# Regenerative therapy in young permanent tooth: Case report

Terapia regenerativa em dente permanente jovem: Relato de caso

Terapia regenerativa en dientes jóvenes permanentes: Relato de caso

Recebido: 27/12/2022 | Revisado: 03/01/2023 | Aceitado: 04/01/2023 | Publicado: 05/01/2023

#### Brenda Silva Araújo

ORCID: https://orcid.org/0000-0001-5425-6819 Faculdade São Leopoldo Mandic, Brasil Email: brendaraujo95@yahoo.com Bruna de Athayde Casadei ORCID: https://orcid.org/0000-0003-1974-2541 Faculdade São Leopoldo Mandic, Brasil

E-mail: casadeibruna@gmail.com Hebertt Gonzaga dos Santos Chaves ORCID: https://orcid.org/0000-0001-8611-3070 Universidade Federal de Minas Gerais, Brasil

E-mail: heberttchaves\_@hotmail.com

#### Abstract

Pulp necrosis in immature permanent teeth represents a challenge for clinical management. The dentin wall in immature teeth is thin and the root is short, leading to an unfavorable long-term prognosis due to the risk of root fracture. Regenerative endodontic procedures have been shown to be effective and improve the prognosis of the compromised immature tooth by re-establishing functional pulp tissue that promotes continued root development and immune competence. The objective of the study was to report a case of a young permanent molar, diagnosed with necrosis and incomplete rhizogenesis. A female patient, 08 years old, attended the clinic of the specialization course in Endodontics, Faculty of Dentistry São Leopoldo Mandic, Belo Horizonte Unit. Regenerative therapy was proposed, which involved the following steps: anesthesia, opening, odontometry, minimal instrumentation, disinfection with 2% chlorhexidine gel, irrigation with saline solution, intracanal medication with calcium hydroxide paste, induction of bleeding to form a blood clot, cervical sealing with mineral trioxide aggregate and composite resin. The patient remained symptom-free up to 5 months after treatment. However, radiographically, an increase in the periapical radiolucent area was noted, so it was decided to carry out the conventional endodontic treatment. Regenerative therapy can be an alternative to apexification in immature teeth in cases of irreversible pulpitis and pulp necrosis associated or not with a periapicalesionson. It is a simple treatment with advantageous results as it promotes an increase in the length and thickness of the dentin wall and apical closure as seen in the case described in this work. Keyword: Necrosis of the dental pulp; Regenerative endodontics; Permanent dentition.

#### Resumo

A necrose pulpar em dentes permanentes imaturos representa um desafio para o manejo clínico. A parede de dentina em dentes imaturos é fina e a raiz curta levando a um prognóstico desfavorável a longo prazo devido ao risco de fratura radicular. Os procedimentos endodônticos regenerativos têm se mostrado eficazes e melhoram o prognóstico do dente imaturo comprometido pelo restabelecimento de um tecido pulpar funcional que promove o desenvolvimento contínuo da raiz e a competência imune. O objetivo do estudo foi relatar um caso de molar permanente jovem, com diagnóstico de necrose e rizogênese incompleta. Paciente do gênero feminino, 08 anos de idade compareceu à clínica do curso de especialização em Endodontia da Faculdade de Odontologia São Leopoldo Mandic, Unidade Belo Horizonte. Foi proposta a terapia regenerativa que envolveu as seguintes etapas: anestesia, abertura, odontometria, instrumentação mínima, desinfecção com de gel clorexidina 2%, irrigação com soro fisiológico, medicação intracanal com pasta de hidróxido de cálcio, indução de sangramento para formação de coágulo sanguíneo, vedamento cervical com agregado trióxido mineral e resina composta. A paciente permaneceu sem sintomas até 5 meses após o tratamento. Porém radiograficamente notou-se um aumento da área radiolúcida periapical desta forma foi optou-se por realizar o tratamento endodôntico convencional. A terapia regenerativa pode ser uma alternativa à apicificação em dentes imaturos em casos de pulpite irreversível e necrose pulpar associada ou não a lesão periapical. É um tratamento simples com resultados vantajosos pois promove aumento do comprimento e da espessura da parede da dentina e fechamento apical como visto no caso descrito neste trabalho.

Palavras-chave: Necrose da polpa dentária; Endodontia regenerativa; Dentição permanente.

#### Resumen

La necrosis pulpar en dientes permanentes inmaduros plantea un desafío importante para el manejo clínico, ya que cesa el desarrollo de la raíz y los ápices permanecen abiertos. La pared de dentina en dientes inmaduros es delgada y la raíz es corta, lo que conduce a un pronóstico desfavorable a largo plazo debido al riesgo de fractura radicular. Se ha demostrado que los procedimientos de endodoncia regenerativa son efectivos y mejoran el pronóstico de los dientes inmaduros comprometidos al restaurar un tejido pulpar funcional que promueve el desarrollo radicular continuo y la competencia inmunológica. El objetivo del presente estudio fue reportar un caso de un molar permanente joven, diagnosticado con necrosis y formación radicular incompleta. Paciente del sexo femenino, de 08 años, acudió a la clínica del curso de especialización en Endodoncia de la Faculdade de Odontologia São Leopoldo Mandic, Unidad Belo Horizonte, para tratamiento de endodoncia. Se planteó una terapia regenerativa que involucró los siguientes pasos: anestesia, apertura, odontometría, mínima instrumentación, desinfección con gel de clorhexidina al 2%, irrigación abundante con solución salina, medicación intraconducto con pasta de hidróxido de calcio, inducción de sangrado para formar coágulo, cervical selle con agregado de trióxido mineral y resina compuesta. El paciente permaneció asintomático hasta 5 meses después del tratamiento. Sin embargo, radiográficamente se observó un aumento del área radiolúcida periapical, por lo que se optó por un tratamiento endodóntico convencional. La terapia regenerativa puede ser una alternativa a la apexificación en dientes inmaduros en casos de pulpitis irreversible y necrosis pulpar asociada o no a lesión periapical. Es un tratamiento técnicamente sencillo con resultados ventajosos en relación a la apexificación, ya que promueve el aumento de la longitud y espesor de la pared dentinaria y el cierre apical, como se ve en el caso descrito en este trabajo.

Palabras clave: Necrosis de la pulpa dental; Endodoncia regenerativa; Dentición permanente.

# 1. Introduction

Conventional endodontic treatment consists in the development and application of techniques aimed at performing chemical-mechanical preparation of root canals in order to eliminate an infection, often difficult to fight due to the complexity of the root canal system (Araújo, 2017; Hameed, 2019; Ramezani, 2019; Xie, 2021). However, this process can become even more complicated in cases of immature teeth with open apexes, whose root walls are fragile due to the thin thickness of the dentin of the root canal, combined with the intense activity and anatomy of an open apex, hindering the complete filling of the root canal, and with risk of extravasation of solid and plastic material to the periapex (Faria, 2019; Nosrat et al., 2019; Chaves et al., 2022; Nicoloso, 2019).

The treatments proposed for this condition include a) apicification with periodic exchanges of calcium hydroxide-based medicinal products; b) placement of apical barrier with Mineral Trioxide Aggregate (MTA), followed by root canal filling with gutta-percha and pulp revascularization (Pereira, 2020; Rombouts, 2016). Pulp revascularization has been consolidated as a viable and effective alternative for the treatment of immature necrotic teeth (El-Tayeb, 2019; Nageh, 2018; Parhizkar, 2018; Yang, 2022). It presents advantages over conventional techniques, such as the possibility of continuous root development and the consequent strengthening of dental structure (Glynis, 2022; He, 2022; Ramezani, 2019). Its steps involve decontamination with root canal irrigators, insertion of intracanal medication, induction of blood clots, and coronary sealing (Montero-Miranelles, 2018).

Pulp revascularization had its first case reported in early 2000. Since then, several studies have been carried out in this sense (He, 2022; Kontakiotis et al., 2015; Zanini, 2019; Chaves et al., 2022). When comparing endodontic procedures in young teeth, studies have shown that pulp revascularization is the only technique that allows a significant increase of root and root wall thickness when compared to the apicification technique with AM or with successive exchanges of calcium hydroxide (Jeeruphan et al., 2012; Nicoloso et al., 2019; Xie, 2021; Wikström, 2021).

According to some studies, pulp revascularization of immature teeth with infected necrotic pulps and/or teeth with apical periodontitis was possible and even predictable (Deluca et al., 2021). The procedure requires disinfection of the pulp space with an effective antibacterial regimen, production of a clot in the pulp space, cervical sealing, and a definitive restoration (Nageh, 2022; Ravikumar, 2021). Thus, regenerative endodontic procedures may improve the prognosis of the immature tooth

compromised by the restoration of functional pulp tissue (Bakhtiar et al., 2022; Caleza-Jiménez, 2022; He, 2022; Law, 2013; Lenzi, 2012).

Therefore, the aim of this study is to report a clinical case in which the pulp revascularization technique was performed in a young permanent tooth diagnosed with pulp necrosis.

# 2. Metodologia

The present study constitutes a clinical case report on regenerative therapy in young permanent tooth. The case study is a structured research method widely used in several areas of health, which can be applied in different situations to contribute to the knowledge of individual or group phenomena, as well as disseminate knowledge of the technique of procedures among professionals (Andrade *et al.*, 2017).

Valuing the legal aspects, all stages were conducted in accordance with the Declaration of Helsinki and Resolution 466/12 of the National Health Council (CNS). The study participant was included after signing the Informed Consent Form (TCLE), signed by the person responsible, declaring to agree to participate in the study and releasing the use of his image for academic purposes. The child signed the Free and Enlightened Assent Term (TALE). The case report described here was approved by the Ethics Committee and is registered on the CAAE number: 46995921.1.0000.5374 and opinion number: 4,805,504.

### 3. Relato de Caso Clínico

A 08-year-old female patient attended the clinic of the Specialization course in Endodontics of the São Leopoldo Mandic School of Dentistry, Belo Horizonte Unit, for endodontic treatment of tooth 46.

Because it is a child, the questions were answered by the person responsible. During anamnesis and clinical examination, the person responsible for the minor reported no deleterious habits or any health problems. However, it was reported by the uncomfortable patient in the dental element 46. The person responsible was informed that emergency care was previously performed for pain relief. On clinical examination, dental element 46 was observed with the presence of endodontic access and temporary sealing (Coltosol®, Coltene, Vigodent). The element was capable of restorative rehabilitation treatment.

On radiographic examination (Figure 1) it was possible to observe bone rarefaction in the periapex and tooth with incomplete rhizogenesis. In view of the clinical and radiographic information, the diagnosis of pulp necrosis was reached and regenerative therapy was proposed as an elective treatment.

### Figure 1 – initial radiograpy of element 46.



Source: From the authors (2022).

Clinical treatment consisted of the following steps: in a first consultation anesthesia of the right lower alveolar nerve was performed, with local infiltrative technique with Alphacaine 2% + Epinephrine (1:100,000) (Nova DFL, Rio de Janeiro, Brazil). The dressing was removed, and absolute isolation was performed with staple 208 (Duflex, SS White, Rio de Janeiro, Brazil), thong, and placement of topDam gingival barrier (FGM, Joinville, Santa Catarina, Brazil) for better sealing of absolute isolation (Figure 2).

Cleaning of the operative field with 70° alcohol, conventional endodontic access with 1016HL high-rotation drill (Komet, São Paulo, Brazil) and low-rotation long rod no. 2 drill (Komet, São Paulo, Brazil) and Chlorhexidine Endogel 2% (LenzaFarm, Belo Horizonte, Brazil).

Cleaning and instrumentation were performed smoothly because the goal of regenerative therapy is to cause an apical closure and not to undo the side walls. Following this protocol, there was no enlargement of the apical foramen.

Canal instrumentation was performed primarily with Cpilot #10 and #15 (VDW GmbH, Munich, Germany) and abundant irrigation using Chlorhexidine Endogel 2% as an auxiliary chemical and physiologic serum as an irrigant solution (Fresenius, Jaguariúna – SP, Brazil).

Instrumentation was performed to avoid unnecessary wear and tear of the walls and apical foramen as much as possible. The reference on the DV cusp was determined; DV: 18mm with reference to the DV cusp; MV: 18 mm with reference to the MV cusp. apparent tooth length (CAD), through the initial radiography, being ML: 18mm with reference in MV cuspid; DL: 18mm.

The entire disinfection and chemical-mechanical preparation process were carried out with physiological serum as an irrigator solution with positive pressure and Chlorhexidine Endogel 2%, as an auxiliary chemical used between instrument exchanges. With the proportions, on average, for each channel, use 5 mL of irrigator solution and 2 mL of auxiliary chemical substance.

#### Figure 2 - Initial aspect after restoration removal.



Source: From the authors (2022).

Then, the channels were filled with BioC temp (Angelus, Londrina, PR, Brazil). The coronium sealing was performed with Maxxion Glass Ionomer Cement (FGM, Joinville, Santa Catarina, Brazil) and a period of 30-35 days was expected (Figure 3).

BioC temp, a bioceramic restorative cement ready for use, has benefits such as tissue regeneration through the release of Ca2+ ions resulting in the formation of mineralized tissue, bactericidal action by high pH, and inhibition of bacterial infiltration by prey expansion and chemical adhesion to dentin.

In a second session, the intracanal bio c temp medication (Angelus, Londrina, PR, Brazil) was retracted, the coagulum stimulus was performed within the root canal, buffer with Bio-C Repair (Angelus, Londrina, PR, Brazil), and provisional restoration. First, anesthesia of the right lower alveolar nerve was applied, with a local infiltrative technique with Mepicain 3% (Nova DFL, Rio de Janeiro, Brazil).

The steps of endodontic access and absolute isolation followed the same protocol as described in the first consultation. The intracanal medication was removed with saline solution and appropriate files, then the stimulation of apical bleeding was induced, in order to promote the formation of a coagulum in this region.



Figure 3 - Radiography after filling the channels with BioC temp.

Source: From the authors (2022).

After the formation of the blood clot inside the root canals, the pulp chamber was cleaned so that the blood clot was only inside the root canals (Figure 4) and then the buffer was performed with BioC repair (Angelus, Londrina, PR, Brazil) (Figure 5).





Source: From the authors (2022).



Figure 5 - Buffer with BioC repair at channel inputs.

Source: From the authors (2022).

For the coronium sealing, a base was carried out with Maxxion Glass Ionomer Cement (FGM, Joinville, Santa Catarina, Brazil), and restoration in composite resin Opalis (FGM, Joinville, Santa Catarina, Brazil) thus promoting a better provisional sealing (Figure 6).

Figure 6 - Final tooth aspect.



Source: From the authors (2022).

After completion of the case, final radiography was performed (Figure 7) and radiographic follow-up for a period of 2 months (Figure 8) and 5 months (Figure 9).



Figura 7 – Final Radiograpy.

Source: From the authors (2022).

In the final X-ray (Figure 7) there is a radiopaque area at the entrance of the root canals which is the plug made with Bio C repair, a barrier with Coltosol, and sealing with restoration in composite resin.

### Figure 8 - Radiography 2 months after the procedure.



Source: From the authors (2022).

In the follow-up ray after 2 months of the procedure (figure 8) we did not notice any changes.



Figure 9 - Radiography 5 months after the procedure.

After 5 months of follow-up, the patient was without clinical signs and symptoms, but radiographically an increase in the periapical radiolucent area (Figure 9), thus, we opted for conventional endodontic treatment.

# 3. Discussion

In view of the characteristics presented in the case: young permanent tooth, diagnosis of pulp necrosis, open apex, and little dentin thickness, regenerative therapy was indicated in order to gain dentin wall thickness and root length.

The concept of regenerative endodontic therapy was introduced in early 1970 when Nygaard-Ostby and Hjortdal verified the growth of new vascularized tissue in the empty apical part of the root canals after super instrumentation and formation of intracanal bleeding (Nygaard-Ostby, 1971). The creation of a blood clot within the root canal was defined by the researchers as responsible for the formation of new vital tissue. However, the practice of regenerative endodontic therapy was substantially initiated in the early 2000s. Since then, several studies have been conducted (Kontakiotis et al. 2015).

Source: From the authors (2022).

There is no consistent pattern to evaluate the efficacy of pulp revascularization. The curative effect has been based mainly on clinical manifestation, pulp vitality examination, and radiographic examination. According to the American Association of Endodontists guidelines, the main objectives are to cure apical periodontitis and eliminate clinical symptoms (Yang, 2022).

Pulp necrosis of immature permanent teeth represents a significant challenge for clinical management, especially in the cleaning and modeling of large canals, due to the extensive root canal space and little root structure. As root development ceases and the apexes remain open, there is a greater difficulty in cleaning and instrumentation of these channels, and errors in apical sealing may occur during canal filling, and possible root fractures caused by thin and weakened root walls. Thus, the pulp regeneration technique is an effective choice in these cases, thus leading to increased thickening of the canal walls and/or continuous root development, as well as a positive response to sensitivity tests (Law, 2013; Yang, 2022).

Immature and necrotic teeth also have as an option the apicification, which consists of the application and exchange of calcium hydroxide paste in the root canal, for a variable period of time, in order to induce the formation of a mineralized barrier in the apical region for the proper accommodation of the obturator material, thus leading to apical closure (Santos, 2022).

When comparing endodontic procedures in young teeth, studies show that regenerative therapy is the only technique that allows the significant increase of root and root wall thickness when compared to apicification with MTA and with calcium hydroxide exchanges, which also provides longer maintenance time for these teeth in the oral cavity. The main process is complete and effective root canal disinfection. Root canal disinfection and chemical irrigation are used to remove infectious materials in the root canal (Jeeruphan et al., 2012; Yang, 2022).

Due to the properties of BioC temp, having as advantages its gradual release of Calcio, biocompatibility, high alkalinity, high radiopacity, and easy removal, was the medication of choice for the case. When comcommenated BioC temp which is an intrachannel medication with bioceramic characteristics and calcium hydroxide pastes, it is noticed that BioC Temp has a great advantage over calcium hydroxide due to the latter presenting low solubility and, thus, allowing the product to be in direct contact with the canal walls for a long period (Viana et al., 2021. Pereira et al., 2014).

Regenerative endodontic procedures may improve the prognosis of the immature tooth compromised by the restoration of a functional pulp tissue that promotes continuous root development and immune competence. The number of evidence has demonstrated the possibility of tissue regeneration within the pulp space and the continuous development of the root in teeth with necrotic pulps and open apexes is increasing. Thus, the stages of regenerative therapy consist of decontamination with root canal irrigators, insertion of intracanal medication, induction of blood clots, and coronary sealing (Law, 2013; Montero-Miranelles, 2018; Torabinejad, 2011).

When performing the regenerative therapy procedure, through washing and disinfection of the root canal, avoiding mechanical preparation, guiding the atrophic stem cells to the root canal, and promoting the continuous development of dental roots, has achieved good clinical curative effects, the tissue formed within the root canal consists of loose connective tissue similar to periodontal ligament tissue with islands of centroid and osteoid tissue (Yang, 2022).

Pulp revascularization is dependent on the differentiation capacity of the epic and periodontal stem cells. These cells have the ability to generate a highly vascularized living tissue rich in connective tissue, it is able to colonize the available pulp space then the stem cells will differentiate into newly formed odontoblasts that will induce a hard tissue apposition. Mineralized tissue, such as cement, forms for apical closure. Thus, regenerative therapy has as advantages when compared to conventional techniques, the possibility of continuous root development and the consequent strengthening of dental structure (Glynis, 2021).

Thus, the tissue formed in the canal of the revitalized tooth is similar to cement and fibrous connective tissue. (Martins et al., 2013; Namour, 2014; Shimizu et al. 2013; Thomson, 2010).

In the clinical case described in this study, after a 5-month follow-up, despite the absence of symptomatology, and the

evidence of decreased periapical injury, it still persisted and the conventional endodontic treatment was chosen. What can be explained since the potential for cleansing, disinfection, healing and the defense mechanism of the pulp has long been recognized, the intensity and nature of the infection are still the determining factors for the result of pulp recovery.

### 4. Final Consideration

In the clinical case described in this study, after a 5-month of follow-up, despite the absence of symptomatology, and the evidence of decreased periapical injury, it persisted and the conventional endodontic treatment was chosen. What can be explained since the potential for cleansing, disinfection, healing and the defense mechanism of the pulp has long been recognized, the intensity and nature of the infection are still the determining factors for the result of pulp recovery.

### References

Alipour M., Aghazadeh Z., Hassanpour M., Ghorbani M., Salehi R. & Aghazadeh M. (2022) MTA-Enriched Polymeric Scaffolds Enhanced the Expression of Angiogenic Markers in Human Dental Pulp Stem Cells. *Stem Cells Int.* 21:7583489.

Araújo P.R.S, Silva L.B., Neto A.P.D.S., Almeida de Arruda J.A., Álvares P.R., Sobral A.P.V., Júnior S.A., Leão J.C., Braz da Silva R., Sampaio G.C. (2017). Pulp Revascularization: A Literature Review. *Open Dent*. 31;10:48-56.

Arshad S., Tehreem F., Rehab Khan M., Ahmed F., Marya A. & Karobari M.I. (2021). Platelet-Rich Fibrin Used in Regenerative Endodontics and Dentistry: Current Uses, Limitations, and Future Recommendations for Application. *Int J Dent.* 15;2021:4514598.

Bakhtiar H., Ashoori A., Rajabi S., Pezeshki-Modaress M., Ayati A., Mousavi M.R., Ellini M.R., Kamali A., Azarpazhooh A. & Kishen A. (2021). Human amniotic membrane extracellular matrix scaffold for dental pulp regeneration in vitro and in vivo. *Int Endod J.* 55(4):374-390.

Banchs F. & Trope M. (2004). Revascularization of immature permanente teeth with apical periodontitis: new treatment protocol. J Endod, 30:196-200.

Bassetti R., Kuttenberger J. & Bassetti M. (2018). Regenerative endodontische Therapie nach Frontzahntrauma. Ein Fallbericht [Regenerative endodontics after front tooth trauma. A case report]. Swiss Dent J. 14;128(5):393-399.

Bezgin T. & Sönmez H. (2015). Review of current concepts of revascularization/revitalization. Dent Traumatol. 31(4):267-73.

Brickhouse T.H., Unkel J.H., Porter A.S. & Lazar EL. (2007). Status do seguro e cárie dentária não tratada em escolares da Virgínia. Pediatr Dent. 29:493 - 9.

Caleza-Jiménez C., Ribas-Pérez D., Biedma-Perea M., Solano-Mendoza B. & Mendoza-Mendoza A. (2022). Radiographic differences observed following apexification vs revascularization in necrotic immature molars and incisors: a follow-up study of 18 teeth. *Eur Arch Paediatr Dent.* 7.

Cehreli Z.C., Erbas Unverdi G., Eymirli P., Mergen I., Arslan E. & Esenturk G. (2022). Combined conventional and regenerative treatment in molars with coexistent closed and open apices: A case series. Aust Endod J. 9.

Cehreli Z.C., Unverdi G.E. & Ballikaya E. (2022). Deciduous Tooth Pulp Autotransplantation for the Regenerative Endodontic Treatment of Permanent Teeth With Pulp Necrosis: A Case Series. *J Endod.* 1:S0099-2399(22)00068-1.

Chauhan R., Rasaratnam L., Alani A. & Djemal S. (2016). Adult Dental Trauma: What Should the Dental Practitioner Know. Prim Dent J. 1;5(3):70-81.

Chaves H.G.S., Moreira T.P.C., Figuereiro B., Macedo I.F.A, Maia I.C., Maia C.A., Ferreira I.C., Silva V.J.L, Nascimento W.M. (2022). Pulp calcification in traumatized teeth – a literature review. *Research, Society and Development*. 11(7).

Chaves H.G.S., Souza L.M.L, Macedo I.F.A., Maia C.A., Figuereiro B., Ferreira I.C., Maia G.C., Ferreira G.C., Silva V.J.L., Casadei B.A. (2022). Regenerative therapy in teeth with incomplete root formation after dental trauma to tooth 21: a case report. *Research, Society and Development*. v. 11(7).

Connert T., Weiger R. & Krastl G. (2022). Present status and future directions - Guided endodontics. Int Endod J. 25.

Deluca M.C.C., Scarparo R.K., Aspesi M., Matte B.F., Brand L.M., Grecca F.S., Casagrande L. & Kopper P.M.P. (2021). Cytotoxic, Migration, and Angiogenic Effects of Photodynamic Therapy and Photobiomodulation Associated with a Revascularization Protocol. *J Endod*. 47(1):69-77.

El-Tayeb M.M., Abu-Seida AM, E.I., Ashry S.H. & El-Hady S.A. (2019). Evaluation of antibacterial activity of propolis on regenerative potential of necrotic immature permanent teeth in dogs. *BMC Oral Health*. 6;19(1):174.

Eramo S., Natali A., Pinna R. & Milia E. (2018). Dental pulp regeneration via cell homing. Int Endod J. 51(4):405-419.

Faria L.V., Chaves H.G.D.S., Borges Silva E.A., Antunes L.S. & Antunes L.A.A. (2020). Minimally invasive treatment of an extruded deciduous tooth - Case report. *Dent Traumatol*. 36(3):303-306.

Flanagan T.A. (2014). What can cause the pulps of immature, permanent teeth with open apices to become necrotic and what treatment options are available for these teeth. *Aust Endod J.* 40:95–100.

Garcia-Godoy F. & Murray P.E. (2012). Recommendations for using regenerative endodontic procedures in permanent immature traumatized teeth. *Dental Traumatology*. 28(1):33-41.

Glynis A., Foschi F., Kefalou I., Koletsi D., Tzanetakis G.N. (2021). Regenerative Endodontic Procedures for the Treatment of Necrotic Mature Teeth with Apical Periodontitis: A Systematic Review and Meta-analysis of Randomized Controlled Trials. *J Endod.* 47(6):873-882.

Hameed M.H., Gul M., Ghafoor R. & Badar S.B. (2019). Management of immature necrotic permanent teeth with regenerative endodontic procedures - a review of literature. J Pak Med Assoc. 69(10):1514-1520.

He W.X. & Yu Q. (2022). New advances in vital pulp therapy and pulp regeneration for the treatment of pulpitis: from basic to clinical application. *Zhonghua Kou Qiang Yi Xue Za Zhi*. 9;57(1):16-22. Chinese.

Huang G.T.J. (2008). A paradigm shift in endodontic management of immature teeth: Conservation of stem cells for regeneration. *Elsevier Ltd. All rights* reserved. 36:379–386.

Jeeruphan T., Jantarat J., Yanpiset K., Suwannapan L., Khewsawai P. & Hargreaves K.M. (2012). Mahidol Study 1: Comparison of Radiographic and Survival Outcomes of Immature Teeth Treated with Either Regenerative Endodontic or Apexification Methods: A Retrospective Study. *JOE*. 38:1330-1336.

Jiménez C.C., Pérez R.D., Perea B.M., Mendonza S.B. & Mendonza M.A. (2022). Radiographic differences observed following apexification vs revascularization in necrotic immature molars and incisors: a follow-up study of 18 teeth. *Eur Arch Paediatr Dent*. 7.

Kontakiotis E.G., Filippatos C.G., Tzanetakis G.N. & Agrafioti A. (2015). Regenerative Endodontic Therapy: A Data Analysis of Clinical Protocols. JOE. 146-154.

Krasner P. & Rankow H. (1995). Nova filosofia para o tratamento de dentes avulsionados. Oral Surg Oral Med Oral Pathol. 79: 616

Law A.S. (2013). Considerations for Regeneration Procedures. Jornal Of Endodontics. 39(3).

Lenzi R. & Trope M. (2012). Revitalization Procedures in Two Traumatized Incisors with Different Biological Outcomes. Jornal Of Endodontics. 38(3).

Luz L.B., Vizzotto M.B., Xavier P.N.I., Vianna-Wanzeler A.M., Dias da Silveira H.L. & Montagner F. (2022). The Impact of Cone-beam Computed Tomography on Diagnostic Thinking, Treatment Option, and Confidence in Dental Trauma Cases: A Before and After Study. *J Endod*. 48(3):320-328.

Martins G., Ricucci, M.D., Jennifer L., Gibbs M.A.S., Louis M. & Lin B.D.S. (2013). Histological Findings of Revascularized/Revitalized Immature Permanent Molar with Apical Periodontitis Using Platelet-rich Plasma. *JOE*. 39:138-144.

Montero-Miralles P., Martín-González J., Alonso-Ezpeleta O., Jiménez-Sánchez M.C., Velasco-Ortega E., Segura-Egea J.J. (2018). Effectiveness and clinical implications of the use of topical antibiotics in regenerative endodontic procedures: a review. *Int Endod J.* 51(9):981-988.

Myers M.C & Fountain S.B. (1974). Dental pulp regeneration aided by blood and blood substitutes after experimentally induced periapical infection. *Oral Surg Oral Med Oral Pathol*. 37:441–50.

Nageh M., Ahmed G.M. & El-Baz A.A. (2018). Assessment of Regaining Pulp Sensibility in Mature Necrotic Teeth Using a Modified Revascularization Technique with Platelet-rich Fibrin: A Clinical Study. *J Endod.* 44(10):1526-1533.

Nageh M., Ibrahim L.A., AbuNaeem F.M. & Salam E. (2022). Management of internal inflammatory root resorption using injectable platelet-rich fibrin revascularization technique: a clinical study with cone-beam computed tomography evaluation. *Clin Oral Investig.* 26(2):1505-1516.

Namour M. & Theys S. (2014). Pulp Revascularization of Immature Permanent Teeth: A Review of the Literature and a Proposal of a New Clinical Protocol. *Scientific World Journal*. 01-09.

Namour M. & Theys S. (2014). Pulp revascularization of immature permanent teeth: a review of the literature and a proposal of a new clinical protocol. *ScientificWorldJournal*. 737503.

Natera M. & Mukherjee P.M. (2018). Regenerative Endodontic Treatment with Orthodontic Treatment in a Tooth with Dens Evaginatus: A Case Report with a 4-year Follow-up. *J Endod.* 44(6):952-55.

Neelamurthy P.S., Kumar R.A., Balakrishnan V., Venkatesan S.M., Narayan G.S. & I K. (2018). Revascularization in Immature and Mature Teeth with Necrotic Pulp: A Clinical Study. J Contemp Dent Pract. 1;19(11):1393-1399.

Nicoloso G.F., Goldenfum G.M., Pizzol T.D.S.D., Scarparo R.K., Montagner F., de Almeida Rodrigues J. & Casagrande L. (2019). Pulp Revascularization or Apexification for the Treatment of Immature Necrotic Permanent Teeth: Systematic Review and Meta-Analysis. J Clin Pediatr Dent. 43(5):305-313.

Nosrat A., Kolahdouzan A., Khatibi A.H., Verma P., Jamshidi D., NevinsA.J. & Torabinejad M. (2019). Clinical, Radiographic, and Histologic Outcome of Regenerative Endodontic Treatment in Human Teeth Using a Novel Collagen-hydroxyapatite Scaffold. *J Endod.* 45(2):136-143.

Nygaard-Ostby B. & Hjortdal O. (1971). Tissue formation in the root canal following pulp removal. Scand J Dent Res. 79:333-49.

Parhizkar A., Nojehdehian H. & Asgary S. (2018). Triple antibiotic paste: momentous roles and applications in endodontics: a review. *Restor Dent Endod*. 20;43(3):28.

Pereira A.C., Oliveira M.L., Cerqueira-Neto A.C.C.L., Gomes B.P.F.A., Ferraz C.C.R., Almeida J.F.A., Marciano M.A., DE-Jesus-Soares A. (2020). Treatment outcomes of pulp revascularization in traumatized immature teeth using calcium hydroxide and 2% chlorhexidine gel as intracanal medication. *J Appl Oral Sci.* 25;28:e20200217.

Pereira, J.C., Anauate-Netto C., Gonçalves S.M.A. (2014). Dentística: uma abordagem multidisciplinar. 1º ed. São Paulo: Artes médicas.

Ramezani M., Sanaei-Rad P. & Hajihassani N. (2019). Revascularization and vital pulp therapy in immature molars with necrotic pulp and irreversible pulpitis: A case report with two-year follow-up. *Clin Case Rep.*19;8(1):206-210.

Ravikumar K., Chakravarthy Y., Kumar A., Samynathan M. & Varshini R.J. (2021). Foreign Body Removal and Revascularization of Teeth with Periapical Radiolucency: 18 Months' Follow-Up. *J Pharm Bioallied Sci*.13(1):S886-S889.

Rombouts C, Giraud T, Jeanneau C, About I. (2017). Pulp Vascularization during Tooth Development, Regeneration, and Therapy. J Dent Res. 96(2):137-144.

Santos P.H.O., dos.; Aguiar K. S., Ogata L.I., & Ribeiro A.L.R. (2022). Revascularização pulpar como alternativa às terapias de apexificação comumente aplicadas em dentes jovens com raízes incompletas. *Research, Society and Development.* 11(15): 2525-3409.

Shah N., Logani A., Bhaskar U. & Aggarwal V. (2008). Efficacy of Revascularization to Induce Apexification/Apexogensis in Infected, Nonvital, Immature Teeth: A Pilot Clinical Study. *J Endod*. 34(8):919-25.

Shimizu E., Ricucci, M.D., Albert J., Alobaid A.S., Gibbs J.L., Huang G.T.J. & Lin L.M. (2013). Clinical, Radiographic, and Histological Observation of a Human Immature Permanent Tooth with Chronic Apical Abscess after Revitalization Treatment. *JOE*. 39:1078-1083.

Stambolsky C., Rodríguez-Benítez S., Gutiérrez-Pérez J.L., Torres-Lagares D., Martín-González J. & Segura-Egea J.J. (2016). Histologic characterization of regenerated tissues after pulp revascularization of immature dog teeth with apical periodontitis using tri-antibiotic paste and platelet-rich plasma. *Arch Oral Biol.* 71:122-128

Thomson A., Kahler B. (2010). Endodontia regenerativa - tratamento de base biológica para dentes permanentes imaturos: um relato de caso e revisão da literatura. *Australian Dental Journal*. 55 (4): 446–452.

Torabinejad M., Turman M. (2011). Revitalization of Tooth with Necrotic Pulp and Open Apex by Using Platelet-rich Plasma: A Case Report. J Endod. 37(2):265–68.

Viana F.L.P., Sampieri M.B.S., Viana P.P., Cruz S.M.L., Vivan R.R., Duaanin I.C.J., Vasconcelos B.C. (2021). Analise do pH e da atividade antimicrobiana de um novo medicamento intracanal bioceramico Bio-C temp. Research Society and Development. 10(7).

Wikström A., Brundin M., Lopes M.F., El Sayed M. & Tsilingaridis G. (2021). What is the best long-term treatment modality for immature permanent teeth with pulp necrosis and apical periodontitis? *Eur Arch Paediatr Dent*.22(3):311-340.

Xie Z., Shen Z., Zhan P., Yang J., Huang Q., Huang S., Chen L. & Lin Z. (2021). Functional Dental Pulp Regeneration: Basic Research and Clinical Translation. *Int J Mol Sci.* 20;22(16):8991.

Yang YQ, Wu BL, Zeng JK, Jiang C, Chen M. (2022). Pulp revascularization on an adult mandibular right second premolar: A case report. World J Clin Cases. 16;10(17):5833-5840.

Zanini M., Hennequin M. & Cousson P.Y. (2019). Which procedures and materials could be applied for full pulpotomy in permanent mature teeth? A systematic review. *Acta Odontol Scand*. 77(7):541-551.

Zhao Y., Liu B. & Zhao Y.F. (2019). Controversies Regarding the Management of Teeth Associated with Cystic Lesions of the Jaws. *Chin J Dent Res.* 22(2):81-92.