

# An Evidence-based Review of the Efficacy of Treatment Approaches for Immature Permanent Teeth with Pulp Necrosis

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## Abstract

**Introduction:** Two fundamental assumptions for teeth treated with regenerative endodontic procedures (REPs) are (1) that the clinical outcome is comparable with the traditional techniques of calcium hydroxide apexification and mineral trioxide aggregate apical barrier techniques and (2) that REPs will result in further root maturation. **Methods:** A systematic review of the electronic databases (Scopus, PubMed, and Web of Science) involved a search for studies that used quantitative assessments of root maturation. The search terms were “dental pulp,” “regenerative endodontic therapy,” “revascularization,” and “revitalization.” The identified studies were further screened for cohort studies that compared clinical outcomes between teeth treated with REPs and apexification/apical barrier approaches. The primary question under review was framed according to the population, exposure, and outcome format. **Results:** Of the 368 studies identified by the search, 6 cohort studies used quantitative assessments of any further root maturation after REPs, and a subset of 4 of these cohort studies assessed and compared clinical outcomes between the different treatment approaches. **Conclusions:** Immature teeth with pulp necrosis treated with REPs generally show further root maturation although the results are variable. Clinical outcomes were similar for both groups. Patient-based criteria such as tooth discoloration, indications for changing the treatment option, and number of treatment appointments are all important for discussion before electing the appropriate treatment plan for the management of immature teeth with pulp necrosis. (*J Endod* 2017; ■:1–6)

## Key Words

Calcium hydroxide apexification, clinical outcomes, clinician- and patient-based criterion, mineral trioxide aggregate apical barrier, quantitative assessment, regenerative endodontic procedures

Immature permanent teeth that develop pulp necrosis result in the cessation of root development, leaving the root walls thin, fragile, and susceptible to cervical root fracture and tooth loss (1). Traditionally, these teeth were treated with the calcium hydroxide apexification technique, which required multiple visits over an extended treatment time with prolonged exposure to calcium hydroxide (2, 3), potentially increasing the susceptibility of cervical root fracture (4). More recently, the use of apical barrier techniques with mineral trioxide aggregate (MTA) being placed at the open apex has shortened the treatment times and resulted in favorable healing outcomes (5, 6). However, neither of these approaches allow for further root maturation with the potential to strengthen the tooth. Since 2001, regenerative endodontic procedures (REPs) provided a biologically based framework in which further root maturation can occur (7).

Recent reviews offer mixed conclusions. One review advocates that REPS should be considered as the first treatment option for immature teeth with pulp necrosis (8), whereas another concludes that the available evidence should be interpreted with caution because studies report different treatment methods and evaluation parameters (9). A third review reported that revascularization of immature teeth was an effective and reproducible technique with 97 of 101 teeth (96%) treated successfully with increases in root length, root width, and apical closure observed in 76.2%, 79.2%, and 55.4% of cases, respectively (10). For REPs, the American Association of Endodontists defines success by 3 parameters (11). The primary goal is the resolution of clinical signs and symptoms. Further root maturation is a secondary goal, and a positive response to vitality testing is a tertiary goal. The American Association of Endodontists has also published “Clinical Considerations for a Regenerative Procedure,” a collection of points to consider when planning or performing REPs in the treatment of immature teeth with pulp necrosis. More recently, it has been advocated that outcome measures of treatment modalities should also include patient-based outcomes in addition to clinician-based criteria (8). Discoloration of teeth, pain, lack of response to treatment,

## Significance

Regenerative endodontic procedures are associated with further root maturation in the treatment of immature teeth with necrotic pulps. However, the amount of development can be variable. In addition, REPs have clinical and radiographic outcomes that are comparable with those of alternative procedures.

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## Review Article

and/or the requirement to change treatment options would be examples of patient-based and clinician-based concerns.

Since 2001, numerous studies reported on immature teeth with pulp necrosis that have been treated with REPs. The literature is dominated by case reports with fewer case series and cohort studies (12). The studies generally have not followed a standardized protocol and, in fact, used a variety of irrigants, medicaments, and materials (13). Furthermore, outcome assessments were often qualitative with the potential for bias. In 2009, a pioneering study was published that used a geometric imaging program to minimize errors of angulation between pre- and postoperative radiographs for outcome assessments and to quantitatively determine and calculate percent changes in root length and width (14).

Although radiographic root development (ie, further root maturation) has been described as a clinician-based outcome (8), a fundamental assumption of REPs is that further root maturation has the potential to strengthen roots and decrease the risk of coronal root fracture, thus likely influencing alternative outcome measures such as tooth survival, an important patient-centered outcome. Secondary to this assumption is that REPs offer successful clinician- and patient-based outcomes despite the lack of long-term outcome studies. Therefore, the purpose of this evidence-based review was 2-fold: first, to undertake a literature review for studies that undertook a quantitative assessment of further root maturation of immature teeth with pulp necrosis after treatment with REPs and, second, to assess cohort studies that assessed different outcomes for calcium hydroxide apexification, MTA apical barrier techniques, and REPs and compare outcomes in terms of clinician- and patient- based criteria.

## Materials and Methods

### Literature Search Strategy

A systematic search limited to English language publications was performed in PubMed, Web of Science, and Scopus databases from their inception through July 1, 2016. The terms used in the electronic research were “dental pulp,” “regenerative endodontic therapy,” “revascularization,” and “revitalization.” Finally, a citation search of the reference lists of all included studies was performed.

### Inclusion Criteria

The primary question under review was framed according to the population, exposure of interest, outcome format (P: immature, nonvital permanent teeth, E: REPs, and O: root maturation [ie, increase in root wall thickness and/or length and/or decrease in apical diameter]). The question generated for the present study to guide the systematic review was as follows: “In human studies evaluating REPs in nonvital immature permanent teeth, what evidence is available to support the premise of achieving further root maturation?” A secondary aim was to investigate other reported outcomes measure of REPs (eg, tooth survival and function, clinical and radiographic resolution of periapical radiolucency, and success/failure) and to compare these against the same for the alternative treatments (calcium hydroxide apexification, and MTA barrier techniques) presented in the included studies.

Studies were included in the systematic review if they met the following inclusion criteria: published in English, performed in humans, included a sample of 5 or more teeth, involved immature necrotic permanent teeth treated with REPs, and performed quantitative assessment of root length and/or width and/or apical diameter changes. Studies in other languages; performed in animals; case reports; and series including less than 5 teeth, not involving immature necrotic permanent teeth treated with REPs, or not including quantitative assessment of root length, root wall thickness, and/or apical diameter were excluded. There were no restrictions on the year of publication.

### Evaluation of the Selected Studies

The title and the abstract of the published studies were evaluated by 2 investigators (B.K. and G.R.F.), and, if not clear enough, the full article was read for accuracy of data gathering. After the initial screening of the title and abstract, full-text evaluation of the relevant articles was performed to identify their eligibility against the inclusion criteria. Disagreements concerning the inclusion of a study were discussed until a decision was obtained by consensus. Data extraction was performed by 2 reviewers (B.K. and G.R.F.).

The following information was extracted for each study and recorded on a data collection sheet: author(s), year of publication, journal, tooth number, sample size, irrigation protocol, medication protocol, use of scaffold, comparators between groups (when present), duration of follow-up, root length changes, root wall thickness changes, apical diameter changes, and other treatment outcomes. The authors of the included studies were contacted for clarification and/or requested to provide further information as needed.

### Data Synthesis

Overall, REPs and alternative treatment(s) success rates were calculated for the different outcome measures if the studies reported the relevant raw data and the outcome definitions were comparable. In the absence of raw data and in the presence of quantitative data and/or differing outcome definitions, the study results were summarized as narrative and tabulated according to the different outcome measures.

## Results

After the removal of duplicates, the electronic search strategy yielded 214 publications. Among the 214 studies, 6 satisfied the inclusion criteria (14–19). The results of the search strategy are presented (Fig. 1) as well as the details and characteristics of the included studies (Table 1).

### Root Maturation

Quantitative outcomes of studies that assessed root maturation after REPs and alternative treatments are reported (Table 1) as well as the comparison of REPs with the traditional techniques (Table 2).

### Outcome Assessment Criteria

A description and comparison of outcome assessment criteria reported in the studies are summarized (Table 3). The outcome measures include tooth survival and function, resolution of disease, and success and failure. Additionally, outcome criteria are also considered as patient- and/or clinician-based outcomes. One study was excluded from outcome assessment analysis except for the root maturation outcomes (14) because it included an assessment of previously published case reports and unpublished data as opposed to the other single-center studies. A second study was excluded from tooth survival analysis because “failed” REP cases were subsequently treated by an MTA barrier (16); thus, study allocation would have been inconsistent. Conversely, the authors of a different study confirmed that all the teeth remained present in the arch throughout the study period and clarified data regarding radiographic healing (17); thus, their data were included for calculation of the relative outcome measures.

Tooth survival data were collected from 4 studies (Tables 2 and 3). An overall survival of 98.6% was found for REPs ( $n = 75$ ), whereas calcium hydroxide and apexification/apical barrier consolidated ( $n = 53$ ) presented with a survival rate of 88.6%.

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