






# Endodontic-surgical- -orthodontic management of maxillary central incisor with root dilaceration and large apical periodontitis using leukocyte and platelet-rich fibrin

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Teeth with root dilaceration represents a challenge in clinical practice when an intervention is needed, especially in cases requiring a multidisciplinary approach to resolve the issue.

**Aim:** This report describes the root dilaceration of a maxillary central incisor with severe apical periodontitis, involving a 4-year follow-up of endodontic surgical-orthodontic management using leukocyte and platelet-rich fibrin (L-PRF).

**Methods:** The planning process included treating the root canal and the central maxillary incisor affected by distoangular root dilaceration, by using orthodontic repositioning of the neighboring tooth, and an endodontic and periapical surgical approach. The operative procedure used cone-beam computed tomography (CBCT) scans of the left maxillary central incisor, taken prior to orthodontic tooth movement maxillary lateral incisor. Orthodontic treatment was performed after the endodontic treatment, and followed by surgical management with periapical lesion curettage, apicoectomy, retro-preparation, retro-filling and grafting with L-PRF, resulting in a successful conclusion. **Conclusion:** The four-year clinical follow-up showed complete alignment of the maxillary lateral incisor and signs of periapical healing based on CBCT images.

**Keywords:** Periapical periodontitis. Apicoectomy. Cone-beam computed tomography. Endodontics. Orthodontics.



## Introduction

Root dilaceration is characterized by an abnormal curvature of the tooth root. Its causes may be related to specific syndromes, such as oculofaciocardiodental syndrome<sup>1</sup>, Kabuki syndrome<sup>2</sup>, Smith-Magenis syndrome<sup>3</sup>, Axenfeld-Rieger syndrome<sup>4</sup>, and the hypermobile type of Ehlers-Danlos syndrome<sup>5</sup>, congenital ichthyosis<sup>6</sup>, and traumatic injuries to the primary tooth, impacting abnormal root formation of its permanent successor<sup>7</sup>.

Although the causal relation of the last named is the most widely accepted hypothesis, it could be said that any mechanical trauma affecting the primary dentition will result in root dilaceration in the permanent dentition. This is because the prevalence of traumatic injuries is significantly higher than the occurrence of root dilaceration<sup>8</sup>. Therefore, other reasons of idiopathic origin must be considered. From an epidemiological point of view, root dilacerations may be found in both the primary and the permanent dentition. However, their incidence in permanent teeth is substantially higher<sup>7,8</sup>. This would partly explain their correlation with traumatic injuries sustained by predecessor teeth and affecting the formation of the permanent dental germ. As for the most prevalent location of root dilacerations, there seems to be no consensus in the scientific literature – some studies show that it is higher in posterior teeth and in the maxilla, while others show that approximately two thirds of the reported dilacerations occur in the mandible. Furthermore, there is no gender predilection<sup>7</sup>.

Mechanical trauma can cause not only root dilaceration<sup>8</sup>, but also pulp necrosis, which develops into apical periodontitis, if not diagnosed and treated early. Complex situations involving different clinical approaches require a high degree of planning. The diagnosis of root dilaceration and apical periodontitis do not always offer sufficient accuracy with two-dimension imaging, such as panoramic and periapical radiographs. Cone beam computed tomography (CBCT) has become an essential tool in diagnostic assessment and clinical planning, by interfering positively in decision making, and rendering more predictable and dependable prognoses<sup>9-12</sup>.

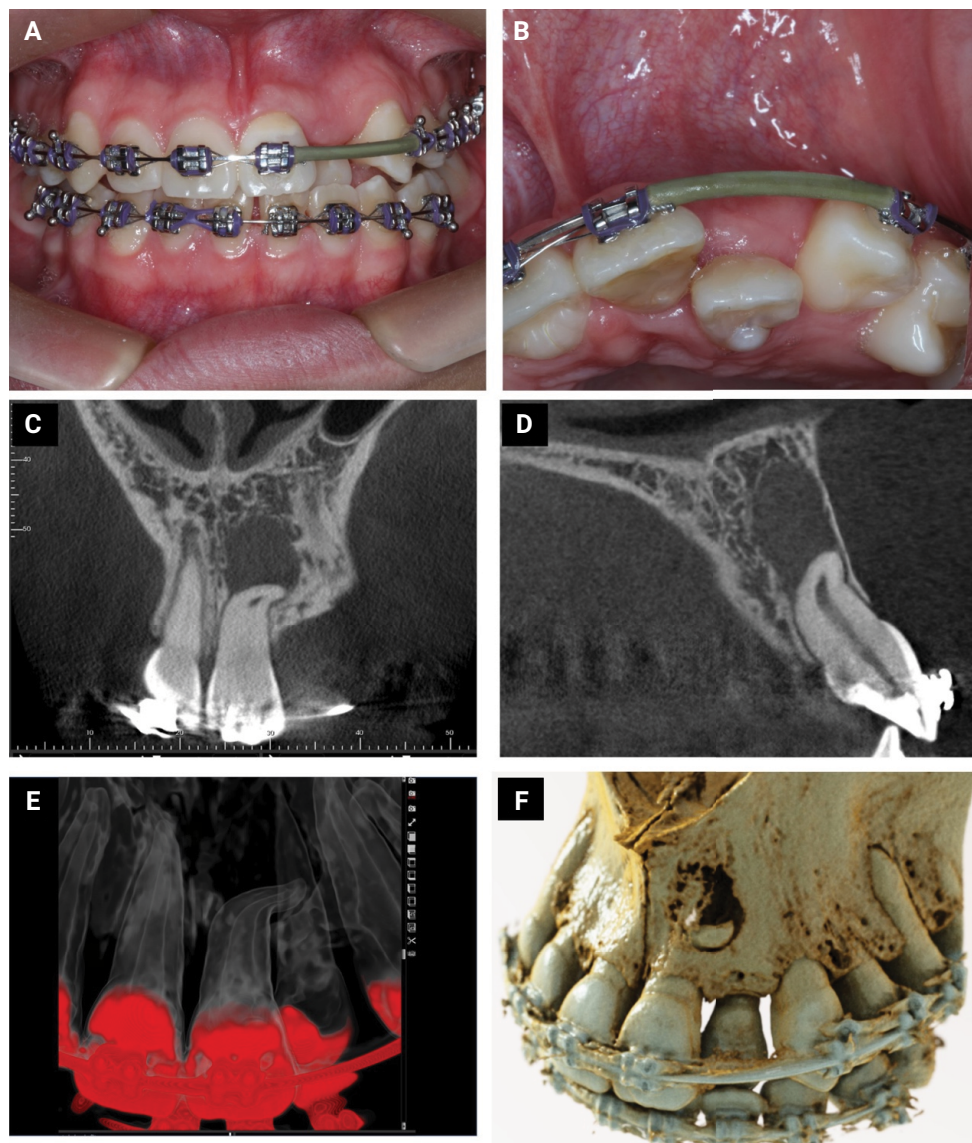
In addition to the benefits of newly developed diagnosis and planning technologies, the use of grafts, especially in large lesions, has been a practice frequently adopted by clinicians in periapical surgical interventions to promote an accelerated healing process and a better postoperative outcome. Among these grafts, platelet aggregates are viewed as interesting alternatives in surgical approaches to endodontic lesion repair, because they are rich in growth factors, promote cell differentiation, and function as a structural matrix in guiding tissue formation. The protocols for obtaining leukocyte- and platelet-rich fibrin (L-PRF) consisted of collecting 1 to 8 tubes of blood (9 to 10 ml, without anticoagulant) by venipuncture, and then centrifuging them at 2,700 or 3,000 rpm for 10-12 minutes. The fibrin can be used in macerated form as a filler, or mixed with other biomaterials, or else prepared as a membrane or buffer, by compressing it in a metal box under light pressure<sup>13</sup>. The clinical applications of L-PRF are based on four healing events optimized by using these membranes, namely angiogenesis, immune control, recruitment of surrounding

precursor cells, and the protection afforded by an epithelial envelope<sup>14</sup>. Angiogenesis consists of the formation of new blood vessels from other pre-existing ones. It requires an extracellular matrix that allows the migration, division, and phenotypic alteration of endothelial cells<sup>15</sup>. Its clinical applicability has gained recognition in implantology and minor oral surgery, such as surgeries of maxillary sinus lifting with and without the association of other biomaterials<sup>16-18</sup>, treatment of maxillary sinus membrane elevation following perforation, treatment of dehiscence / fenestrations and gingival recession, furcation defects and gingival plastic surgery, filling of fresh alveoli, and regenerative endodontic procedures associated with endodontic microsurgery<sup>15-25</sup>.

This study reported a clinical case involving a multidisciplinary approach to the endodontic-surgical-orthodontic management of a maxillary central incisor with root dilaceration, and large apical periodontitis lesions, using leukocyte- and platelet-rich fibrin, with a 4-year follow-up.

## Case Report

A 15-year-old female white patient, in good general condition, sought care at the Senador Canedo Dental Specialties Center, Goiás, Brazil, complaining of "crooked anterior teeth." She reported that she had started orthodontic treatment 4 years ago, and that her anterior teeth were still misaligned. Clinical examination revealed that an upper and lower fixed appliance, together with an open spring between teeth left maxillary central incisor and left maxillary canine, had been installed to gain space for the vestibularization of the palatinized left maxillary lateral incisor (Figure 1). There was no pain, nor were there any clinical signs of inflammation of the mucosa, such as fistula, erythema or edema. The patient was medically fit and healthy at the initial consultation. The patient's family history was non-contributory. CBCT scans (PreXion Inc., San Mateo, USA) were acquired to obtain a more accurate assessment, and promote more predictable planning. The imaging exams revealed severe root dilaceration and a circumscribed, periapical hypodense area around the apex of left maxillary central incisor, with destruction of the buccal cortical bone, and with the left maxillary lateral incisor palatal to the central incisor and canine (Figure 1). A dental team composed of specialists in the areas of endodontics, oral surgery, oral pathology, and orthodontics defined the planning strategy according to the results of the exams. After reviewing the risks, benefits, and treatment options with the patient and her parent, informed consent was obtained to perform the planning strategy on tooth left maxillary central incisor.



**Figure 1.** Upper and lower fixed appliance with an open spring between central incisor and canine, installed to gain space for vestibularization of left maxillary lateral incisor (A,B). CBCT scans show root dilaceration maxillary central incisor in the coronal and sagittal planes with a periapical hypodense area and rupture of the buccal cortical bone (C,D). Three-dimensional reconstruction - specific filter of e-Vol DX CBCT software program indicates apical periodontitis; photorealistic reconstruction images of the e-Vol DX CBCT software program confirm destruction of the buccal cortical bone (E,F).

A multidisciplinary approach was adopted based on diverse types of clinical intervention, starting with endodontic treatment, followed by apical surgery, and final orthodontic treatment, supported by radiographic clinical monitoring every 6 months.

### **Endodontic treatment**

Previous root canal treatment of left maxillary central incisor was performed using a 1012 diamond bur (KG Sorensen, SP, Brazil) for coronary access, followed by root

canal preparation with rotary Protaper Universal instruments (Dentsply Maillefer, Ballaigues, Switzerland) up to the F3 instrument, and filling of the canals with AH Plus root canal sealer, using the hybrid Tagger technique.

### ***Leukocyte and platelet-rich fibrin (L-PRF) preparation***

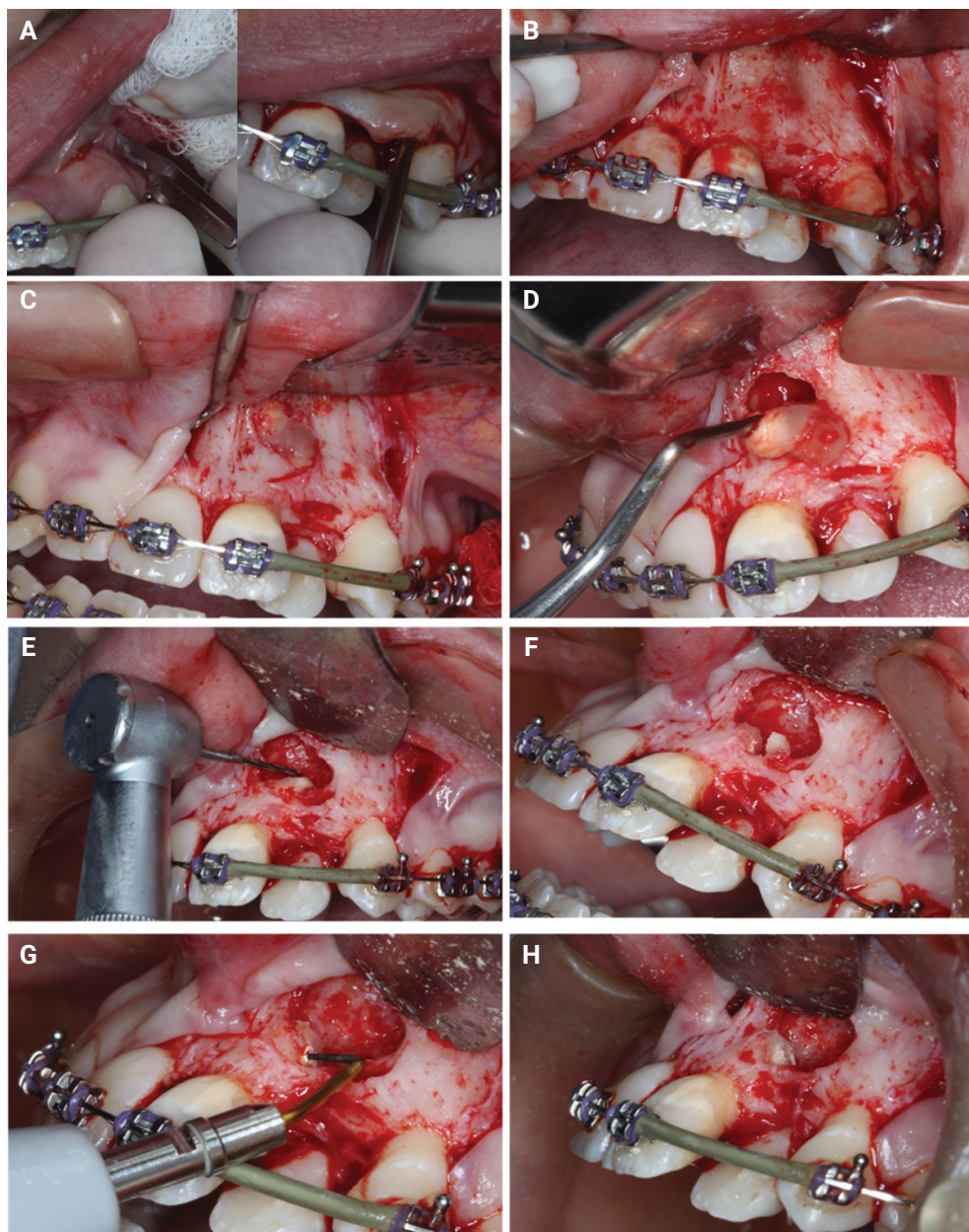
The protocol for obtaining leukocyte- and platelet-rich fibrin (L-PRF) was performed by collecting 8 tubes of blood (10 mL without anticoagulant) by venipuncture, and centrifuging them at 2,700 rpm for 12 minutes. Next, the fibrin clots from the centrifugation were placed in a metal box used specifically for this type of procedure (Fibrin box). L-PRF membranes obtained from 2 of the 8 tubes were made by light compression on the metal box. The rest were kept intact until placed inside the surgical cavity.

### ***Periapical surgery***

An incision and full-thickness flap were performed with only 1 relief incision. Since there was only a thin layer of cortical buccal bone, a Lucas curette was sufficient for the osteotomy and removal of the periapical lesion (Figure 2) Then, a Zekrya drill (Dentsply Maillefer, Ballaigues, Switzerland) was used to perform the apicectomy; in this case, it was positioned parallel to the long axis of the tooth due to the extensive root dilaceration. The retro-preparation was performed with an ultrasonic insert, and the cavity was sealed with white MTA (Angelus, Londrina, Brazil) (Figure 2). Then, the bone crypt was filled with L-PRF (fibrin clots). Finally, 2 L-PRF membranes were placed over the remaining clots, covering the vestibular bone fenestration, and the flap was sutured (Figure 3 A-D). The lesion was referred for anatomopathological examination, and the diagnosis was compatible with a periapical granuloma (Figure 3E).

### ***Orthodontic treatment***

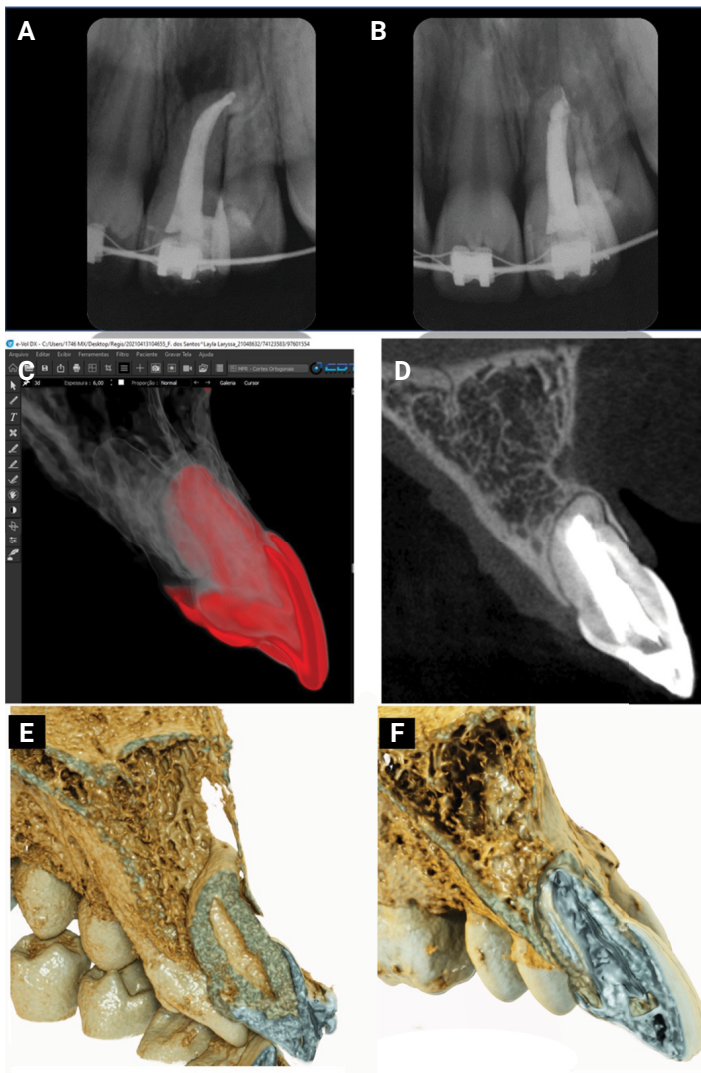
Thirty days after the surgical procedure, orthodontic traction for vestibularization of the left maxillary lateral incisor began. A bite lift was performed to properly position maxillary central incisor, and treatment continued for the next three years. In the first months of orthodontic traction, promising results were observed in relation to the vestibularization of the maxillary lateral incisor. In the fifth month after traction began, the tooth was in almost total alignment with the adjacent teeth. Figure 3 shows the clinical follow-up of orthodontic traction at different time points: one month after surgery (F), 5 months later (G) and 4 years after removal of the orthodontic appliance (H, I). Figure 4A and 4B show the radiographic aspect of the root canal obturation before surgery and immediately after apicectomy and retro-obturation, respectively, while Figure 4 C-F shows the CBCT scans indicating complete periapical healing and formation of the vestibular bone cortex with no signs of root resorption. The patient currently remains asymptomatic, with normal gingival mucosa, and without any signs of inflammation.



**Figure 2.** Incision and full-thickness flap with a relief incision (A,B); osteotomy of a thin layer of buccal cortical bone (C) and removal of root apex by Lucas curette (D); apicectomy parallel to the long axis of the tooth (E); apical fragment removed (F); retro-preparation (G) and retro-cavity sealed with white MTA (H).



**Figure 3.** L-PRF (fibrin clots) placed in the bone crypt (A); bone crypt completely filled by the graft (B); L-PRF membranes placed covering the vestibular bone fenestration (C) and sutured flap (D); anatomopathological examination compatible with periapical granuloma (E); clinical follow-up of orthodontic traction at various times, one month after surgery (F); 5 months later (G), and 4 years following orthodontic appliance removal (H, I).



**Figure 4.** Radiographic images showing before (A) and immediately after (B) apicectomy of maxillary central incisor; CBCT scans (C-D) suggest complete periapical healing and neof ormation of buccal cortical bone. CBCT images with cinematic rendering reconstruction using e-Vol DX CBCT software before (E), and 4 years after (F) endodontic-surgical-orthodontic management.

## Discussion

Multidisciplinary planning can make clinical procedures safer when managing complex cases. Cone beam computed tomography (CBCT) scan provides a greater amount of information on anatomical structures that appear superimposed on periapical radiographs. In this study, CBCT scans were essential toward achieving promising results in the preoperative period.

The visualization of both the compromised cortical bone and the periapical lesion in relation with neighboring structures facilitates surgical planning and helps prevent iat-

rogenic diseases. The overlapping of anatomical structures seen in two-dimensional exams represents a significant obstacle in clinical practice. What differentiates the CBCT imaging technique from others is that different planes (coronal, axial, sagittal, oblique) can be viewed, and both resolution and contrast are higher<sup>12</sup>. In this particular case, the CBCT technique made it possible to identify how close the root dilaceration of the maxillary central incisor was to the adjacent tooth. This ultimately provided a plan that had the best approach angle for the apicoectomy, and that enabled removing only what was necessary for the correct orthodontic repositioning of the left maxillary lateral incisor.

The e-Vol DX software program (CDT, São José dos Campos, Brazil) was used to improve the quality of the images obtained by CBCT. This is an additional tool that can be used to improve periapical surgical interventions, not only for the planning of clinical cases, but also for their documentation. Its main advantages include compatibility with all current CBCT scanners, ability to export DICOM data, better adjustment of brightness, contrast and sharpness, advanced noise reduction algorithm, and dedicated endodontic volume rendering filters capable of large enlargements without affecting the quality of the image<sup>12</sup>. A recent advance in 3D data visualization is the cinematic rendering reconstruction method, a technique that generates photorealistic 3D images from CBCT DICOM<sup>10,11</sup>. Figure 4 (C-F) shows CBCT images with cinematic rendering reconstruction using e-Vol DX CBCT software.

Regarding autologous grafting, it should be borne in mind that ongoing research in the health sciences has been focusing on pioneering the biomaterials that accelerate bone neof ormation and a tissue network. In dentistry, platelet aggregates have been frequently used to repair oral tissues, even though their therapeutic capabilities still must have more studies<sup>23-26</sup>. In the late 1990s, the first generation of platelet aggregates emerged, namely platelet-rich plasma (PRP)<sup>24</sup> and plasma rich in growth factors (PRGF)<sup>26</sup>. However, the complexity of their preparation, the time required to obtain the aggregates, and the need for additive substances, such as anticoagulants (sodium citrate) and coagulants (calcium chloride or bovine thrombin)<sup>27</sup>, attributed few clinical advantages to their production. In 2001, the second generation of platelet aggregates appeared in the form of platelet and leukocyte-rich fibrin (L-PRF), developed by Choukroun et al.<sup>14</sup>. This aggregate is an autologous biomaterial formed by incorporating leukocytes, platelets and growth factors into an autologous fibrin matrix, acquired through a blood sample from the very patient. It acts as an immunomodulator with the ability to control the inflammatory process. Most leukocyte growth factors and cytokines are trapped in the fibrin matrix of the L-PRF, and have no acellular plasma or exudate, even after the matrix is compressed and reduced in the membrane. Use of L-PRF enables incorporation of these molecules closely into the architecture of fibrin polymers and precludes losing the molecules along with the exudate<sup>14</sup>. Thus, unlike the other platelet concentrates used, these involve a simplified technique that simulates the natural coagulation process, producing a bioactive, biocompatible, simple, and economical membrane that functions as a fibrin network, providing more efficient cellular migration and proliferation<sup>28,29</sup>. It has been suggested that these growth factors may accelerate the healing of soft and hard tissues<sup>15</sup>. The regenerative

endodontic procedure associated with endodontic microsurgery represents a therapeutic alternative for patients with incomplete root formation, and large apical lesions<sup>22</sup>. L-PRF may be used as pulp regeneration and revitalization material in immature teeth with necrotic pulps, given that it is rich in growth factors. In addition, there are cases in apexification procedures, where the combination of L-PRF as a lesion filler and mineral trioxide aggregate (MTA) as a protective root tip cover is a highly effective alternative to aid in forming artificial apical barriers, and to induce the rapid healing of larger periapical lesions<sup>28,29</sup>.

The reason the L-PRF autogenous graft was chosen for this study is broadly based on literature, and also on affording the economy-minded advantage of avoiding the extra costs incurred in purchasing hetero-graft materials. It is noteworthy to bear in mind that the present case could have also been successful without using any type of grafted. However, when alternatives are used to improve the postoperative period and tissue repair, the prospect of clinical comfort and chances of success increase substantially. Soto-Peñaloza et al.<sup>30</sup> conducted a randomized clinical trial to evaluate pain and quality of life after endodontic surgery with or without application of advanced platelet-rich fibrin (A-PRF +) and membrane. Although the clinical evidence of the effects of platelet concentrates on the perception of postoperative pain in endodontic surgeries is limited, and does not present statistically significant differences, clinical findings have shown that the A-PRF + group had less pain perception than the controls. In addition, altered quality of life parameters were more prevalent in the control group, and were found to be significant for speech and sleep functions. The results obtained in the current clinical case are compatible with those described in the literature. The patient reported that her postoperative experience was very favorable, and that there were no complications. Clearly, there are many variables that can have a significant impact on the quality of the postoperative period, such as the duration of the surgery, the general health of the patient, the use of medications, and professional experience. However, any procedure that proves clinically advantageous, and that offers no risk is warranted, and should be introduced in the surgical plan whenever possible.

With respect to the orthodontic treatment, since the force of movement involved in tooth traction is gentle, and does not dissipate abruptly, it was decided to initiate traction (left maxillary lateral incisor) as soon as possible (30 days). Another reason was that it does not affect the tissue phenomenon, or the cells related to apical and periapical repair, such as angiogenesis and collagen synthesis, or even interfere with the microbiota of the canal or with the external periapical areas<sup>31</sup>.

Multidisciplinary clinical management of complex cases that are well discussed and structured are less likely to fail. The decision-making process for each clinical stage of this case report was planned to use advanced imaging resources, such as CBCT scans. These enabled more organized and improved visualization of the anatomical structures, so that the best treatment could be given to resolve the situation. Other tools included a coherent and conservative approach to root canal treatment, use of an autologous graft, confirmation of the diagnosis by anatomopathological examination, and performance of the orthodontic treatment. Future randomized controlled studies are needed to confirm the promising effects of

using leukocyte – plasma rich fibrin in endodontic procedures associated with apical surgery.

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## Conflict of Interest

The authors have no conflict of interest to disclose.

## Data availability

Datasets related to this article will be available to the corresponding author upon request.

## Author Contribution

**Regis Augusto Aleixo Alves:** Conceptualization, Formal analysis, Diagnosis Investigation, Writing – review & editing. **André Luiz Gomide Morais:** Formal analysis, Investigation, Visualization. **Larissa Emanuelle Sestari:** Formal analysis, Investigation, Visualization. **Guilherme Lopes Angelino:** Formal analysis, Investigation, Visualization. **Carlos Estrela:** Software, Conceptualization, Formal analysis, Diagnosis, Investigation, Visualization, Writing – review & editing. All authors actively revised and approved the final version of the manuscript.

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## References

1. Martinho J, Ferreira H, Paulo S, Paula A, Marto CM, Carrilho E, et al. Oculo-facio-cardio-dental syndrome: a case report about a rare pathological condition. *Int J Environ Res Public Health*. 2019 Mar;16(6):928. doi: 10.3390/ijerph16060928.
2. do Prado Sobral S, Leite AF, Figueiredo PT, Ferrari I, Safatle HP, Córdoba MS, et al. Craniofacial and dental features in kabuki syndrome patients. *Cleft Palate Craniofac J*. 2013 Jul;50(4):440-7. doi: 10.1597/11-052. Epub 2011 Oct 24.
3. Tomona N, Smith AC, Guadagnini JP, Hart TC. Craniofacial and dental phenotype of Smith-Magenis syndrome. *Am J Med Genet A*. 2006 Dec;140(23):2556-61. doi: 10.1002/ajmg.a.31371.
4. Jena AK, Kharbanda OP. Axenfeld-Rieger syndrome: report on dental and craniofacial findings. *J Clin Pediatr Dent*. 2005 Fall;30(1):83-8. doi: 10.17796/jcpd.30.1.v1732398454r0244.
5. Yassin OM, Rihani FB. Multiple developmental dental anomalies and hypermobility type Ehlers-Danlos syndrome. *J Clin Pediatr Dent*. 2006 Summer;30(4):337-41. doi: 10.17796/jcpd.30.4.72426m58695tg2h0.
6. Gebhardt R. [Ear and tooth abnormalities as marginal symptoms in common ichthyosis]. *Z Haut Geschlechtskr*. 1966 Dec;41(12):465-7. German.
7. Jafarzadeh H, Abbott PV. Dilaceration: review of an endodontic challenge. *J Endod*. 2007 Sep;33(9):1025-30. doi: 10.1016/j.joen.2007.04.013.

8. Valladares Neto J, de Pinho Costa S, Estrela C. Orthodontic-surgical-endodontic management of unerupted maxillary central incisor with distoangular root dilaceration. *J Endod.* 2010 Apr;36(4):755-9. doi: 10.1016/j.joen.2009.12.032.
9. Estrela C, Bueno MR, Leles CR, Azevedo B, Azevedo JR. Accuracy of cone beam computed tomography and panoramic and periapical radiography for detection of apical periodontitis. *J Endod.* 2008 Mar;34(3):273-9. doi: 10.1016/j.joen.2007.11.023.
10. Estrela C, Couto GS, Bueno MR, Bueno KG, Estrela LRA, Porto OCL, et al. Apical foramen position in relation to proximal root surfaces of human permanent teeth determined by using a new cone-beam computed tomographic software. *J Endod.* 2018 Nov;44(11):1741-8. doi: 10.1016/j.joen.2018.07.028.
11. Bueno MR, Estrela C, Granjeiro JM, Estrela MRA, Azevedo BC, Diogenes A. Cone-beam computed tomography cinematic rendering: clinical, teaching and research applications. *Braz Oral Res.* 2021 Feb;35:e024. doi: 10.1590/1807-3107bor-2021.vol35.0024.
12. Bueno MR, Estrela C, Azevedo BC, Diogenes A. Development of a new cone-beam computed tomography software for endodontic diagnosis. *Braz Dent J.* 2018 Nov-Dec;29(6):517-29. doi: 10.1590/0103-6440201802455.
13. Choukroun J, Adda FB, Vervelle AG. [An opportunity in perio-implantology: PRF]. *Implantodontie.* 2001;42:55-62. French.
14. Choukroun J, Diss A, Simonpieri A, Girard MO, Schoeffler C, Dohan SL, 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 Endod.* 2006 Mar;101(3):299-303. doi: 10.1016/j.tripleo.2005.07.012.
15. Dohan DM, Choukroun J, Diss A, Dohan SL, Dohan AJ, Mouhyi J, 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 Mar;101(3):e51-5. doi: 10.1016/j.tripleo.2005.07.010.
16. Mazor Z, Horowitz RA, Del Corso M, Prasad HS, Rohrer MD, Dohan Ehrenfest DM. 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 Dec;80(12):2056-64. doi: 10.1902/jop.2009.090252.
17. Simonpieri A, Choukroun J, Del Corso M, Sammartino G, Dohan Ehrenfest DM. 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 Feb;20(1):2-12. doi: 10.1097/ID.0b013e3181faa8af.
18. Tajima N, Ohba S, Sawase T, Asahina I. Evaluation of sinus floor augmentation with simultaneous implant placement using platelet-rich fibrin as sole grafting material. *Int J Oral Maxillofac Implants.* 2013 Jan-Feb;28(1):77-83. doi: 10.11607/jomi.2613.
19. Diss A, Dohan DM, Mouhyi J, Mahler P. Osteotome sinus floor elevation using Choukroun's platelet-rich fibrin as grafting material: a 1-year prospective pilot study with microthreaded implants. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2008 May;105(5):572-9. doi: 10.1016/j.tripleo.2007.08.021.
20. Miron RJ, Zucchelli G, Pikos MA, Salama M, Lee S, Guillemette V, et al. Use of platelet-rich fibrin in regenerative dentistry: a systematic review. *Clin Oral Investig.* 2017 Jul;21(6):1913-27. doi: 10.1007/s00784-017-2133-z.
21. Castro AB, Meschi N, Temmerman A, Pinto N, Lambrechts P, Teughels W, et al. Regenerative potential of leucocyte- and platelet-rich fibrin. Part A: intra-bony defects, furcation defects and periodontal plastic surgery. A systematic review and meta-analysis. *J Clin Periodontol.* 2017 Jan;44(1):67-82. doi: 10.1111/jcpe.12643. Epub 2016 Nov 24.

22. Pinto N, Harnish A, Cabrera C, Andrade C, Druttman T, Brizuela C. An innovative regenerative endodontic procedure using leukocyte and platelet-rich fibrin associated with apical surgery: a case report. *J Endod.* 2017 Nov;43(11):1828-34. doi: 10.1016/j.joen.2017.07.002.
23. 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 Mar;27(3):158-67. doi: 10.1016/j.tibtech.2008.11.009.
24. Marx RE, Carlson ER, Eichstaedt RM, Schimmele SR, Strauss JE, Georgeff KR. Platelet-rich plasma: growth factor enhancement for bone grafts. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 1998 Jun;85(6):638-46. doi: 10.1016/s1079-2104(98)90029-4.
25. Al-Hamed FS, Tawfik MA, Abdelfadil E, Al-Saleh MAQ. Efficacy of platelet-rich fibrin after mandibular third molar extraction: a systematic review and meta-analysis. *J Oral Maxillofac Surg.* 2017 Jun;75(6):1124-35. doi: 10.1016/j.joms.2017.01.022.
26. 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 Jul-Aug;14(4):529-35.
27. Jovani-Sancho MD, Sheth CC, Marqués-Mateo M, Puche-Torres M. Platelet-rich plasma: a study of the variables that may influence its effect on bone regeneration. *Clin Implant Dent Relat Res.* 2016 Oct;18(5):1051-64. doi: 10.1111/cid.12361. Epub 2015 Jul 1.
28. Saravanakumar B, Julius A, Sarumathi T, Aarthinisha V, Manisundar N. Therapeutic effects and concepts in the use of platelet – rich fibrin (PRF) on alveolar bone repair – A literature review. *Middle East J Sci Res.* 2014;19(5):669-73. doi: 10.5829/idosi.mejsr.2014.19.5.82246.
29. Shivashankar VY, Johns DA, Vidyanath S, Kumar MR. Platelet rich fibrin in the revitalization of tooth with necrotic pulp and open apex. *J Conserv Dent.* 2012 Oct;15(4):395-8. doi: 10.4103/0972-0707.101926.
30. Soto-Peñaloza D, Peñarrocha-Diago M, Cervera-Ballester J, Peñarrocha-Diago M, Tarazona-Alvarez B, Peñarrocha-Oltra D. Pain and quality of life after endodontic surgery with or without advanced platelet-rich fibrin membrane application: a randomized clinical trial. *Clin Oral Investig.* 2020 May;24(5):1727-38. doi: 10.1007/s00784-019-03033-5. Epub 2019 Oct 14.
31. Consolaro A, Miranda DAO, Consolaro RB. Orthodontics and endodontics: clinical decision-making. *Dental Press J Orthod.* 2020 May;25(3):20-9. doi: 10.1590/2177-6709.25.3.020-029.oin.