



Bone regeneration around immediate placed implant of molar teeth with autologous platelet-rich fibrin

Two case reports

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Abstract

Rationale: There are some challenges concerning immediate implant placement in molar region. Platelet-rich fibrin (PRF), a second generation platelet concentrate, is an autologous fibrin matrix and contains platelets, growth factors, and leukocytes. It is used for tissue healing and regeneration in periodontal and oral-maxillofacial surgery. We report 2 cases of immediate placed implant of molar teeth with autologous PRF to improve and accelerate tissue healing.

Patient concerns: Case 1 was a 38-year-old female patient with masticatory discomfort. Case 2 was a 43-year-old male patient with a demand for his left mandibular posterior tooth restoration.

Diagnoses: Through the clinical and radiographic examination, the patient in case 1 was diagnosed with vertical root crown fracture of the maxillary right first molar. The patient in case 2 was diagnosed with residual root of the left mandibular first molar via cone-beam computer tomography and clinical examination.

Interventions: The 2 patients underwent extraction of the molar teeth and immediate placed implant of molar teeth with autologous PRF was performed. In case 1, the gap between the implant surface and the socket walls of freshly extracted tooth was filled with PRF mixed with a commercial spongious bone substitute, followed by 2 PRF membranes coverage for protection. In case 2, PRF was used as a sole bone substitute material, placed between immediate implant and the socket wall of freshly extracted tooth.

Outcomes: Follow-up of 2 cases revealed successful osseointegration and matured gingiva with optimal form and function.

Lessons: The results suggested that PRF could solely serve as a bone scaffold in 4-wall bony defects, or can be combined with xenograft in 3-wall bony defects during immediately placed implants in molar regions, exhibiting excellent biocompatibility and good soft and hard tissue healing.

Abbreviations: CBCT = cone-beam computer tomography, PRF = platelet-rich fibrin.

Keywords: bone regeneration, immediate implant placement, molar tooth, platelet-rich fibrin

1. Introduction

Recently, immediate implant placement has rapidly gained popularity as this procedure definitively shortens the duration

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Received: 16 June 2018 / Accepted: 9 October 2018 http://dx.doi.org/10.1097/MD.000000000013058 of the treatment, reduces the number of surgical sessions, and minimizes the discomfort of patients. However, the clinical effectiveness of immediate implantation in the molar regions has rarely been challenged. It has been reported that immediate implant placement does not seem to counteract alveolar ridge alteration and reconstruction after tooth extraction.^[1] However, the application of inorganic bone grafts with/without barrier membranes simultaneously to immediate implant placement could reduce the extent of the horizontal resorption of the original buccal dimension to about 15%.^[2]

Compared with platelet-rich plasma, platelet-rich fibrin (PRF) has several advantages including easier preparation, denser fibrin, and not requiring chemical manipulation of the blood.^[3] The 3-dimensional mesh architecture of PRF can capture platelets, white blood cells, cytokines, growth factors, and matrix glycoproteins during a centrifugation process after an anticoagulant-free blood harvest.^[4] It is hypothesized the natural fibrin framework of PRF protect growth factors from proteolysis, and slow release of polypeptide growth factors such as transforming growth factor $\beta 1$, platelet-derived growth factor, vascular endothelial growth factor, and matrix glycoproteins gradually over at least 1 week, which are beneficial for promoting bone regeneration.^[5] PRF was found in a time-dependent manner to increase the proliferation of osteoblasts and up-regulate osteoprotegerin production in osteoblasts, which inhibits the



Figure 1. Preoperative and intraoperative photographs of case 1. (A) Clinical view of the vertical root crown fracture; (B) radiographic aspect of the tooth.

differentiation of osteoclast.^[6] Moreover, several clinical studies also indicated the use of PRF as the sole filling material during a simultaneous sinus floor elevation and implantation achieved a noticeable bone again.^[7] In addition, interleukin (IL)-1 β , IL-4, IL-6, vascular endothelial growth factor, and transforming growth factor- α released from PRF play important roles in regulation of inflammation.^[8] Literatures stated that PRF might enhance the healing and regeneration of soft and hard tissue, and reduce the side effects simultaneously.^[9]

This report describes 2 clinical cases in which implants placed immediately into fresh extraction sites of molar teeth with PRF solely or PRF mixed with a xenograft (Bio-oss) as filling materials.

2. Case report

For both cases, informed written consent was obtained from the patient for publication of this case report and accompanying images

2.1. Case 1

A 38-year-old female patient presented to the Department of Oral Implantology with masticatory discomfort. Her medical history was unremarkable, but clinical examination found that the maxillary right first molar presented with silver amalgam filling treated and vertical root crown fracture in mesial-distal direction (Fig. 1A). The available bone height and furcation defect were evaluated using the panoramic radiography (Fig. 1B). This patient had good oral hygiene, good systemic health, and without any contraindications to implant surgery. After extensive discussion with the patient, a treatment plan was immediate postextractive implantation of the fractured tooth.

Patient rinsed with 0.12% chlorhexidine mouthwash for 3 min/time for 3 times before the operation. After local anesthesia using articaine with adrenaline 1:100000, #16 was removed as atraumatically as possible and the socket walls were debrided and irrigated (Fig. 2A). A surgical procedure of osteotome-mediated sinus floor elevation was performed. To get adequate primary stability, an implant (NobelReplace, Sweden, $\Phi 5.0 \text{mm} \times 13 \text{ mm}$) was inserted with a torque of at least 35 N/cm. A gap between the

implant surface and the socket walls can be observed after implant placement (Fig. 2B). Before the surgical procedure, 20 mL whole blood was taken without artificial biochemical modification in 2 glass-coated plastic tubes and was immediately centrifuged at 3000 rpm for 10 minutes. A natural fibrin clot was formed in the middle of the tube. To fill the space around the implant, a mix of the bottom part of 1 PRF and deproteinized bovine bone (Bio-oss 0.25–1 mm; Geistlich Biomaterials, Switzerland, 0.25 g) was placed (Fig. 2C). Finally, the rest of PRF clots were pressed into membranes with sterile dry gauze and covered the bone graft as a barrier (Fig. 2D), and nontight suture was used with 4-0 polyglactin dyed vicryl sutures (Fig. 2E).

The patient received antibiotic therapy with cefuroxime axetil 0.25g q12h and tinidazole tablets 0.5g bid for 5 days after surgery. Chlorhexidine (0.12%) was used for mouthwash for 7 days in accordance with the instruction. The patient was instructed to use modified oral hygiene procedures and informed to avoid chewing in the surgical area.

At 6 months after the surgery, the periapical x-ray examination of the tooth demonstrated a better osteointegration (Fig. 3A). Also, the tissues presented a positive healing characteristic (Fig. 3B). During re-entry surgery, new bone regeneration around the neck of implant was found (Fig. 3C). After healing abutment (NobRpl WP, Sweden, Φ 6.0mm × 5.0mm) was placed for 2 weeks, the keratinized gingiva presented a cuff morphology, and the width of keratinized gingiva was wider than 2 mm (Fig. 3D). Two weeks later, the morphology of the cuff was stable. When a zirconia ceramic crown was constructed, the final result appears to be satisfactory.

2.2. Case 2

A 43-year-old male patient, without any systemic disease, came to the Department of Oral Implantology, demanded to restore his left mandibular posterior tooth. Clinical examination showed his left mandibular first molar was a residual root. The cone-beam computer tomography (CBCT) show the distance between the apex of #36 and inferior alveolar nerve was greater than 12 mm (Fig. 4). Patient had good oral hygiene without any contraindications to implant surgery. After extensive discussion, the patient referred for immediate implant placement.



Figure 2. Intraoperative photographs and illustration describing each step of the surgery. (A) The tooth was carefully removed; (B) a bone defect gap around the implant; (C) A mix of PRF and Bio-oss fully filled in the space; (D) 2 PRF membranes covered the alveolar crest; (E) no-tight suture was applied.

Patient rinsed with 0.12% chlorhexidine mouthwash for 3 min/ time for 3 times before the operation. After local anesthesia using articaine with adrenaline 1:100000, the tooth was carefully removed, and a thorough curettage of socket walls was performed to clean any remaining granulation tissue (Fig. 5A). Afterwards, an implant (SLA, Straumann, Switzerland, Φ 4.8mm × 10 mm, bone level implant) was placed into the fresh extraction site with an insertion torque of 35 N/cm. The bone and soft tissues around the implant were insufficient (Fig. 5B). The PRF membranes were prepared as mentioned in case 1. Afterwards, the PRF membranes as grafting materials were packed into the space between the implant and the fresh extraction site to regenerate the bone (Fig. 5C) and periodontal tissue without tight suture.

Postsurgical care included the administration of antibiotic for 5 days (500 mg azithromycin), and mouthwash followed the instructions for 10 days (0.12% chlorhexidine). Patient was



Figure 3. Postoperative photos of case 1. (A) Periapical radiographs aspect 6 months postsurgery; (B) clinical view of surgery site at 6-month follow-up; (C) bone regenerated around the neck of implant; (D) keratinized gingiva formed a cuff and the morphology was stable.



Figure 4. Preoperative CBCT of case 2. The preoperative CBCT exhibited the alveolar ridge height of 36 was greater than 12mm. CBCT=cone-beam computer tomography.

instructed to use modified oral hygiene procedures and informed to avoid chewing in the surgical area.

Three months later, the regeneration of periodontal tissue was visible under clinical examination, and the keratinized gingiva formed a cuff (Fig. 6A). Then a final restoration was fabricated (Fig. 6B). The periapical film demonstrated that the space around the implant was filled with a dense bone-like tissue (Fig. 6C). The clinical and periapical x-ray examinations revealed the alveolar bone and gingival margin has stabilized at a 4-month follow-up (Fig. 7A and B). The clinical examination and the radiological examination by CBCT showed the alveolar ridge height around the implant and the gingival margin were not remarkably changed at a one-year follow-up (Fig. 7C and D).

For both the above cases, ethical approval was not required, because there are no pictures in which the patients are not identifiable. For both patients, informed consent agreement was signed before surgery.

3. Discussion

Immediate implant placement has several advantages, including decreased rehabilitation treatment time, fewer surgical sessions,



Figure 5. Intraoperative photographs of case 2. (A) The tooth was carefully removed; a thorough curettage of socket walls was performed; (B) the bone and soft tissue around the implant were insufficient; (C) PRF membranes as grafting materials were filled into the space around the implant. PRF=platelet-rich fibrin.

and positive psychological impact on the patient. Most available studies on immediate implant placement have described their use in the anterior area for aesthetic reason. Few studies have focused on immediate implantation in molar area. A recent clinical study showed that immediate dental implantation in molar and premolar regions had better clinical and radiographic outcomes than delayed dental implanta-tion.^[10] Kamel and Abd-Elwahab^[11] Radi have proved that immediate implant placement could be an alternative to delayed implants in molar regions through a randomized clinical trial (RCT). Recently, bovine xenograft grafting combined PRF was successfully applied on the top of the extraction socket, indicating that this guided bone regeneration (GBR) technology can promote the release of growth factors and proteins during the first few days and accelerate the healing of soft tissue in immediate implant placement.^[12] Therefore, immediate implant placement with suitable GBR technology will become a more favorable surgical approach in posterior area.

However, because of the anatomic and physiologic limitations, the immediate placement of dental implants in the posterior maxillary and mandibular regions presents specific challenges, which may be adversely affected by the bone defect, insufficient soft tissue for closure, and flap dehiscence over the extraction site.^[13] A literature review of the most common biomaterials used for immediate dental implants concluded that the appropriate graft material can increase the level of immediate implant osseintergration.^[14] Deproteinized bovine bone has been widely used as excellent bone substitute material in regenerative dentistry. However, compared with autogenous bone deproteinized bovine bone demonstrated an inferior osteogenic potential.^[15] The other problem with the grafts was the flap closure. Once exposures had occurred, it could seriously affect the effect of bone augmentation, even lead to implant failure.

Platelet-rich fibrin is increasingly applied to oral implantology as it may affect both hard and soft tissue healing through the sustained release over time of growth factors. Choukroun et al^[16] suggested using PRF in company with freeze-dried bone allograft in sinus lift reduced the healing time by half. A mixture of PRF with a bone graft placed in bone defects around implant in case of immediate implant achieved satisfactory clinical results.^[17] In a recent clinical trial, the effect of a combination of PRF and demineralized freeze-dried bone allograft at a proportion of 1:1 (v/v) for the treatment of infrabony periodontal defects is particularly significant.^[18] The fibrin of PRF enriched with polypeptide growth factors. When mixed with bone graft, the



Figure 6. Postoperative photos of case 2. (A) The keratinized gingiva presented a cuff morphology; (B) final prosthetic crown was fabricated 3 months postsurgery; (C) the radiograph demonstrated that the space around the implant was filled with a dense bone-like tissue.

fibrin of PRF favors the migration of osteoprogenitor cells to the center of the graft, and allows the association of some growth factors involved in the angiogenic process.^[19] In case 1, the PRF as grafting materials with deproteinized bovine bone was packed into the space between the implant and the fresh extraction site,

and in case 2, considering that the bone defects around the implant were less and bone walls were intact, the PRF as the grafting materials alone was used. In both cases, the PRF increased local cytokines and growth factors, reduced local inflammation, and promoted the formation of new bone. There were no allergic reactions, and the radiographic parameters revealed the new bone formation was found in the both cases (Table 1). The finding was similar with other studies that revealed that PRF was used with other biomaterials in bone regeneration (GBR).^[20] A pilot study showed growth factor concentrated mainly on lower-thirds, the bottom part of PRF.^[21] Likewise in case 1, we selected the bottom part of PRF to mix with deproteinized bovine bone.

Regenerative techniques have been widely tested with membrane alone, whether the membrane is absorbable or not, and the membrane in conjunction with bone substitutes.^[1,14] Some hold that application of bone substitutes accompanied with a membrane has shown significant effects on preserving alveolar ridge height, and also ridge width, [22,23]¹ but this idea is controversial.^[2,24] In case 1, we used PRF membrane to cover the graft material. The PRF concentrates almost all leukocytes of the blood harvest.^[3] Moreover, it was documented that plateletderived growth factor, epidermal growth factor, vascular endothelial growth factor, and TGF-B are important factors for soft tissue repair.^[25] When released from PRF, these growth factors played important roles in differentiation, migration, and proliferation of cells, leading to soft tissue regeneration promotion. Therefore, the PRF membranes covering the alveolar crest can not only play the role of mechanical barrier, protecting open wounds from oral environment and preventing infection, but also provide substrate for cell migration, inducing soft tissue regeneration. In the 2 cases, the width of the keratinized gingiva was more than 2 mm (Table 1). The results of this study indicated the effect of PRF on the gingival regeneration in accordance with similar studies.^[26,27] Because PRF is easy and inexpensive to prepare, and exists in the form of PRF clots and membranes that may affect both hard and soft tissue healing through the sustained release over time of growth factors, such auto-biomaterial may be an alternative to classic GBR procedures for alveolar bone preservation with immediate implant placement.^[3] Nevertheless, the major limitation of these 2 cases is that the individual medical condition may affect the effect of PRF on hard and soft tissue regeneration.

4. Conclusions

Though only 2 patients were treated, the follow-up results of clinical view and radiographic demonstrated that: this procedure, using PRF solely as a bone scaffold in 4-wall bony defects or combine with xenograft in 3-wall bony defects, is suitable for use during immediately placed implants in molar regions; and PRF could enhance the regeneration of soft and hard tissue.

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Author contributions

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Figure 7. Follow-up photos of case 2. (A and B) The alveolar bone and gingival margin has stabilized at 4 months; (C and D) intraoperative photographs and CBCT show that the alveolar ridge height around the implant and gingival margin were stabilized at 1-year follow-up. CBCT = cone-beam computer tomography.

Table 1

Clinical details of patients in 2 cases.

	Age	M/F	Smoker	Teeth replaced	Type of defect	Surgical protocol	Allergic reactions	Osseointegration (wks)	Keratinized gingiva
1	38	F	Ν	#16	3-wall bony defects	GBR: deproteinized bovine bone + PRF; PRF as a barrier	Ν	24	≥2 mm
2	43	Μ	Ν	#36	The wall was intact	PRF	Ν	12	≥2 mm

F=female, M=male.

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References

- Clementini M, Tiravia L, De Risi V, et al. Dimensional changes after immediate implant placement with or without simultaneous regenerative procedures: a systematic review and meta-analysis. J Clin Periodontol 2015;42:666–77.
- [2] Chen ST, Darby IB, Reynolds EC. A prospective clinical study of nonsubmerged immediate implants: clinical outcomes and esthetic results. Clin Oral Implants Res 2007;18:552–62.
- [3] Dohan Ehrenfest DM, Rasmusson L, Albrektsson T. Classification of platelet concentrates: from pure platelet-rich plasma (P-PRP) to leucocyte- and platelet-rich fibrin (L-PRF). Trends Biotechnol 2009;27: 158–67.
- [4] Kang YH, Jeon SH, Park JY, et al. Platelet-rich fibrin is a bioscaffold and reservoir of growth factors for tissue regeneration. Tissue Eng Part A 2011;17:349–59.
- [5] Dohan Ehrenfest DM, Bielecki T, Del Corso M, et al. Shedding light in the controversial terminology for platelet-rich products: platelet-rich plasma (PRP), platelet-rich fibrin (PRF), platelet-leukocyte gel (PLG), preparation rich in growth factors (PRGF), classification and commercialism. J Biomed Mater Res A 2010;95:1280–2.
- [6] Chang IC, Tsai CH, Chang YC. Platelet-rich fibrin modulates the expression of extracellular signal-regulated protein kinase and osteoprotegerin in human osteoblasts. J Biomed Mate Res A 2010;95:327–32.

- [7] 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.
- [8] Masuki H, Okudera T, Watanebe T, et al. Growth factor and proinflammatory cytokine contents in platelet-rich plasma (PRP), plasma rich in growth factors (PRGF), advanced platelet-rich fibrin (A-PRF), and concentrated growth factors (CGF). Int J Implant Dent 2016;2:19.
- [9] Lee JW, Kim SG, Kim JY, et al. Restoration of a peri-implant defect by platelet- rich fibrin. Oral Surg Oral Med Oral Pathol Oral Radiol 2012;113:459–63.
- [10] Kim JK, Yoon AJ. Clinical and radiographic outcomes of immediate and delayed placement of dental implants in molar and premolar regions. Clin Implant Dent Relat Res 2017;1–7.
- [11] Kamel S, Abd-Elwahab Radi I. Limited evidence suggests immediate implant placement could be an alternative to delayed implants in molar regions. J Evid Based Dent Pract 2018;18:260–2.
- [12] Valenzuela S, Olivares JM, Weiss N, et al. Immediate implant placement by interradicular bone drilling before molar extraction: clinical case report with one-year follow-up. Case Rep Dent 2018;2018:6412826.
- [13] Griffin TJ, Cheung WS. The use of short, wide implants in posterior areas with reduced bone height: a retrospective investigation. J Prosthet Dent 2004;92:139–44.
- [14] Santos PL, Gulinelli JL, Telles Cda S, et al. Bone substitutes for periimplant defects of postextraction implants. Int J of Biomater 2013;2013:307136.
- [15] Broggini N, Hofstetter W, Hunziker E, et al. The influence of PRP on early bone formation in membrane protected defects. A histological and histomorphometric study in the rabbit calvaria. Clin Implant Dent Relat Res 2011;13:1–2.
- [16] Choukroun J, Diss A, Simonpieri A, et al. Platelet-rich fibrin (PRF): a second-generation platelet concentrate. Part V: histologic evaluations of PRF effects on bone allograft maturation in sinus lift. Oral Surg Oral Med Oral Pathol Oral Radiol 2006;101:299–303.
- [17] Del Corso M, Mazor Z, Rutkowski JL, et al. The use of leukocyte- and platelet-rich fibrin during immediate postextractive implantation and

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loading for the esthetic replacement of a fractured maxillary central incisor. J Oral Implantol 2012;38:181–7.

- [18] Agarwal A, Gupta ND, Jain A. Platelet rich fibrin combined with decalcified freeze-dried bone allograft for the treatment of human intrabony periodontal defects: a randomized split mouth clinical trail. Acta Odontol Scand 2016;74:36–43.
- [19] Dohan Ehrenfest DM, Bielecki T, Jimbo R, et al. Do the fibrin architecture and leukocyte content influence the growth factor release of platelet concentrates? An evidence-based answer comparing a pure platelet-rich plasm (P-PRP) gel and a leukocyte- and platelet-rich fibrin (L-PRF). Curr Pharm Biotechnol 2012;13:1145–52.
- [20] Tatullo M, Marrelli M. Platelet rich fibrin in reconstructive surgery of atrophied maxillary bones: clinical and histological evaluators. Int J Med Sci 2012;9:872–80.
- [21] Nishimoto S, Fujita K, Sotsuka Y, et al. Growth factor measurement and histological analysis in platelet rich fibrin: a pilot study. J Maxillofac Oral Surg 2015;14:907–13.
- [22] Park SH, Lee KW, Oh TJ, et al. Effect of absorbable membranes on sandwich bone augmentation. Clin Oral Implants Res 2008;19:32–41.
- [23] Greenstein G, Carpentieri JR. Utilization of d-PTFE barriers for postextraction bone regeneration in preparation for dental implants. Compend Contin Educ Dent 2015;36:465–73.
- [24] Brkovic BM, Prasad HS, Rohrer MD, et al. Beta-tricalcium phosphate/ type I collagen cones with or without a barrier membrane in human extraction socket healing: clinical, histologic, histomorphometric, and immunohistochemical evaluation. Clin Oral Investig 2012;16:581–90.
- [25] Dohan DM, Choukroun J, Diss A, et al. Platelet-rich fibrin (PRF): a second-generation platelet concentrate. Part III: leucocyte activation: a new feature for platelet concentrates? Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2006;101:e51–5.
- [26] Aroca S, Keglevich , Barbieri B, et al. Clinical evaluation of a modified coronally advanced flap alone or in combination with a platelet-rich fibrin membrane for the treatment of adjacent multiple gingival recessions: a 6-month study. J Periodontal 2009;80:244–52.
- [27] Sculean A, Gruber R, Bosshardt DD. Soft tissue wound healing around teeth and dental implants. J Clin Periodontol 2014;41:6–22.