Application of advanced platelet-rich fibrin for through-and-through bony defect during endodontic surgery: Three case reports and review of the literature

Algahtani FN et al. Platelet-rich fibrin in endodontic surgery

Abstract

BACKGROUND

The use of advanced platelet-rich fibrin (A-PRF) membranes for guided bone and tissue regeneration in through-and-through defects after endodontic surgery was explored in three cases.

CASE SUMMARY

Herein, three patients presented to the endodontic clinic suffering from apical periodontitis, associated with large bone resorption and related to previously endodontically treated teeth. Periapical surgery was indicated in these cases and the osteotomy site was covered by A-PRF membrane. Cone-beam computed tomography (CBCT) was used to assess the cases before and after the surgery.

CONCLUSION

Four months post-surgery, the recall CBCT scan showed complete obliteration of the osteotomy with newly formed bone. A-PRF membrane showed promising results and was an advantageous addition to surgical endodontic treatment.

Key Words: Cone-beam computed tomography; Endodontic; Periapical disease; Platelet-rich fibrin; Surgery; Tunnel defect; Alveolar bone loss; Case report

INTRODUCTION
The major reason for failed periapical healing after primary endodontic therapy is the presence of bacteria and diseased tissue\textsuperscript{1}. Orthograde retreatment is the first treatment of choice for such cases. However, there are situations where it is not feasible, too complicated or unsuccessful. In such circumstances, apical surgery has proved to be a sound treatment option to save the tooth\textsuperscript{2}.

Modern technology, materials, and techniques have improved the prognosis of endodontic surgery\textsuperscript{2}. Cone-beam computed tomography (CBCT) enabled more accurate determination of the root anatomy and its proximity to critical anatomical structures such as the inferior alveolar nerve which led to better planning of the surgical approach\textsuperscript{3}. When the root-end resections and retrograde fillings are performed using microsurgical instruments with current materials and techniques, the success rates was 85\% to 97\%\textsuperscript{4}.

In certain clinical situations where lesions have eroded the lingual/palatal cortex (with or without erosion of buccal cortex), resulting in a through-and-through (tunnel) defect, the success of endodontic surgery is less predictable\textsuperscript{5-8}. Since the healing usually results in the development of scar tissue in the post-operative area\textsuperscript{5-7},

Mesenchymal stem cells are pluripotent cells that have the ability to differentiate into osteoblasts thereby promoting bone healing. This often depends on an adequate stimulator of stem cell gene expression, as well as the presence of platelet derivatives which include within them various pro-inflammatory markers that direct the cells’ maturation. Local administration of hormones, growth factors, ascorbic acid. Plasma derivatives has been advised to promote bone regeneration and soft tissue repair after oral surgery\textsuperscript{9,10}. Moreover, bone morphogenic proteins, parathyroid hormone, and enamel matrix proteins have been administered locally to increase the healing capacity of the surgical site\textsuperscript{9,11}. However, their usefulness in endodontic surgery is still debatable, and the benefits they bring to both surgeon and patient are modest and debatable\textsuperscript{12-14}.

Due to the local and continuous release of growth factors and proteins, platelet-rich fibrin (PRF) is frequently utilized to stimulate and accelerate soft tissue and bone
healing. This mimics the natural wound healing and reparative tissue processes\textsuperscript{[15]}. Because it is entirely composed of the patient's blood, PRF acts as a reservoir for growth factors that could be used without exposing the patient to immunogenicity or infection risks\textsuperscript{[16]}.

The use of such a specialized biomaterial in endodontic surgery has been discussed in case reports and a randomized clinical trial\textsuperscript{[17,18]}. However, many of these studies excluded through-and-through bony defects\textsuperscript{[17,18]}. Furthermore, many of these cases were assessed and evaluated solely through the use of periapical radiographs\textsuperscript{[19,20]}. As a result, the current study examined three clinical cases in which CBCT was used to assess the success of advanced platelet-rich fibrin (A-PRF) membrane for bone regeneration in through-and-through bony defects following periapical endodontic surgery.

**CASE PRESENTATION**

*Chief complaints*

**First case:** A 32-years-old female, medically fit and unaware of any allergies, was referred to the endodontic clinic for the assessment and treatment of the maxillary right second premolar. The patient complained of persistent pain while chewing, localized to the area of that tooth. The pain intensity was six out of ten according to the verbal numerical rating scale (VNRS).

**Second case:** A 24-year-old female patient was referred to the endodontic clinic for the assessment and treatment of the maxillary left second premolar. She was medically fit and unaware of any allergies.

**Third case:** A medically fit, 55 years-old female patient was referred to the endodontic clinic for assessment and treatment of the maxillary right lateral incisor.

*History of present illness*
**First case:** Root canal treatment (RCT) had been performed on that tooth several weeks ago, but it did not reduce the symptoms. She was prescribed 500 mg amoxicillin (500 mg) to be taken orally every eight hours with analgesics for five days. However, this measure did not help reduce the symptoms.

**Second case:** The patient received an RCT on her left maxillary second premolar a year ago, but was continuously complaining of mild pain while chewing, related to that tooth. The pain intensity was four out of ten according to the VNRS.

**Third case:** The patient had all ceramic dental crowns on the maxillary anterior teeth, placed three to five years ago.

**Physical examination**

**First case:** Upon clinical examination, the tooth had a permanent composite core restoration. It did not respond to the cold test, but was tender to the palpation and percussion tests. Periodontal probing was within the normal range.

**Second case:** Upon clinical examination, the tooth was restored with a porcelain fused to metal crown. Periodontal probing was within the normal range. It did not respond to the cold test, but was tender to percussion.

**Third case:** The tooth responded negatively to cold, percussion, and palpation. The radiographic examination revealed a localized radiolucency surrounding the apex of the maxillary right lateral incisor (Table 1). The tooth had an adequate RCT, a metallic post, and a ceramic crown. The radiographic quality of the recently performed RCT and crown were adequate

**Imaging examinations**
**First case:** The periapical radiograph showed a localized radiolucency surrounding the apex of the tooth, an overextended root canal filling in the buccal canal, and a fiber post-supported core restoration (Table 1).

**Second case:** The periapical radiograph showed a localized radiolucency surrounding the apex and the tooth had two canals (Table 1).

**Third case:** The radiographic examination revealed a localized radiolucency surrounding the apex of the maxillary right lateral incisor (Table 1). The tooth had an adequate RCT, a metallic post, and a ceramic crown. The radiographic quality of the recently performed RCT and crown were adequate.

**FINAL DIAGNOSIS**

*First case*

The endodontic diagnosis was previously treated with symptomatic apical periodontitis. Treatment options were discussed with the patient, and they included orthograde retreatment, periapical surgery, extraction, and no treatment.

*Second case*

The endodontic diagnosis was previously treated with symptomatic apical periodontitis. After discussing the endodontic treatment options with the patient, which included: Orthograde retreatment, periapical surgery, extraction, and no treatment, the treatment of choice was periapical surgery.

*Third case*

The endodontic diagnosis was previously treated with asymptomatic apical periodontitis. The risks and benefits of the treatment options: Orthograde retreatment, periapical surgery, extraction, and no treatment were discussed with the patient.
TREATMENT

First case
After the risks and benefits of each option were considered, the treatment of choice was periapical surgery. Small field of view (FOV) CBCT imaging was taken for the area and endodontic microsurgical protocol was followed (Table 2, Figure 1). The osteotomy site was covered by A-PRF membrane (Figure 1). The histological examination revealed granulation tissue. The patient responded negatively to the percussion and palpation tests two weeks and six months after the surgery.

Second case
After discussing the endodontic treatment options with the patient, which included: Orthograde retreatment, periapical surgery, extraction, and no treatment. The treatment of choice was periapical surgery, since the radiographic quality of the recently performed RCT was adequate, in addition, the tooth had been recently restored with an adequate crown. Small FOV CBCT imaging was taken for the area and endodontic microsurgical protocol was followed (Table 2, Figure 2). Upon accessing the root tip, the osteotomy site was void and filled with a small amount of blood. The osteotomy was proximal to the maxillary Schneider membrane. After the placement of MTA retro-filling material, the osteotomy site was covered by plasma and A-PRF membrane (Figure 2). A histological examination revealed a traumatic bone cyst. The patient responded negatively to the percussion and palpation tests two weeks after the surgery and at the four months follow up. The recall CBCT scan four months after the surgery showed obliteration of the osteotomy with newly formed bone. The patient was content that the procedure went well, and the prognosis was favorable.

Third case
The patient opted for periapical surgery. Small FOV CBCT imaging was taken for the area and endodontic microsurgical protocol was followed (Table 2, Figure 3). The osteotomy was closed with a bone graft and A-PRF membrane. The histological
examination revealed a radicular cyst. The patient responded negatively to the percussion and palpation tests two weeks and six months post-surgery. The recall CBCT scan four months after the surgery showed obliteration of the osteotomy with bone (Figure 3). The patient was content that the procedure went well, and the prognosis was favorable.

OUTCOME AND FOLLOW-UP

First case
The recall CBCT scan four months after the surgery showed obliteration of the osteotomy with newly formed bone (Figure 1). The patient was advised to have a permanent crown placed immediately. The patient was content that the procedure went well, and the tooth has favorable prognosis.

Second case
The recall CBCT scan four months after the surgery showed obliteration of the osteotomy with newly formed bone. The patient was content that the procedure went well, and the prognosis was favorable.

Third case
The recall CBCT scan four months after the surgery showed obliteration of the osteotomy with bone (Figure 3). The patient was content that the procedure went well, and the prognosis was favorable.

DISCUSSION
Non-surgical endodontic treatment was found to be successful in the management of dental periapical lesions[21,22]. This is related to the ability to eliminate microorganism within the root canal system and the absence of extra-radicular infection. However, a few cases cannot be managed by a non-surgical approach alone and require surgical intervention[1,4].
The modern approach to endodontic surgery has improved the prognosis of peri-radicular surgery\cite{4}. This modern endodontic surgery incorporates the use of CBCT, a microscope, ultrasonic tips, and bio-ceramic materials\cite{4}. Additionally, evidence-based methods were adapted for surgical flap design, root resection, and root end preparation\cite{4}. However, the prognosis of modern endodontic surgery is less predictable in cases with periodontal involvement or through-and-through (Tunnel) defects\cite{5-7}. A through-and-through defect in endodontic surgery is defined as a bony defect that has eroded the buccal and lingual plate caused by the inflammatory lesions, or as a result of buccal access during the osteotomy procedure, in the presence of eroded lingual bone\cite{8}. The first and third cases had inflammatory lesions that caused erosion of the buccal and palatal plates. However, in the second case, the buccal access during the osteotomy resulted in a through-and-through defect after the surgery, as the opposing palatal side was the maxillary sinus. In these configurations, three walls are present (mesial, distal, and caudal) and two walls are missing (buccal and lingual/palatal)\cite{8}. The healing of bone defects after peri-radicular surgery can be summarized in two main events: The first event is the healing of the surgical flap, which takes place during a few days, up to two weeks after surgery\cite{23}. The following event is the healing of the osseous defect, which takes place over several months\cite{24,25}. Usually, the complete healing of an osseous defect can take up to one year; however, the sign of progressive bone formation could become radiographically visible after six months\cite{25}. The use of CBCT for the evaluation of bone healing after periapical surgery is recommended\cite{26}.

The usefulness of guided tissue regeneration (GTR) for healing bony defects after peri-radicular surgery was debatable\cite{27}. However, techniques for GTR were considered in through-and-through defects to occupy the space in the bony defect and prevent marginal migration of epithelial cells\cite{27}. Since the epithelium turnover rate is faster than bony stem cells, scar tissue healing was seen in the absence of cortical bone in through-and-through lesions\cite{27}.

However, the disadvantage of external bone graft material and membranes is the possibility of infection and foreign body rejection\cite{28}. This can be seriously considered
when dealing with infectious lesions that could hold possible residual bacteria\textsuperscript{29}. Moreover, the addition of bony grafts and membranes will add to the expense of apical procedures, which could hinder access to care for a few patients.

The centrifuging machine used in this study produces three types of PRF: A-PRF, S-PRF, and I-PRF. The A-PRF is a smart blood concentrate that employs a higher amount of white blood cells in addition to platelet and fibrin to uniquely obtain the A-PRF membrane or plug\textsuperscript{30}. The white blood cells in the membrane or plug are meant to become active in stimulating the transformation of monocytes into macrophages\textsuperscript{30}. This rapid transformation will speed up the inflammatory cascade and stimulate bone healing\textsuperscript{30}. When the A-PRF to the PRF were compared in the regenerative endodontic procedure, it was found that the A-PRF increased the root thickness and length within 13 mo\textsuperscript{31}. This can be explained as the amount of growth factors released by the A-PRF was greater than PRF\textsuperscript{30}. Moreover, the use of bone graft in comparison to A-PRF clot alone in periapical surgery yielded in remarkable size reduction of the bony defect in the A-PRF group within 6 mo\textsuperscript{32}. The significant role of PRF in bony healing is the release of growth factors trapped in platelets that happens during the centrifugation\textsuperscript{33}. These growth factors are essential for the stimulation of cellular migration and proliferation\textsuperscript{33}. They also assist in guiding tissue maturation and remodeling which promotes healing in injured tissues\textsuperscript{32,33}.

The main objective of using the bone graft in the third case was to provide structural support and to prevent the A-PRF membrane from collapsing in the deep bony defect\textsuperscript{34}. The bone graft in this case was mixed with collected concentrated A-PRF blood clot to benefit from the growth factors embedded there to further promote bone healing. The presence of blood clot is essential to promote the osseousductive properties of bone graft\textsuperscript{35}. The histological studies confirmed that mixing the PRF with bone accelerates bone healing, as new bone formation was evident within 30 d to 60 d in animals and up to four months in humans\textsuperscript{36-38}. However, one of the disadvantages of the bone graft is that it has the same radiopacity as the bone, but it looks like bony chips with voids in the radiograph\textsuperscript{39}. In the present case report, the combination of the
radiographic appearance in the CBCT together with the absence of clinical signs and symptoms was sufficient to confirm the postsurgical healing.

Generally, the advantages of PRF membranes are their low expense and low risk of body rejection and infection\textsuperscript{[40]}. Not to mention that the use of PRF is recommended in the patients treated with bisphosphonates with periapical lesions to improve bone repair and prevent osteonecrosis\textsuperscript{[41]}. The PRF membrane was used to cover the bony defect in several case reports\textsuperscript{[17,18]}. In accordance with the present case report series, they found that PRF promoted accelerated bone healing evident after 6 mo\textsuperscript{[15]}. However, in many of these reports, the through-and-through defect was excluded\textsuperscript{[17,18]}. Moreover, this study incorporated CBCT to evaluate bone healing after using PRF in periapical surgery. The CBCT proved to be superior to periapical radiographs in sensitivity and specificity\textsuperscript{[42,43]}. The evidence of bone healing was seen in all cases at four months postsurgery, thus reducing the period needed to evaluate the short-term success of surgical endodontic treatment. The CBCT imaging was better than the periapical radiograph in identifying the volumetric changes in the size of the lesion after periapical surgery\textsuperscript{[44]}. Moreover, postsurgical cases that were identified as uncertain or incompletely healed in periapical radiographs can be classified in CBCT imaging\textsuperscript{[44]}. Especially in the third case, the CBCT was better at detecting bone healing after periapical surgery compared to the periapical radiograph.

While the short-term follow up could be considered a limitation of this study, the long-term prognosis of endodontic treatment is multifactorial. Factors such as coronal leakage and occlusal overload could contribute to the final outcome of the procedure, and it will be difficult to attribute the success of the procedure to the use of PRF membrane in periapical surgery\textsuperscript{[45]}. Moreover, short term recall and the use of CBCT allowed accurate assessment of the healing while reducing the incidence of patient dropout that usually happen in longer period. Recently, a randomized clinical trial used CBCT to evaluate the healing of postsurgical endodontic procedures after six months of the surgery only\textsuperscript{[52]}. The main reason for patient dropout in dental clinics was the improvement of symptoms\textsuperscript{[46]}. In all of the three presented clinical cases, patients were
asymptomatic two weeks after the surgery and the patients responded negatively to percussion and palpation. Further clinical studies that explore the benefits of using A-PRF in other complex clinical scenarios, such as apico-marginal bone defects, are recommended.

CONCLUSION
Within the limitations of this study, the use of A-PRF membrane for GTR in the management of through and through osseous defects was successful. In three cases, the use of A-PRF membrane resulted in the complete healing of peri-radicular tissue and the preservation of root canal-treated teeth that would otherwise be extracted. The advantages of A-PRF membrane in endodontic surgery were low expense, low risk of post-surgical infection, and foreign body rejection.

Figure Legends

Figure 1 Bone regeneration using advanced platelet-rich fibrin membrane in through-and-through bony defects following periapical endodontic surgery on the maxillary right second premolar. A: The cone-beam computed tomography (CBCT) shows localized radiolucency surrounding the apex of maxillary right second premolar. The lesion is perforating the labial cortical bone and displaced sinus periosteum upward which is a typical feature of periapical osteoperiostitis. The root canal treatment appears to be overextended with a uniform density; B: The CBCT shows bony healing of the resected area within four months; C: A clinical photo of the resected root; D: A clinical photo of the MTA retro-filling; E: The platelet-rich fibrin membrane handled using a tweezer and placed to seal the bony defect.

Figure 2 Periapical endodontic surgery on the maxillary left second premolar using advanced platelet-rich fibrin membrane. A: The cone-beam computed tomography
(CBCT) shows localized radiolucency surrounding the apex of the maxillary left second premolar in the sagittal section. There is a thin layer of the labial bone surrounding the apex and a displaced sinus periosteum upward which is a typical feature of periapical osteoperiostitis in the sagittal section. The root canal treatment appears to be adequate with a uniform density; B: The CBCT shows bony healing of the resected area within four months and a normal appearance of the maxillary sinus; C: A clinical photo of the labial bone before root resection; D: A clinical photo of the bony defect after resection shows a hollow space adjacent to the maxillary sinus; E: The platelet-rich fibrin membrane is used to seal the bony defect.

Figure 3 Periapical endodontic surgery on the maxillary right lateral incisor advanced platelet-rich fibrin membrane. A: The cone-beam computed tomography (CBCT) shows a well-defined radiolucency surrounding the apex of the maxillary right lateral anterior in the sagittal section. The lesion appears to be perforating the labial and palatal bone surrounding the apex in the coronal section. The root canal appears to be adequate and uniform in density; B: The CBCT shows the bone formation and healing surrounding the apex and bony defect within four months post-operatively in the coronal and sagittal section; C: A clinical photo shows the resected surface of the root and the bony defect; D: The placement of bone graft mixed with the blood clot; E: The platelet-rich fibrin membrane is used to seal the defect and hold the bone graft in place.
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