties, such as platelet-rich fibrin (PRF) was recently introduced as replacement or additional materials in sinus augmentation procedures [20].



The biologic mediators have osteoinductive properties and they are considered to accelerate the formation of new bone and to reduce the time interval. The strengths of PRF comes from promoting the vascularization of bone tissue, reducing tissue inflammation, improving scaffold mechanics and accelerating new bone formation [20]. Newly, researchers have paid greater attention to the success of PRF application in maxillary sinus lifting procedures, but no consensus has been reached. Some researchers have reported positive effects of PRF application in sinus augmentation procedures.

Platelet concentrates have been used to accelerate bone generation and improve healing by releasing growth factors such as transforming growth factor  $\beta$ 1 and  $\beta$ 2, platelet-derived growth factor and vascular endothelial growth factor, which are able to induce angiogenesis and activate cell proliferation.

In the literature there are some different application techniques for PRF in the sinus augmentation such as PRF as a sole grafting material, PRF with allografts or PRF with xenografts. All of these techniques have variable clinical, radiographic and histologic and histomorphometric outcomes.

Mazor et al. [21] and Simonpieri et al. [22] performed sinus lift by using lateral approach and PRF was used as a sole grafting material and implants were applied immediately to serve as tent pegs. During the healing period there were no complications. A 100% survival rate was observed in total of 57 sinus lift procedures and 110 implants during the follow-up period (2 years). Radiographic examination was performed by CT scan or panoramic radiographs about 6 months after the sinus augmentation to examine the bone volume, where the average bone gain was 9.8 mm. Histologic and histomorphometric examination accomplished by Mazor et al. showed that dense collagen matrix, easily identified osteocytes and osteoblasts in the lacunae and well-organized and vital bone with structured trabeculae with more than %30 bone matrix.

Choukroun et al. [23] performed sinus augmentation with PRF in combination with demineralized freeze-dried bone allograft (DFDBA). They found the rate of vital bone/inert bone%20 both in test and control group but with a reduced healing time at PRF group.

Zhang et al. [24] applied the PRF/xenograft mixture for the test group and xenograft as a sole graft material for the control group. They found no statistically significant difference between the two groups.

In light of this information, although there is not a consensus statement about the effect of PRF as a grafting material at sinus lifting procedure, still it is a good alternative material with its osteoinductive properties to enhance hard tissue healing.

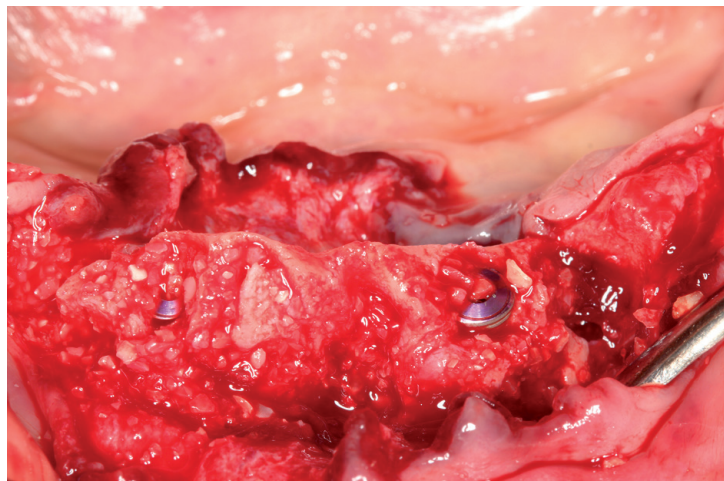
## **1.6 PRF for preserving bone around implants**

Marginal bone loss is an inevitable process which starts immediately following implant placement. There have been done plenty of studies since decades to minimize it. Previous studies about preserving bone around implants, has focused on soft tissue thickness and it was hypothesized, adequate soft tissue volume around implants has a positive effect in preserving marginal bone and PRF is perfect material to augment soft tissue. We know PRF is a good autologous material to enhance soft tissue healing with its growth factors including VEGF, PRGF, etc. However researches about PRF usage to augment hard tissue have contradictory results and there is need to do further detailed randomized controlled clinical studies to know about the effect of PRF preserving marginal bone [25] (**Figures 6** and **7**).

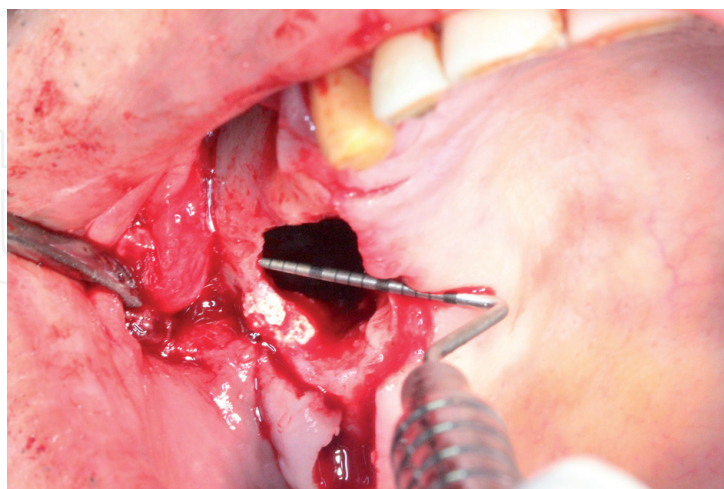




**Figure 6.**  
*Liquid PRF combined with MPM (Mineralized Plasmatic Matrix) and B-TCP graft material for sinus lifting.*



**Figure 7.**  
*PRF pieces combined with xenograft in guided bone regeneration.*



**Figure 8.**  
*Large sinus membrane perforation.*

### 1.7 PRF in rare clinical scenarios

PRF could also be beneficial with growth factors including in rare clinical scenarios such as cyst treatment, sinus membrane perforations, oroantral fistulae closure and osteonecrosis.

Oroantral fistula (OAF) constitution is defined a pathological way between maxillary sinus and oral cavity. It is an unnatural epithelial connection filled with granulation tissue or polypoid extension of sinus membrane. It can either come into existence spontaneously following a large maxillary cyst or tumor or as iatrogenic after tooth extraction or dental implant surgery [26]. An OAF is highly iatrogenic and depending on the perforation of sinus membrane during surgical interventions at maxilla. Either this or that way the treatment of perforated sinus membrane is bringing the tissue free from infection, cleaning the epithelium and repairing the membrane (**Figure 8**).

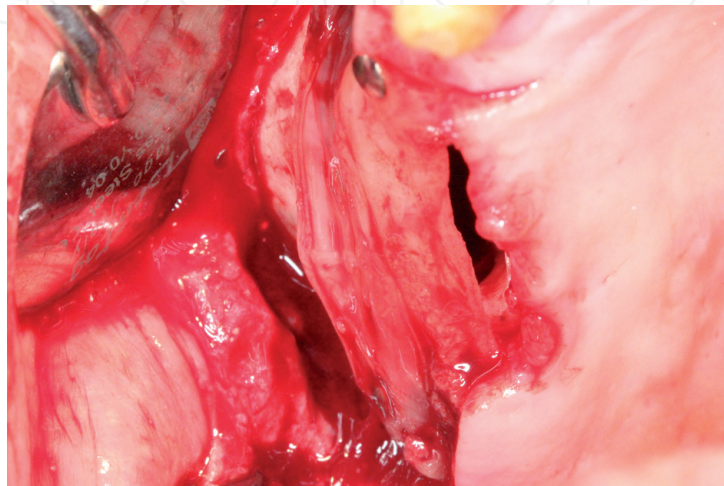
There are plenty of methods maintaining with OAF. PRF is one of them which is recently introduced. The technique is as following; PRF clots obtained by centrifugation should be isolated from PPP (Platelet Poor Plasma) and red blood cells, prepared as thin membranes and applied perforated area layer by layer. The researches about PRF in OAF closure conclude that, wound healing is faster and there was an increase in soft tissue thickness during healing. Due to its natural ingredients, there are no need to use additional materials, thus less donor site morbidity occurs.

Osteonecrosis is another rare clinical scenario which is defined as avascular bone area surrounding soft tissue on occasion. Various clinical and medical considerations can cause osteonecrosis. It can occur in consequence of bisphosphonates (including denosumab), medications or iatrogenic dental malpraxis (In proper use of NaOH<sub>2</sub>, formaldehyde, devitalizing agents). Either this or that way the healing of necrotic bone takes 8 weeks at least in appropriate circumstances. Osteonecrosis can conclude either with a demarcation line or heal just as avascular necrosis. Clinician should choose the treatment modality according to the clinical situation.

The main factor of osteonecrosis is the disturbance of vascular blood supply. The management of patient with compromised healing in bone is controversial. Despite the conventional treatment modalities, curettage of necrotic bone, antibiotic usage, chlorhexidine glukonate; with more complex treatment modalities hyperbaric oxygen therapy, ozone and low dose laser; PRF utilization alone or with these treatment modalities takes place in recent years (**Figure 9**) [27].

The use of PRF in cyst depends on the same rationale with the enhancement of soft and hard tissue healing. Researches related to this topic conclude that using PRF as a graft material is beneficial for shortening healing time and increasing bone mineral density (**Figures 10–12**).

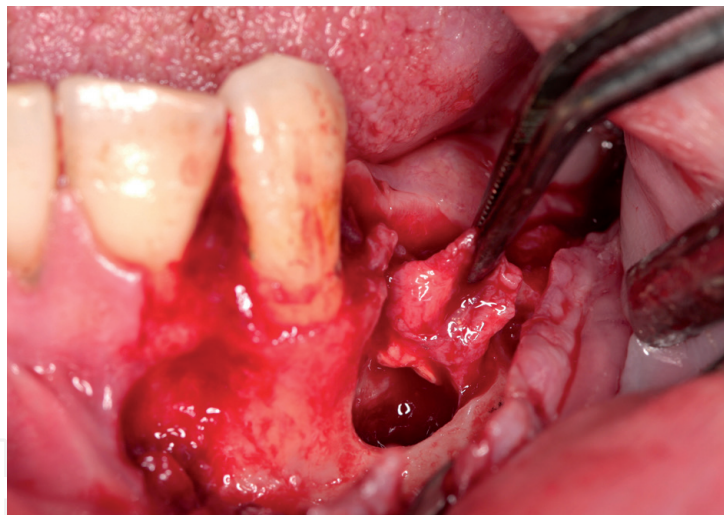
Since it has been discovered the synergetic effect of PRF in healing enhancement of covering oral mucosa, these platelet derivatives became even more important. PRF



**Figure 9.**  
*Sinus membrane perforation closure with PRF membrane.*



**Figure 10.**  
*2 weeks follow up after PRF application of avascular necrosis area in mandible.*



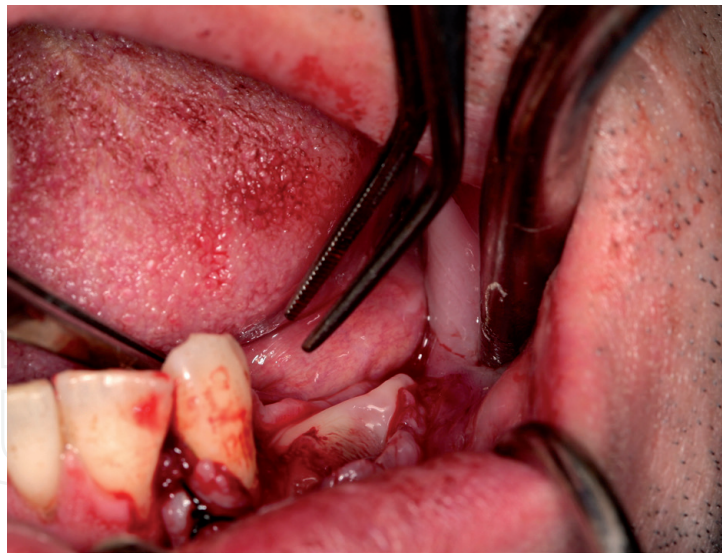
**Figure 11.**  
*Radicular cyst enucleation.*

involves cytokines, chemokines, and antimicrobial derivatives with growth factors such as VEGF, which are crucial to support hard and soft tissue in order to heal (**Figure 13**).

## 2. Conclusion and future perspectives

PRF with its strong fibrin matrix, including growth factors and slow release, has a positive effect on wound healing. The most important factor for success in oral surgical procedures is early wound healing. This improvement will decrease the healing time and enhance relatively the healing of underlying bone. PRF's effect on decreasing pain, swelling and edema is evidenced based. Thus it is very promising material in applications mostly associated with soft tissue healing such as third molar extractions, oroantral fistula closure and alveolar cleft reconstructions.





**Figure 12.**  
*PRF utilization after cyst enucleation.*



**Figure 13.**  
*Healing 2 months follow up after PRF augmentation.*

However studies have sparsely mentioned about the positive effect of new bone formation at sinus lifting, periodontal and peri-implant bone preservation and alveolar bone augmentation. For future perspectives, with the use of new generations of PRF with increased growth factor capacity, combined with graft materials, PRF will appear in more areas in oral surgery applications.

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### **Conflict of interest**

The authors declare no conflict of interest.



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