

## Clinical evidence of pulp Revascularization in necrosed and immature teeth: a literature review

### Evidências clínicas da Revascularização pulpar em dentes necrosados e imaturos: uma revisão de literatura

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#### **ABSTRACT**

Introduction: Endodontic treatment in teeth with incomplete root formation and necrotic pulp has been constantly studied and new approaches are being carried out, with revascularization being the most recent of them. Objective: This work is a literature review, which sought to elucidate the clinical aspects of pulp revascularization, about its longevity as a treatment modality. Methods: Articles from the last 7 years were used in the PUBMED, Scielo and VHL databases in English and Portuguese. Randomized clinical studies, clinical cases with follow-up, systematic reviews and meta-analysis were considered. Results and Discussion: Among the various recommendations, due to the clinical cases exposed, the importance of disinfection of root canal systems by the use of irrigating solutions with antimicrobial action, the use of intracanal medication, and calcium hydroxide can be used or the tri-antibiotic paste, both with the aim of eliminating bacteria present on dentin surfaces. Apical revascularization facilitates tooth root development, but it is uncertain how much root length and thickness, or apical

closure, is achieved. However, regenerative techniques seem to have superior results, in these aspects, when compared to the Apexification technique. Among the clinical studies evaluated, it was observed that the revascularization technique with blood clot associated with the use of PRP and PRF as a scaffold was more effective for the longevity and success of the technique. Conclusion: After the reviewed articles, it can be concluded that the apical root closure technique, through the induction of the blood clot, is effective in enabling root strengthening and development, being safe, traumatic, and low cost and can be performed in any age, covering a significant number of patients with incomplete apex associated with pulp necrosis.

**Keywords:** apexification, immature teeth, pulp necrosis, Revascularization.

## RESUMO

**Introdução:** O tratamento endodôntico em dentes com rizogênese incompleta e polpa necrosada, vem sendo constantemente estudado e novas abordagens estão sendo realizadas, sendo a revascularização a mais recente delas. **Objetivo:** Este trabalho trata-se de uma revisão de literatura, onde se buscou elucidar os aspectos clínicos da revascularização pulpar, acerca da sua longevidade como modalidade de tratamento. **Métodos:** Foram utilizados artigos dos últimos 7 anos, nas bases de dados PUBMED, Scielo e BVS na língua inglesa e portuguesa. Foram considerados estudos clínicos randomizados, casos clínicos com preservação, revisões sistemáticas e meta-análise. **Resultados e Discussão:** Dentre as diversas recomendações, em razão dos casos clínicos expostos, destaca-se a importância da desinfecção dos sistemas de canais radiculares pelo uso de soluções irrigadoras com ação antimicrobiana, o uso da medicação intracanal, podendo ser utilizado o hidróxido de cálcio ou a pasta tri-antibiótica, ambas com o intuito de eliminar as bactérias presentes nas superfícies dentinárias. A revascularização apical facilita o desenvolvimento da raiz do dente, mas é incerto o quanto se alcança de comprimento e espessura radicular, ou fechamento apical. Entretanto, as técnicas regenerativas parecem ter resultados superiores, nestes quesitos, quando comparadas a técnica de apicificação. Dentre os estudos clínicos avaliados, observou-se que a técnica de revascularização com o coágulo sanguíneo associado ao uso do PRP e PRF como “scaffold” se mostrou mais eficaz para a longevidade e sucesso do tratamento. **Conclusão:** A técnica de fechamento apical radicular, por meio da indução do coágulo sanguíneo mostrou-se eficaz em possibilitar o fortalecimento e desenvolvimento radicular, sendo segura, a traumática, de baixo custo e podendo ser executada em qualquer idade, abrangendo um número expressivo de pacientes com ápice incompleto associado à necrose pulpar.

**Palavras-chave:** apexificação, dentes imaturos, necrose pulpar, Revascularização.

## 1 INTRODUCTION

Endodontics aims to preserve the dentition with its physiological and functional characteristics in order to maintain the oral and systemic health of the patient (LAW et al., 2012). When teeth are approached, not completely formed and diagnosed with pulp necrosis, the challenge to maintain these characteristics is even greater (BUKHARI et al., 2016; CHAN et al., 2017; ESTEFAN et al., 2016; ANTUNES et al., 2015).

According to the American Association of Endodontics (AAE), immature teeth have smaller-thick dentin walls, and sharp instrumentation can further weaken these structures.

Another factor to be observed in these teeth is the absence of apical constriction. Due to these characteristics, conventional filling is not indicated, which may lead to extravasation of the obturator material (ALBUQUERQUE et al., 2012). Thus, conventional endodontic treatment should undergo changes in its protocol, aiming mainly at decontamination of dentin walls by chemical and mechanical means (LAW et al., 2012).

The conservative treatment of the pulp should, whenever possible, be indicated, being of paramount importance, first check, whether or not the tooth has pulp vitality. If the pulp is vital, interventions in the root canal should be avoided, and if necessary, the intervention should be restricted to the coronary pulp part, aiming at maintaining the root pulp and cells of the Epithelial Sheath of Hertwig, allowing the physiological process of root formation to progress (CAO et al., 2015).

When pulp necrosis diagnosis is detected, root canal intervention becomes inevitable, and should be performed. Pulp revascularization is a highly commented treatment option currently studied because it is a procedure that aims to stimulate the end of root development in necrotic teeth with incomplete rhizogenesis. It is suggested that its mechanism involves stimuli to the penetration of periradicular tissue inside the root canal, thus reestablishing the vitality of previously necrotic teeth, allowing tissue repair and regeneration (CHAN et al., 2017; SILUJJAI et al., 2016; CAO et al., 2015).

According to studies conducted, the pulp revascularization procedure seems to be the most indicated alternative for these teeth, as it is related to a conduct that restores the vitality of non-vital teeth, enabling tissue repair and regeneration (CHAN et al., 2017; SILUJJAI et al., 2016; CAO et al., 2015; PARYANI et al., 2013). Revascularization, when compared to Apexification, has a greater number of benefits, because after the control of pulp infection, it results in a shorter treatment time, and can be completed in one or two sessions. If there is an induction of the end of root development with thickening of walls, we will have, as a result, the strengthening of them (BUKHARI et al., 2016).

The revascularization technique boils down to the formation of a blood clot rich in undifferentiated cells through stimulation of periapical bleeding. This clot will fill the root canal space, forming in the future a new "pulp" tissue, which will differentiate and provide continuity of the formation of the root apical third. The protocols studied in the present study refer to the techniques of induction and formation of the blood clot, in addition to verifying the existence of other approaches that are still being studied, such as stem cell therapy and the use of Platelet-rich Plasma (PRP) and Plasma Rich in Fibrins (PRF), currently promising and recent research in the literature (SHIVASHANKAR et al., 2017; WANG et al., 2015; ZHUJIANG et al., 2015).

Thus, the objective of this work is to review the literature, addressing the clinical aspects of pulp revascularization therapy, about the most used modalities, as well as to analyze the longevity and predictability of this treatment when in necrotic, immature teeth presenting apical periodontitis or not.

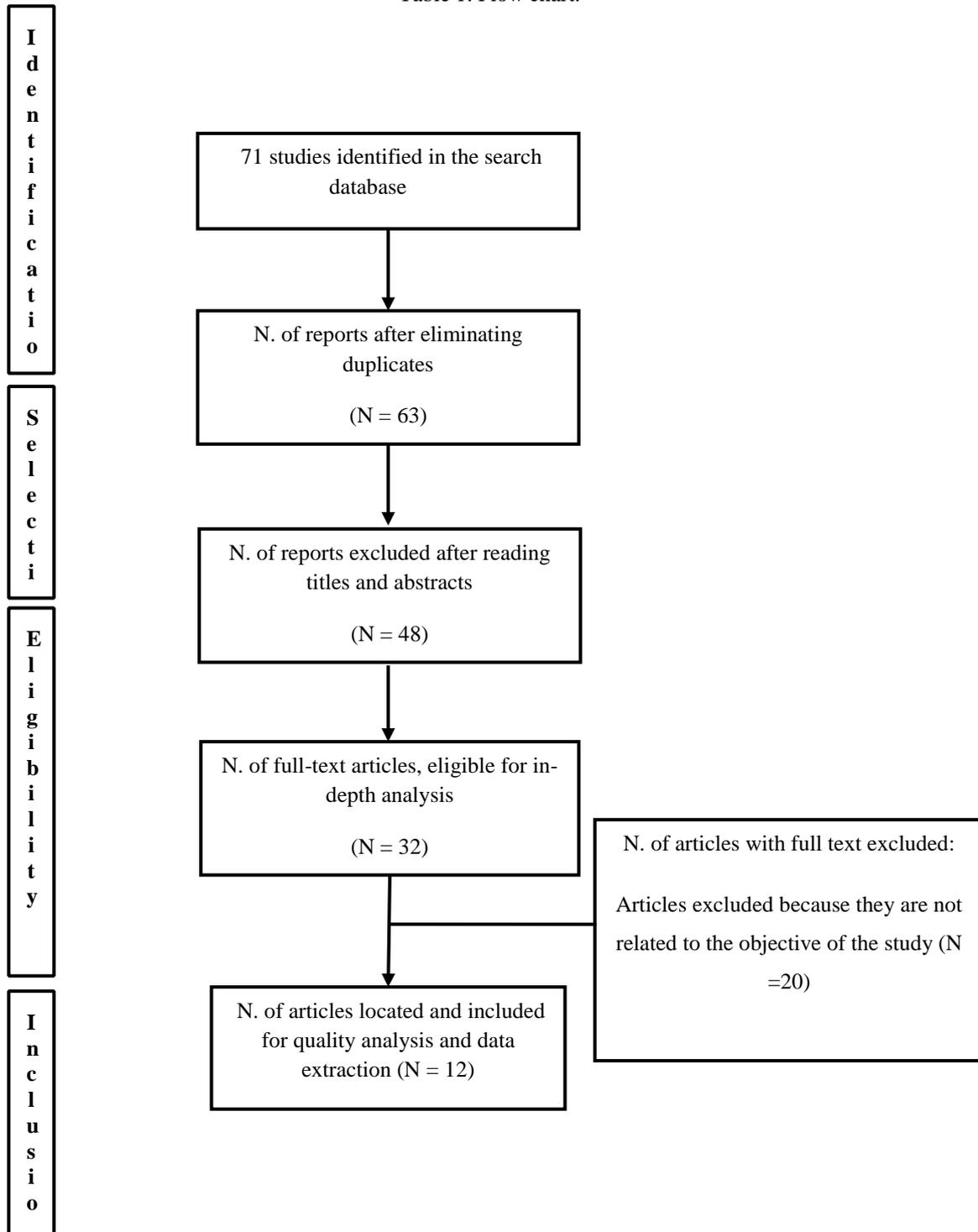
## **2 METHODOLOGY**

This is a descriptive literature review, which sought scientific evidence to explain the clinical methods pulp revascularization therapy as well as to ascertain the longevity of treatment.

Information collection was performed through pubmed (National Library of Medicine), Scielo (Scientific Electronic Library Online) and VHL (Virtual Health Library) databases using the following descriptors: "Apexification", "Immature Teeth", "Pulpal Necrosis", "Revascularization".

The inclusion criteria used for the bibliographic survey, were scientific papers in The English Portuguese, literature reviews, case reports, systematic reviews. Studies published in other languages and repeated, as well as articles that ran away from the theme studied, were excluded. The first stage of the selection of articles was performed through a reading and analysis of titles and abstracts, applying the inclusion and exclusion criteria. The second stage proceeded with a complete reading of the articles that supported the research, separate them according to the proposed objective, observing the results found. Subsequently, a qualitative analysis was performed among the articles, which resulted in 12 articles selected for the preparation of this review.

Table 1. Flow chart.



Source: The authors.

### 3 RESULTS

Table 2. Characterization of selected studies.

AUTHOR/YEAR	STUDY OBJECTIVE	MAIN FINDINGS
Bukhari et al., 2016.	Evaluate the outcome of the revascularization procedure in necrotic immature teeth.	The result of revascularization, in which periapical periodontitis healing and root maturation occur, is very promising, making it a viable treatment option compared to Apexification.
Chan et al., 2016.	To evaluate root growth and thickening through radiographs, using the revascularization protocol as a treatment.	The teeth treated with revascularization presented resolution of the symptoms. Although significant clinical alteration was not achieved in all cases, there was an increase in root thickness and length and apical closure after 30 months.
Silujjai et al., 2017.	To evaluate the clinical and radiographic results of Apexification and revascularization with MTA in non-vital immature permanent teeth and analysis of the factors that influence the outcome of treatment.	The success rates of Apexification were higher than revascularization with MTA. In revascularization, there was an increase in root length ranging from 4% to 58%. The fracture was the main cause of failure in the apicified teeth with MTA. None of the treatments provided predictable and satisfactory root development.
Shivashankar et al., 2017.	Radiographic evaluation of root development continuation, increased dentin wall thickness and canal space narrowing, apical closure and resolution of periapical lesion with the use of PRF and clinical evaluation of response to pulp sensitivity tests and response to percussion and palpation tests using PRP.	The protocol with the use of PRP was better than the PRF and induced hemorrhage in relation to periapical wound healing. It is important to establish the induced hemorrhage technique as a standard procedure for revascularization.
He et al., 2017.	Perform a meta-analysis on revascularization;	Apical revascularization facilitates the development of the tooth root, but is uncertain in root elongation, enlargement or apical closure.
Guerrero, Guerrero, Mendonza; Ribas; Aspiazu, 2018.	To evaluate the clinical cases related to the evaluation of Apexification and revascularization in immature permanent teeth.	The MTA barrier as Apexification treatment is a technique applied in place of calcium hydroxide Apexification; this technique does not require several consultations, and the conformation of the barrier does not require an external factor to develop, as well as in the regeneration of the pulp.
Dhiman; Duhan, D.C.; Juneja; Tewari; Sangwan, 2019.	Case report describing two immature teeth with pulp necrosis and apical periodontitis that were treated through revascularization.	Both cases proved to be a clinical and radiographic success for long follow-up periods.
Hameed; Gul, I'm not going to Ghafoor; Bada; 2019.	Review in the literature the evidence on the treatment of immature necrotic permanent teeth through regenerative endodontic procedures.	Complete biological regeneration of periodontal and endodontic tissues is not yet obtained predictably due to the histological nature of the regenerated tissue, suggesting that regenerative procedures promote guided endodontic repair rather than regeneration of the pulpdent complex. The development of this endodontic therapy may eliminate the need for more complex treatments in the future, such as extractions and replacement by implants.
Mittmann et al., 2020.	Evaluate the clinical and radiographic outcome of	Revascularization is a promising approach for the treatment of immature incisors to regain sensitivity,

	revascularization therapy in traumatized permanent incisors.	improve apical closure, maintain alveolar bone in terms of alveolo preservation. However, a complete root development in length and thickness cannot be expected and the prognosis for the teeth is limited by the risks of trauma.
Wikström et al., 2021.	To evaluate the current knowledge about Apexification and regenerative techniques as an effective treatment modality for the management of immature teeth with pulp necrosis and apical periodontitis.	Regeneration and Apexification techniques had similar rates of success and survival, were effective in the treatment of permanent immature necrotic teeth. However, regenerative techniques seem to be superior, as they stimulate root maturation, i.e., root wall thickening and root elongation.
Cui et al., 2021.	Review in the literature the understanding of the biological basis of clinical treatments for immature permanent teeth with pulp necrosis and the roles of dental Mesenchytous Stem Cells during this process and update the progress of endodontic regeneration procedures based on these in the treatment of permanent immature necrotic teeth.	Revascularization is successful in resolving apical periodontitis and disrupted root formation, it is widely applied in the treatment of immature permanent teeth with necrotic pulp. However, histological studies show that the pulp - dentin complex is absent in these cases, although some studies show a positive response to the vitality test.
Xie et al.,2021.	This is a systematic review and meta-analysis that summarizes data and results of randomized clinical trials that directly compared revascularization with Apexification in immature necrotic teeth.	Revascularization therapy and Apexification were effective options in relation to the healing of periapical periodontitis or the closure of open apexes. Pulp revascularization is more effective for increasing root length and thickness.

Source: The authors.

#### 4 DISCUSSION

The treatment of pulp regeneration is indicated for interventions in teeth with pulp necrosis and incomplete rhizogenesis, however, there is still no assent in relation to clinical practice. When talking about a better prognosis, it is necessary to pay attention to the time dedicated to treatment, such as the postoperative period and the biological issues involved during the process (ALCALDE et al., 2014).

With regard to pulp regeneration, it aims to eliminate symptoms and promote repair of periapical injury, enlarge the thickness of walls and lengths of root canals, as well as restore pulp vitality. Thus, it remains the most indicated alternative for young teeth with incomplete rhizogenesis. Thus, pulp regeneration has been a viable alternative and in many cases replacing the Apexification treatment, which was fundamental as a pioneer treatment for clinical cases of necrotic teeth (BUKHARI et al., 2016).

The pulp regeneration protocol, according to some researchers and following the criteria of THE, usually occurs in two clinical sessions. In the first, the protocols of cleaning and

disinfection of root canals with 2.5% NaOCl, insertion of MIC and sealing with temporary restorative material are performed. In the second, abundant and careful irrigation is performed with the EDTA 17%; induction of bleeding inside the root canal (blood clot), or use of PRP, PRF or injectable scaffold with basic fibroblast growth factor and MTA sealing (ANTUNES et al., 2015; PRAMILA; MUTHU, 2012).

One of the most important steps is the complete disinfection of root canals correctly (PRAMILA; MUTHU, 2012). Subsequently, the irrigating solutions should act on bacteria and other organisms that can proliferate and hinder treatment, and it is necessary to correctly choose existing ones (CAO et al., 2015). There is a preference among researchers for the NaOCl solution because it has antimicrobial properties that help in the success of treatment. It is noteworthy that the concentrations can range from 0.5% to 6%, and it is of paramount importance that irrigation occurs 3 mm below the working length, thus avoiding future damage. Even though NaOCl is the most indicated, several authors question its toxicity and opt for another irrigating solution, such as 2% chlorhexidine gluconate (ANTUNES et al., 2015).

To optimize the growth of the human dentin matrix, it is necessary to use chelating. Among these, we can mention EDTA and citric acid, and EDTA is the most used, as it helps in the conservation of stem cells present at the apex (GALLER et al., 2016).

Regarding intra-channel medication (MIC), there is a consensus among the authors (BANCHS; TROPE, 2004; ANTUNES et al., 2015), regarding the indication and use of the triantibiotic paste, which is the association of three antibiotics (Metronidazole, Ciprofloxacin and Minocycline). According to Sato, in 1996, such paste can eliminate microorganisms, even those of the deepest dentinal layers.

Even with all the scientific development, a negative aspect about this paste stands out: the darkening of the dental crown through Minocycline. For this to do not occur, research has proven that the use of an adhesive system that protects the dentin exposed to this factor optimizes the process, avoiding darkening (ALCADE, 2014).

Namour and Theys (2014) reported that Minocycline is a semisynthetic derivative of Tetracycline, with a similar spectrum of action, and can be replaced, in the composition of the paste, by Cefaclor to prevent some risk of coronary pigmentation that compromises aesthetics. Although not common, the authors Soares et al. (2013), report as an alternative to antibiotic paste, the use of calcium hydroxide associated with CHX gel 2%, due to the antibacterial action of both, as it can become a MIC of choice to endodontics in the treatment of the pulp revascularization technique.

Regarding the use of PRP and PRF, studies have proven their efficacies through the results observed in healing, apical closure and thickening of the dentin walls, in a short period of time, when compared to the conventional technique with the use of blood clot; however, despite showing excellent results, some researchers suggest maintaining the blood clot technique as a standard for the revascularization procedure, as it is less uncomfortable and does not require biochemical manipulation of the patient's blood (SHIVASHANKAR, 2017).

For Chan et al. (2017) and Estefan et al. (2016), the blood clot induction technique is effective in eliminating symptoms and enabling root strengthening and development; and because it is less traumatic and low cost, it can be implemented at any age. Regarding its efficacy, an increase in root thickness and length was observed, as well as apical closure after 30 months.

Regarding root elongation, some authors found that there was a significant increase in dentin wall thickness and root length after revascularization in teeth with incomplete rhizogenesis (ESTEFAN et al., 2016, CHAN et al., 2017, BUKHARI et al., 2016). The follow-up time for these cases ranged from 6 months to 6 years.

Other authors opted for platelet concentrates in the pulp space, aiming to increase growth factors and improve the revascularization process. Wang et al., (2015) and Antunes et al., (2015) added PRP to the blood clot as scaffold. Shivashankar et al., (2017); Pramila and Muthu (2012) used PRF or PRP as a scaffold option in their cases, and obtained excellent results. Shivashancakar et al. (2017), for example, observed that the use of PRF as scaffold in regenerative endodontic procedures increases the predictability of results, since it is a more stable matrix than a simple blood clot and contains a large amount of growth factors.

## 5 CONCLUSION

When we refer to the treatment of pulp regeneration, there is still no concrete standard protocol. However, it can be affirmed that endodontic regeneration has been highlighted through the technique with blood clot and with PRP and PRF, both are effective. Advances in the subject are increasingly diligent, always bringing as an objective the development of benefits for people who need this type of treatment.

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