ORIGINAL ARTICLE
ISSN 2645-4351

https://doi.org/10.22037/jds.v43i1.46750

Outcome of Regenerative Endodontic Procedures in Permanent Immature Necrotic Teeth

Shiva Shojaeian[a], Nazanin Zargar[a], Arman Rafiezade Rafiee[a], Sara Zamaheni[a], Mohadeseh Asgari[a,*]

[a]Department of Endodontics, school of dentistry, Shahid Beheshti university of medical science, Tehran, Iran.

*Correspondence to: Mohadeseh Asgari, Email: mohadeseh.asgari96@gmail.com

Submitted: 16 November 2024
Revised: 23 December 2024
Accepted: 24 December 2024
Published: Winter 2025

How to cite:
Shojaeian S, Zargar N, Rafiezade Rafiee A, Zamaheni S, Asgari M. Outcome of Regenerative Endodontic Procedures in Permanent Immature Necrotic Teeth. J Dent Sch 2025;43(1):10-17.

Abstract:

Objective(s): This study assessed the outcome of regenerative endodontic procedures (REPs) in permanent immature necrotic teeth. **Methods:** This longitudinal cross-sectional study was conducted on permanent immature necrotic teeth that had undergone REPs from 2013 to 2018. The patients were contacted by phone and asked to show-up for clinical and radiographic examinations of their treated teeth. The preoperative parallel periapical (PA), 6-18-month postoperative radiographs, and clinical examination results were collected and compared. Functional presence of the respective tooth in dental arch with no need for an endodontic treatment in the follow-up sessions was considered as treatment success. Data were analyzed by paired t-test (alpha=0.05). **Results:** Twelve patients (N=16 teeth) met the inclusion criteria; of which, 9 (N=12 teeth) showed up for the follow-up. The mean age of patients was 15±8.44 years (range 10 to 23 years). Ten teeth had experienced trauma, and the remaining two were necrotic due to anomalies (Turner's hypoplasia and supernumerary tooth). Six teeth had undergone REPs with calcium-enriched mixture (CEM) cement, 4 with Biodentine, and 2 with mineral trioxide aggregate (MTA). Eleven out of 12 teeth were functional with no clinical sign/symptom at 6-12, and 18-month follow-ups, and were considered as treatment success. Closure of apical opening was significant (P=0.049). **Conclusion:** REPs through revascularization by using CEM cement, Biodentine, and MTA can be successful and increase the chance of completion of root development in permanent immature necrotic teeth.

Keywords: Patient Outcome Assessment; Calcium-Enriched Mixture Cement; Mineral Trioxide Aggregate; Regeneration; Regenerative Endodontics

Introduction

Immature teeth are defined as those with wide canals, thin root dentinal walls, and open apices. Thus, their instrumentation, working length determination, control of irrigants, and obturation are highly difficult, if not impossible.[1-3] Moreover, even in case of an ideal root canal treatment, such teeth are always at higher risk of fracture due to thin root dentinal walls. Therefore, root canal treatment of permanent immature teeth with a necrotic pulp is a challenge for dental clinicians.[4]

Long-term intracanal application of calcium hydroxide (CH) is the routine treatment for immature open-apex teeth; leading to apexification at the root end.[5] However, long-term treatment course is one of the most important drawbacks of this method, since it may take up to 6 months, and requires multiple patient visits during this period.[6] Another shortcoming is that long-term application of CH can change the physical properties of dentin, and decrease the root strength.[7]

To overcome the shortcomings of apexification treatment with CH, formation of a mechanical barrier induced by mineral trioxide aggregate (MTA) was suggested.[8] Apexification with MTA has shown relatively more favorable results compared with long-term treatment with CH in terms of periapical signs and symptoms.[9] Also, treatment duration and session frequency are decreased in treatment with MTA compared to CH. Despite all these advantages, application of MTA does not affect the root length or root canal wall thickness, and therefore, cannot change the root strength, still leaving the treated tooth at high risk of fracture.[3]

Regenerative endodontic procedures (REPs) and revascularization of the periapical region have been recently proposed as a possible alternative treatment for management of permanent immature necrotic teeth. In this technique, bleeding is induced at the periapical area for subsequent formation of a blood clot at the root canal end. Subsequently, providing a scaffold, growth factors, or stem cells at the site can lead to root development.[10, 11] Many studies have shown that this treatment protocol led to an increase in root length and canal wall thickness in immature teeth with a necrotic pulp.[12, 13] Nonetheless, sufficient evidence does not exist to support the use of REPs with regard to their long-term outcome compared with the conventional treatment. Thus, this study aimed to assess the outcome of REPs in permanent immature necrotic teeth.

Methods

This longitudinal cross-sectional study was conducted on permanent immature necrotic teeth that had undergone REPs at the Pediatric Dentistry and Endodontics Departments of Shahid Beheshti Dental School from 2013 to 2018. The study protocol was approved by the ethics

committee of the university (IR.SBMU.RIDS.REC.1396.584).

Sample size:

Considering the exploratory nature of the study, a confidence level of 85% (Z = 1.44), a precision (Δ) of 0.15, and an estimated standard deviation (σ) of 0.228 for paired differences, the following formula was used to calculate the required sample size:

$n = (Z_{a}/_{2} + Zβ)^2 * σ^2 / Δ^2$

Substituting the values:

$n = (1.44 + 0.84)^2 * 0.228^2 / 0.15^2$

Calculations:

$n = (2.28)^2 * 0.051984 / 0.0225 = 5.1984 * 0.051984 / 0.0225 ≈ 12$

The estimated sample size required for this study was calculated to be 12 participants. This sample size was deemed sufficient to provide preliminary insights and assess general trends in the outcomes of the procedure. While this approach may reduce the statistical power and precision of the results, it remains suitable for an initial evaluation and hypothesis generation.

Eligibility criteria:

The inclusion criteria were (I) permanent open-apex immature necrotic teeth that had undergone revascularization treatment according to the protocol of the American Association of Endodontists [14], (II) a minimum of 6 months passed since the revascularization treatment, (III) no underlying systemic disease affecting the study variables, (III) no intake of medications affecting the study variables, (IV) no history of trauma during the time interval between treatment and follow-up session, (V) age between 8 to 24 years (mean age of 16 years) at the time of treatment, (VI) availability of complete patient records in the archives, and (VII) the respective tooth had to be permanently restored within three months after completion of revascularization treatment.

Data collection:

Dental records of patients who had presented to the Pediatric Dentistry and Endodontics Departments of Shahid Beheshti Dental School from 2013 to 2018 for REPs were retrieved from the archives, and eligible patients were contacted by phone and asked to show up for clinical and radiographic examinations. A total of 12 eligible patients (N=16 teeth) were contacted; out of which, 9 (N=12 teeth) showed up for a follow-up.

All patients signed informed consent forms for participation in the study. The preoperative periapical (PA) radiograph of patients was retrieved from their records and saved. Clinical and radiographic examinations were performed at 6-12 months and 18 months after the treatment. All clinical examinations were performed by a dental student, and the following items were assessed on clinical examination:

- Survival rate: Is the respective tooth present in dental arch without requiring retreatment?
- Function: Assessment of the masticatory function of the respective tooth in dental arch.
- Symptoms: The patient was asked about spontaneous or evoked pain.
- Pulp sensibility tests including the heat and cold tests, and electric pulp test (EPT): The respective tooth was completely dried with a cotton pellet and isolated. The tests were performed for both buccal and lingual surfaces of the respective tooth, and also on a sound control tooth. The heat test was performed by placing a heated gutta-percha on the tooth surface for a minimum of one minute. The cold test was performed by using a cold spray (Denronic cool spray, Germany) for a minimum of one minute. EPT (Gentle Pulse, Parkell, USA) was also performed. In EPT, the intensity was gradually increased from 0 to 10. Each test was repeated twice.
- Periapical tests including percussion and palpation: These tests were performed using a dental mirror handle and fingertips.
- Tooth mobility: A dental mirror handle was used for this purpose. The mobility intensity was categorized as < 1 mm horizontally (score 1), > 1 mm horizontally (score 2), and presence of both horizontal and vertical movements (score 3).
- Presence/absence of sinus tract or swelling and abscess
- Radiographic examination: A parallel PA radiograph was obtained from each tooth, and evaluated by CS Imaging Patient Browser 7.0.20 software. For alignment of the preoperative and follow-up radiographs, the percentage of changes was calculated using the following formula [12,13]:

For horizontal magnification:

$$\frac{a}{a'} = w$$

Where “a” is the mesiodistal root width at the cementoenamel junction (CEJ) on the preoperative radiograph, and “a'” is the mesiodistal root width at the CEJ on the follow-up radiograph

For longitudinal magnification:

$$\frac{\frac{i}{i'} + \frac{j}{j'}}{2} = l$$

Where “i” is the longitudinal distance from the mesial border of the crown to the CEJ of the mesial surface on the preoperative radiograph; “i'” is the longitudinal distance from the mesial border of the crown to the CEJ of the

mesial surface on the follow-up radiograph; "j" is the longitudinal distance from the distal border of the crown to the CEJ of the distal surface on the preoperative radiograph; and "j'" is the longitudinal distance from the distal border of the crown to the CEJ of the distal surface on the follow-up radiograph.

- Root length: The method described by Alobaid et al.[15] was used for this purpose. Accordingly, a straight line was drawn from the mesial and distal borders of the CEJ to the radiographic apex. The mean of these two was recorded as the root length. The mean distance between the apex end and the mesial and distal border of the CEJ was calculated using the software.

Percentage of change in root length:

$$\frac{l\left(\frac{g'+h'}{2}\right)-\frac{g+h}{2}}{\frac{g+h}{2}}\times 100$$

Where "g" is the longitudinal distance between the mesial end of the apex and mesial border of the CEJ on the preoperative radiograph; "g'" is the longitudinal distance between the mesial end of the apex and mesial border of the CEJ on the follow-up radiograph; "h" is the longitudinal distance between the distal end of the apex and distal border of the CEJ on the preoperative radiograph; and "h'" is the longitudinal distance between the distal end of the apex and distal border of the CEJ on the follow-up radiograph.

- Root width: Root width was measured at the apical third (two-thirds of the root length) and coronal third (one-third of the root length) before the treatment, and at the same region after the intervention according to Jiang et al [16].

The percentage of change in root width at the coronal third of the root was calculated as follows:

$$\frac{wb'-b}{b}\times 100$$

Where "b" is the root width at the coronal third of the root on the preoperative radiograph, and "b'" is the root width at the coronal third of the root on the follow-up radiograph.

The percentage of change in root width at the apical third of the root was calculated as follows:

$$\frac{wc'-c}{c}\times 100$$

Where "c" is the root width at the apical third of the root on the preoperative radiograph, and "c'" is the root width at the apical third of the root on the follow-up radiograph.

- Dentin width: Root width at baseline and follow-up session minus the pulp width at the same time point in the apical and coronal thirds of the root.

The percentage of change in dentin width at the coronal third of the root (one-third of the root length) was calculated as follows:

$$\frac{w(b'-e')-(b-e)}{b-e}\times 100$$

Where e is the canal width at the coronal third of the root on the preoperative radiograph, and "e'" is the canal width at the coronal third of the root on the follow-up radiograph.

The percentage of change in dentin width in the apical third of the root (two-thirds of the root length) was calculated as follows:

$$\frac{w(c'-f')-(c-f)}{c-f}\times 100$$

Where "f" is the canal width in the apical third on the preoperative radiograph, and "f'" is the canal width in the apical third on the follow-up radiograph.

Percentage of change in apical opening:

It was calculated as follows:

$$\frac{wd'-d}{d}\times 100$$

Where "d" is the size of apical opening on the preoperative radiograph, and "d'" is the size of apical opening on the follow-up radiograph.

- Apical shape: It was categorized as blunderbuss and non-blunderbuss.

- The percentage of change in mesiodistal dimension of the PA lesion was calculated using the following equation:

$$\frac{wk'-k}{k}\times 100$$

Where "k" is the mesiodistal dimension of the PA lesion on the preoperative radiograph, and "k'" is the mesiodistal dimension of the PA lesion on the follow-up radiograph.

The percentage of change in the height of the PA lesion was calculated using the following equation:

$$\frac{lm'-m}{m}\times 100$$

Where "m" is the height of the PA lesion on the preoperative radiograph, and "m'" is the height of the PA lesion on the follow-up radiograph.

Figure 1 shows the measurements.

All data were recorded in a checklist, and preoperative and follow-up radiographic data were compared. All measurements were made in the software in triplicate to minimize errors.

Functional presence of the respective tooth in dental arch with no need for endodontic treatment during the follow-ups were considered as treatment success.[15]

Statistical analysis:

Root length and width, dentin width, and apical opening were compared among the follow-up sessions by paired samples t-test. The mean and frequency values were

reported for the survival rate, tooth function, symptoms, pulp sensibility tests, PA tests, PD, bleeding, edema, sinus tract, scarring, mobility and PA index. All statistical analyses were carried out using SPSS 25 (SPSS Inc., IL, USA), and P<0.05 was considered statistically significant. The normality of the data was assessed using the Kolmogorov–Smirnov test in SPSS.

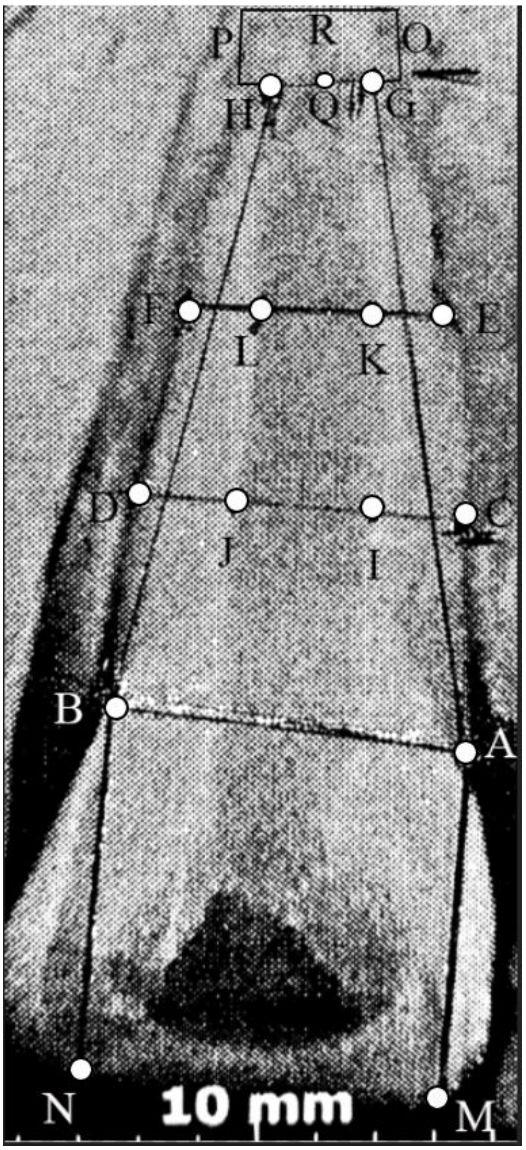

Figure 1: Measurements: AB: a, CD: b, EF: c, GH: d, IJ: e, KL: f, AG: g, BH: h, AM: I, OPQR: periapical lesion

Results

A total of 12 eligible patients (N=16 teeth) were contacted; out of which, 9 (N=12 teeth) showed up for a follow-up. Two teeth were excluded due to change in treatment plan, and two others were excluded since the patients did not show-up. The mean age of patients was 15±8.44 years (range 10 to 23 years), and 41.66% were females.

Ten teeth had experienced trauma, and the remaining two were necrotic due to anomalies [Turner's hypoplasia (case 3), and supernumerary tooth (case 8)]. Of all teeth, five were right maxillary central incisors, five were left maxillary central incisors, one was mandibular left first premolar, and one was maxillary right lateral incisor. Twelve teeth had undergone revascularization; six teeth had been treated with calcium-enriched mixture (CEM) cement, four with Biodentine, and two with mineral trioxide aggregate (MTA). Triple antibiotic paste had been applied as intracanal medicament in all teeth, except one, where only CH was used (case 11). In three teeth (cases 3, 4 and 6), CollaPlug was used as collagen scaffold. All teeth had pulpal necrosis before treatment. In three teeth (cases 3, 5 and 6), CH had been previously used for apexification treatment; however, they eventually underwent revascularization treatment due to their blunderbuss apical shape. Four teeth were non-blunderbuss (cases 5, 6, 10, and 12) at the treatment onset, and the rest were blunderbuss.

All teeth were painless at the treatment onset except one maxillary right central incisor (case 9), which had intermittent pain and acute apical abscess. It underwent revascularization with Biodentine. All teeth were painless at the one-year follow-up. All teeth were discolored at the onset of treatment except four teeth (cases 5, 6, 10, and 12). Two teeth had veneers, 8 had composite restorations, and 2 had temporary glass ionomer restoration. At the 12-month follow-up, 5 teeth (cases 1, 2, 4, 7 and 8) showed discoloration. All teeth, except for a maxillary right lateral incisor (case 8, which had grade I mobility) had normal mobility. Table 1 presents a summary of the information of patients.

In the first follow-up session (between 6 to 12 months after the treatment), 12 teeth were evaluated. All showed a successful treatment, except one tooth treated in 2014, which underwent retreatment in 2018 due to the increase in lesion size and mobility (case 8). Three teeth showed a reduction in root length (cases 3, 7, and 8). All teeth experienced an increase in root width which was slight in the coronal third, and greater in the apical third. One tooth (case 8) showed a reduction in dentin width in the coronal and apical region. Also, the size of apical opening decreased in 11 cases, and only increased in a maxillary right lateral incisor (case 8). The mean percentage of change in lesion size was -4.333% in the mesiodistal dimension and -8.967% in height.

In the second follow-up session (12 to 18 months after the treatment), 11 teeth were evaluated (all cases except for case 8, i.e., a maxillary right lateral incisor). Two teeth had

a reduction in root length, including a mandibular right premolar (case 3) and a maxillary left central incisor (case 7). All teeth showed a slight increase in root width at the coronal third and apical third. Also, all teeth experienced an increase in coronal and apical dentin width. The size of apical opening decreased in all cases. The mean percentage of change in lesion size was -6.519% in mesiodistal and -12.544% in height. Figure 2 shows 12-month follow-up of a tooth.

Table1- A summary of information of patients

Case number	Age	Tooth number	Cause	Type of treatment	PA status at treatment onset
1	14	UR1	Trauma	Revascularization (CEM)	SAP
2	14	UL1	Trauma	Revascularization (CEM)	CAA
3	10	LL4	Turner hyperplasia	revascularization (Biodentine)	SAP
4	23	UR1	Trauma	Revascularization (CEM)	N
5	11	UL1	Trauma	revascularization (Biodentine)	N
6	11	UR1	Trauma	revascularization (Biodentine)	N
7	10	UL1	Trauma	Revascularization (CEM)	N
8	19	UR2	Supernumerary tooth	revascularization (Biodentine)	SAP
9	22	UR1	Trauma	Revascularization (CEM)	AAA
10	16	UL1	Trauma	Revascularization (CEM)	N
11	15	UL1	Trauma	Revascularization (MTA)	CAA
12	15	UR1	Trauma	Revascularization (MTA)	AAP

SAP: Symptomatic apical periodontitis / AAA: Acute apical abscess / N: Normal / CAA: Chronic apical abscess / AAP: Asymptomatic apical periodontitis

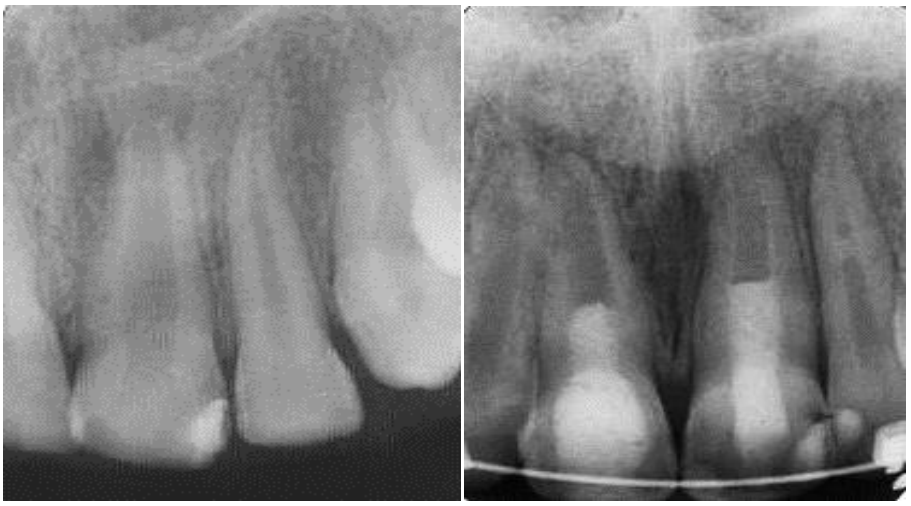

Figure 2: (Left) Immature maxillary left central incisor with a periapical lesion; (right) 12-month follow-up of the same tooth after revascularization treatment. Resolution of periapical lesion, increased root length and dentinal wall thickness, and apex closure can be seen.

In the third follow-up session (after 2 years), only 5 teeth (3 patients; cases 5, 6, 10, 11, and 12) were evaluated. All teeth showed an increase in root length, a slight increase in root width in the coronal third, and greater increase in root width in the apical third. Also, all teeth showed an increase in coronal and apical dentin width. The normality of variables was tested (by kolmogorov Smirnov test) and they were normally distributed so the repeated measure

Anova was done. The size of apical opening decreased in all cases.

Statistically, closure of apical opening was significant (P=0.049). Other changes were not statistically significant (P>0.05). Table 2 presents radiographic changes at the three follow-ups.

Table 2- Radiographic changes at the three follow-ups

Parameter	First follow-up	Second follow-up	Third follow-up	P value
	Mean± SD	Mean± SD	Mean± SD	
Changes in root length	3.412 ± 6.562	5.754 ± 6.495	9.194 ± 7.636	0.096
Changes in coronal root width	3.483 ± 3.809	5.390 ± 3.305	1.735 ± 4.840	0.705
Changes in apical root width	9.101 ± 7.644	11.670 ± 6.439	11.321 ± 6.224	0.330
Changes in coronal dentin width	9.841 ± 14.781	14.951 ± 12.089	12.197 ± 18.964	0.408
Changes in apical dentin width	11.628 ± 15.961	30.077 ± 12.159	24.895 ± 10.082	0.455
Changes in apical opening	-10.036 ± 8.078	-13.971 ± 12.497	-31.626 ± 12.633	0.049

SD: Standard deviation

Discussion

This study assessed the outcome of REPs in permanent immature necrotic teeth. Evidence shows that at least six months are required for radiographic assessment of the change in PA lesions and 12 to 18 months are required to assess root development.[17] Thus, the follow-ups were scheduled at 6, 12, and 18 months in the present study. Twelve necrotic teeth that underwent revascularization with CEM cement, Biodentine, and MTA were evaluated. At the follow-ups, the root length of the majority of the teeth had increased and the root apex was closed. Root length, apical root width, and apical dentin width significantly increased compared with the preoperative state, and 11 out of 12 teeth were clinically asymptomatic and had normal function, pointing to the success of revascularization treatment, at least in the short-term.

Petrino et al.[18] used triple antibiotic paste and MTA for dentin-pulp regeneration in six immature anterior teeth. At the follow-up session, three teeth showed root development and two teeth showed a positive response to sensibility tests. The success rate at the 12-18-month follow-up in the present study (root development in 81% of the teeth) was higher than that of their study, which may indicate the effectiveness of the adopted treatment approach. Simon et al,[19] in their study, performed apexification with MTA for 57 teeth. At the 1-year follow-up, 43 teeth were assessed. The PA index showed PA healing in 81%; this rate was 33.33% in the present study. In the current study, cases with PA lesions at baseline showed a reduction in lesion size at the follow-up sessions, but the changes were not statistically significant.

A cohort study [15] compared 19 teeth treated by revascularization with 12 teeth treated by apexification. Only one tooth failed in revascularization group, and the majority of the cases showed clinical success. However, side effects were more frequently seen in the revascularization group. Thus, this treatment should be performed carefully and utmost attention should be paid to case selection.

A clinical trial [16] assigned 46 non-vital immature teeth treated by REP with Bio-Gide and without it. All teeth were treated successfully, and dentin thickness in the apical third of the root was greater in teeth treated by REPs. In the present study, three cases received intracanal collagen (CollaPlug). Another clinical trial [20] evaluated 118 teeth in two groups of REPs and apexification. Each group had two subgroups of dent evaginatus and trauma according to etiology. The PA lesions were resolved in all teeth; however, the REP group showed greater root length and thickness; in this group, dent evaginatus teeth showed greater root length and thickness than traumatized teeth. These findings may indicate that non-vital immature teeth may also heal without REPs and by using other approaches; however, REPs can lead to greater root dentin formation, and therefore may be preferred. In a systematic review by Kontakiotis et al [21] on REPs, 51 studies which were mainly case reports were

assessed. They reported resolution of most clinical signs and symptoms after treatment, and an increase in root length and thickness at the follow-ups. In the present study, all clinical symptoms were resolved at the one-year follow-up, and root development was seen in 81% of the teeth after 12 to 18 months. In a more recent systematic review by Torabinejad et al, [22] REPs were compared with MTA apical plug in 144 studies, mostly case reports. No significant difference existed in clinical success rate and tooth survival between the two groups although the success percentage of MTA apical plug was slightly higher (94.6% versus 91.3%). However, there is still need for studies with higher methodological quality.

Studies on REPs with CEM cement are scarce. Asgary et al. [23] used CEM cement apical plug and REPs with CEM cement for two immature maxillary central incisors. At the 3-year follow-up, root development was seen in the tooth treated with REPs; nonetheless, both treatments were successful. In the present study, CEM cement was used in 6 teeth and all of them showed treatment success after 12 months. Root development was seen in all teeth except one.

Risk of discoloration exists in treatment with CEM cement and MTA due to oxidation of heavy metals such as bismuth. Madani et al. [24] treated 68 extracted anterior teeth with Biodentine, MTA, and CEM cement and reported significantly lower discoloration in the Biodentine group than the MTA group after six months; however, the difference between Biodentine and CEM cement was not significant. This topic was not evaluated in the present study due to small sample size.

Small number of cases treated by REP and poor cooperation of patients in showing up for the follow-up sessions especially in the long-term were among the limitations of this study. Also, due to its retrospective design, comprehensive data collection was problematic. Radiographic assessment was performed by PA radiography, and CBCT was not used due to ethical constraints. Future multi-center studies with a larger sample size and longer follow-ups are required to obtain more reliable results.

Conclusion

REPs through revascularization using CEM cement, Biodentine, and MTA can be successful, and increase the chance of completion of root development in permanent immature necrotic teeth.

Acknowledgement: This study was part of a post-graduate thesis in partial fulfillment of the requirements for the M.S. degree in Shahid Beheshti University, School of Dentistry.

Author Contributions:
S.S.: Contributed to the study concept and design; provided administrative, technical, and material support; supervised the study; and performed statistical analysis.
N.Z.: Contributed to the analysis and interpretation of data.
Arman Rafiezade Rafiee: Responsible for the acquisition of data.
S.Z.: Conducted critical revision of the manuscript for important intellectual content.
M.A.: (Corresponding Author): Drafted the manuscript and critically revised it for important intellectual content.

Funding: No funding was received for this research.

Ethical Approval Code: This study was approved by the Ethics Committee of Shahid Beheshti university of medical sciences with approval code: (IR.SBMU.RIDS.REC.1396.584)."

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: "Data Availability Statement: The datasets generated during and/or analyzed during the current study are available from the corresponding author upon reasonable request."

Conflict of Interest: The authors declare no conflict of interest.

References

1. Trope M. Treatment of the immature tooth with a non–vital pulp and apical periodontitis. Dental clinics. 2010;54(2):313-24. doi: 10.1016/j.cden.2009.12.006
2. Cvek M. Prognosis of luxated non-vital maxillary incisors treated with calcium hydroxide and filled with gutta-percha. A retrospective clinical study. Endod Dent Traumatol. 1992;8(2):45-55. doi: 10.1111/j.1600-9657.1992.tb00228.x
3. Jeeruphan T, Jantarat J, Yanpiset K, Suwannapan L, Khewsawai P, Hargreaves KM. Mahidol study 1: comparison of radiographic and survival outcomes of immature teeth treated with either regenerative endodontic or apexification methods:

a retrospective study. J Endod. 2012;38(10):1330-6. doi: 10.1016/j.joen.2012.06.028

4. Murray PE. Review of guidance for the selection of regenerative endodontics, apexogenesis, apexification, pulpotomy, and other endodontic treatments for immature permanent teeth. Int Endod J. 2023:56 Suppl 2:188-99. doi: 10.1111/iej.13809

5. Jadhav K, Vaidya MJ, Hegde V, Kawle S. Management of non-vital immature teeth-A review. J Dent Med Sci. 2021; 20:35-40. doi.org/10.9790/0853-2007093540

6. Sheehy E, Roberts G. Use of calcium hydroxide for apical barrier formation and healing in non-vital immature permanent teeth: a review. Br Dent J. 1997;183(7):241-6. doi: 10.1038/sj.bdj.4809477

7. Al-Hiyasat AS, El-Farraj HS, Alebrahim MA. The effect of calcium hydroxide on dentine composition and root fracture resistance of human teeth: An in vitro study. Eur J Oral Sci. 2021;129(4):e12798. doi: 10.1111/eos.12798

8. Gupta S, Sodhi SP, Brar GK, Bansal RN. Endodontic treatment of immature tooth-a challenge. J Pre Clin Clin Res. 2020;14(3):73-9. doi.org/10.26444/jpccr/126280

9. Kandemir Demirci G, Kaval ME, Güneri P, Çalışkan MK. Treatment of immature teeth with nonvital pulps in adults: a prospective comparative clinical study comparing MTA with Ca (OH) 2. Int Endod J. 2020;53(1):5-18. doi: 10.1111/iej.13201

10. Murray PE, Garcia-Godoy F, Hargreaves KM. Regenerative endodontics: a review of current status and a call for action. J Endod. 2007;33(4):377-90. doi: 10.1016/j.joen.2006.09.013

11. Lovelace TW, Henry MA, Hargreaves KM, Diogenes A. Evaluation of the delivery of mesenchymal stem cells into the root canal space of necrotic immature teeth after clinical regenerative endodontic procedure. J Endod. 2011;37(2):133-8. doi:10.1016/j.joen.2010.10.009

12. Youssef A, Ali M, ElBolok A, Hassan R. Regenerative endodontic procedures for the treatment of necrotic mature teeth: A preliminary randomized clinical trial. Int Endod J. 2022;55(4):334-46. doi: 10.1111/iej.13681

13. Li J, Zheng L, Daraqel B, Liu J, Hu Y. Treatment outcome of regenerative endodontic procedures for necrotic immature and mature permanent teeth: a systematic review and Meta-analysis based on randomised controlled trials. Oral Health Prev Dent. 2023:21:141-52. doi: 10.3290/j.ohpd.b4100877

14. Rossman LE. American Association of Endodontists. J Am Coll Dent. 2009;76(1):4-8.

15. Alobaid AS, Cortes LM, Lo J, Nguyen TT, Albert J, Abu-Melha AS, et al. Radiographic and clinical outcomes of the treatment of immature permanent teeth by revascularization or apexification: a pilot retrospective cohort study. J Endod. 2014;40(8):1063-70. doi: 10.1016/j.joen.2014.02.016.

16. Jiang X, Liu H, Peng C. Collagen membrane in regenerative endodontics: a randomized, controlled clinical trial. J Endod. 2017;43(9):1465-1471. doi: 10.1016/j.joen.2017.04.011.

17. Bose R, Nummikoski P, Hargreaves K. A retrospective evaluation of radiographic outcomes in immature teeth with necrotic root canal systems treated with regenerative endodontic procedures. J Endod. 2009;35(10):1343-9. doi: 10.1016/j.joen.2009.06.021

18. Petrino JA, Boda KK, Shambarger S, Bowles WR, McClanahan SB. Challenges in regenerative endodontics: a case series. J Endod. 2010;36(3):536-41. doi: 10.1016/j.joen.2009.10.006

19. Simon S, Rilliard F, Berdal A, Machtou P. The use of mineral trioxide aggregate in one-visit apexification treatment: a prospective study. International endodontic. Int Endod J. 2007;40(3):186-97. doi: 10.1111/j.1365-2591.2007.01214.x

20. Lin J, Zeng Q, Wei X, Zhao W, Cui M, Gu J, et al. Regenerative endodontics versus apexification in immature permanent teeth with apical periodontitis: a prospective randomized controlled study. J Endod. 2017;43(11):1821-7. doi: 10.1016/j.joen.2017.06.023

21. Kontakiotis EG, Filippatos CG, Agrafioti A. Levels of evidence for the outcome of regenerative endodontic therapy. 2014;40(8):1045-53. doi: 10.1016/j.joen.2014.03.013

22. Torabinejad M, Nosrat A, Verma P, Udochukwu O. Regenerative endodontic treatment or mineral trioxide aggregate apical plug in teeth with necrotic pulps and open apices: a systematic review and meta-analysis. J Endod. 2017 Nov;43(11):1806-1820. doi: 10.1016/j.joen.2017.06.029

23. Asgary S, Fazlyab M, Nosrat A. Regenerative endodontic treatment versus apical plug in immature teeth: three-year follow-up. J Clin Pediatr Dent. 2016;40(5):356-60. doi: 10.17796/1053-4628-40.5.356.

24. Madani Z, Alvandifar S, Bizhani A. Evaluation of tooth discoloration after treatment with mineral trioxide aggregate, calcium-enriched mixture, and Biodentine® in the presence and absence of blood. Dent Res J (Isfahan). 2019 Nov 12;16(6):377-383.