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Comparison of Scaffold Materials on CBCT-assessed Root Development Outcomes after Regenerative Endodontic Treatment of Immature Permanent Teeth: A Systematic Review

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Abstract

Introduction: Regenerative endodontic therapy (RET) promotes root maturation in immature necrotic permanent teeth; however, the relative efficacy of various scaffolds remains unclear. This review synthesizes cone-beam computed tomography (CBCT)-based evidence to evaluate and compare post-RET root development across different scaffold materials. **Materials and Methods:** The review followed PRISMA 2020 and was prospectively registered in PROSPERO. Electronic databases and grey literature were searched for records published between January 2000 and February 2026. Clinical studies assessing root development by CBCT used alone or alongside conventional radiography were eligible and grouped by scaffold material to enable inter-material comparison. Root length change, dentinal wall thickness change, and apical closure served as the CBCT-assessed outcomes. Methodological quality was appraised using RoB-2 and ROBINS-I, and certainty of evidence was rated with GRADE. Owing to substantial heterogeneity, findings were synthesized narratively. **Results:** Twelve studies (466 teeth) were included. All scaffold types showed root-length increases (0.21–2.42 mm). Specifically, the conventional blood clot group exhibited root-length gains of 0.50–1.64 mm and apical closure in 65–73% of teeth. The blood clot produced modest but reproducible improvements; platelet concentrates (PRP, PRF) showed inconsistent outcomes; concentrated growth factor and chitosan-based scaffolds yielded favourable but limited evidence; L-PRF was comparatively less effective. Head-to-head comparisons, drawn from small, heterogeneous studies, were study-specific and did not establish clear superiority of any scaffold. Overall certainty of evidence was low to very low. **Conclusions:** Low- to very-low-certainty evidence suggests root maturation post-RET, though the superiority of scaffolds over blood clots remains inconclusive. Future research requires standardized CBCT protocols, consistent outcome reporting, and adequately powered comparative trials.

Keywords: Cone-beam Computed Tomography; Immature Permanent Teeth; Regenerative Endodontics; Scaffolds

Introduction

Immature permanent teeth affected by pulp necrosis constitute a substantial clinical challenge in endodontics, as arrested root formation results in thin dentinal walls and an open apex that impede conventional treatment and heighten susceptibility to root fracture [1]. Regenerative endodontic therapy (RET) has developed as a biologically based alternative intended to restore the vitality of the pulp–dentin complex and to permit continued root maturation [2, 3]. Founded on tissue-engineering principles, RET depends on the coordinated interaction of stem cells, growth factors, and scaffolds to promote tissue regeneration [4]. Clinically, this is typically accomplished by thorough canal disinfection followed by the induction of periapical bleeding into the canal space, whereby the resultant blood clot functions as a natural scaffold that supports the migration and differentiation of stem cells [5]. The success of this approach is contingent upon an adequate population of stem cells derived from the apical papilla and the concomitant release of bioactive molecules that stimulate regeneration and continued root growth [6]. For terminological consistency, the designation RET is applied throughout this review to encompass the related terms regenerative endodontic procedures (REP) and revascularization.

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In addition to the conventional blood clot, numerous alternative biomaterials have been investigated with the aim of enhancing regenerative outcomes. Platelet concentrates, namely platelet-rich plasma (PRP) and platelet-rich fibrin (PRF), have attracted considerable interest owing to their elevated growth-factor content, which can stimulate cellular proliferation and tissue repair [7, 8]. More recently, additional scaffolds, including leukocyte–platelet-rich fibrin (L-PRF), concentrated growth factor (CGF), treated dentin matrix, and synthetic materials such as chitosan-based hydrogels, have been explored [9, 10]. Each is designed to optimize the regenerative microenvironment by providing structural support and by delivering signaling molecules that promote tissue formation.

The efficacy of regenerative procedures is conventionally assessed by the degree of continued root development, comprising increases in root length, thickening of the dentinal walls, and narrowing or closure of the apical foramen. These parameters have traditionally been evaluated exclusively through imaging, ranging from two-dimensional periapical radiography to the more recent three-dimensional cone-beam computed tomography (CBCT). Two-dimensional radiography is nonetheless constrained by image distortion, superimposition of adjacent anatomical structures, and limited accuracy in representing the true three-dimensional morphology of the root [11]. Consequently, CBCT has become an important endodontic modality, as its high-resolution volumetric imaging enables a markedly more accurate assessment of dental structures and, in particular, of root development and dentinal wall thickness [12].

In recent years, CBCT has been increasingly employed to quantify the outcomes of regenerative endodontic procedures, affording a three-dimensional evaluation of root maturation, dentinal wall thickening, and apical closure. Various scaffold materials, including the blood clot, PRP, and PRF, have been investigated, with studies reporting variable outcomes. However, differences in scaffold type, treatment protocols, outcome measures, and CBCT assessment methods contribute to considerable heterogeneity in the available evidence, rendering definitive conclusions regarding the comparative effectiveness of the different scaffolds difficult to establish [13, 14].

Although several previous systematic reviews [14, 15] of regenerative endodontic therapy have concentrated predominantly on clinical success rates or on outcomes assessed by conventional radiography, more recent evidence, for instance, the randomized controlled trial reported by Mittal *et al.* [4] emphasizes the utility of CBCT for a more accurate, three-dimensional evaluation of post-treatment root development. Conversely, certain contemporary trials, such as the randomized controlled study by Rizk *et al.* [16], relied solely on periapical radiography, thereby limiting the accuracy with which genuine three-dimensional changes in root morphology can be characterized. A synthesis restricted specifically to CBCT-based assessment of regenerative outcomes is therefore warranted.

Accordingly, the present systematic review aimed to evaluate the available clinical evidence concerning regenerative endodontic therapy in immature permanent teeth with pulp necrosis, employing CBCT as the principal outcome-assessment modality. Specifically, the review sought to collate data on post-treatment changes in root length, dentinal wall thickness, and apical closure and to compare the relative performance of the various scaffold materials. In contrast to earlier reviews that amalgamated outcomes obtained from both two-dimensional radiography and CBCT, the present work is distinguished by restricting its synthesis to CBCT-derived measurements, thereby minimizing the distortion and superimposition inherent to conventional radiography and enabling a more accurate three-dimensional comparison of scaffold performance. Although earlier evidence syntheses have confirmed the overall effectiveness of regenerative endodontics across a range of clinical protocols [17], none has restricted its outcome assessment exclusively to CBCT-derived three-dimensional measurements; this methodological restriction constitutes the principal novelty and added value of the present review.

Materials and Methods

The review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines, and the protocol was prospectively registered with the International Prospective Register of Systematic Reviews (PROSPERO) on January 2026 under registration number CRD420261278764. The focused question was formulated according to the population, intervention, comparison, and outcomes (PICO) framework (Table 1).

Review question

How do different intracanal scaffold materials influence CBCT-assessed root development, quantified as change in root length, change in dentinal wall thickness, and degree of apical closure in immature permanent teeth with pulp necrosis undergoing regenerative endodontic therapy?

Eligibility criteria (Table 1)

Several eligible studies employed CBCT in conjunction with conventional periapical radiography rather than as the sole imaging modality. Such studies were included provided that CBCT-based measurements of root development were reported

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Table 1. Eligibility criteria according to the PICOS framework

Parameter	Inclusion criteria	Exclusion criteria
Population	Human patients with immature permanent teeth (open apex, incomplete root development) diagnosed with pulp necrosis on clinical and radiographic assessment, treated by regenerative endodontic therapy. No restriction on age, sex, or ethnicity.	Primary teeth; mature permanent teeth with closed apices; non-human subjects, including animal and *in vitro* investigations; case reports and series of fewer than five patients
Intervention	Regenerative endodontic therapy by any protocol intended to promote continued root development, including blood-clot induction (revascularization), platelet-rich plasma, platelet-rich fibrin, leukocyte- and platelet-rich fibrin, concentrated growth factor, chitosan hydrogel, treated dentin matrix and other scaffold-based strategies	Apexification or MTA plug evaluated alone, without a regenerative intervention; other non-regenerative treatments
Comparison	Another regenerative scaffold (head-to-head); apexification or re-calcification with calcium hydroxide or MTA; a contralateral healthy tooth as normative reference; or pre-treatment CBCT measurements for within-group comparison. Single-arm studies without a concurrent comparator were eligible and were included with caution, provided that within-subject change could be quantified from CBCT.	Studies from which no CBCT-based comparison, either between groups or against baseline, could be derived
Outcomes	CBCT-based measurement of root development: change in root length (mm from a predetermined reference point to the radiographic apex); change in dentinal wall thickness (mm at standardized levels from the apex); and apical closure (binary, or the proportion of teeth achieving complete closure). Studies using CBCT alongside conventional periapical radiography were eligible provided CBCT-derived measurements were reported or derivable; only the CBCT-derived data were extracted and synthesised.	No CBCT evaluation; root development assessed exclusively by two-dimensional radiography; no CBCT-based outcome reported
Study design	Randomized controlled trials; non-randomized controlled trials; prospective cohort studies; retrospective cohort studies	Case reports and series of fewer than five cases; narrative and systematic reviews; editorials, commentaries and letters; *in vitro* studies; animal studies; conference abstracts without full text
Context	No geographical, demographic or setting restrictions. No language restriction; published and unpublished studies, including theses, dissertations and preprints, were eligible.	—

CBCT, cone-beam computed tomography; MTA, mineral trioxide aggregate; PICOS, population, intervention, comparison, outcomes, study design. The Comparison row has been revised so that the criteria match both the review protocol, which lists single-arm studies as eligible, and the study designs actually included.

or could be derived; in these instances, only the CBCT-derived data were extracted and synthesized, whereas outcomes assessed exclusively by two-dimensional radiography were excluded. Studies that reported no CBCT-based outcome were not eligible.

Information sources

To identify all relevant studies irrespective of language or publication status, a comprehensive search was undertaken. Four principal electronic databases-PubMed (MEDLINE), Embase, Scopus, and Web of Science constituted the core search, which was supplemented by grey literature and additional sources (Google Scholar, ProQuest Dissertations & Theses, OpenGrey, and SSRN) to retrieve records not indexed in the primary databases.

Search strategy

The search covered MEDLINE (via PubMed), Embase, Scopus and Web of Science, with additional records identified from supplementary sources. The database-specific search expressions, reported search dates and retrieval counts are summarized in Table 2. These details are reproduced from the available study report and could not be independently verified against original search histories. The Web of Science search expression was not recoverable in executable form; the reported retrieval count is retained for consistency with the original study-selection record. No separately verifiable CENTRAL search or CENTRAL-derived records were available for inclusion in the documented search totals.

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Table 2. Information sources and search strategies as reported, with search dates (January 15–18, 2026).

Source	Platform	Search expression reported in manuscript (execution not independently verified)	Records
MEDLINE	PubMed	((("Regenerative Endodontics"[Mesh] OR "Dental Pulp Necrosis"[Mesh] OR "Tooth Apex"[Mesh] OR regenerative endodontic*[tiab] OR regenerative endodontic therap*[tiab] OR pulp regeneration[tiab] OR pulp revascularization[tiab] OR revascularization procedure*[tiab] OR revitalization[tiab] OR cell homing[tiab] OR platelet rich fibrin[tiab] OR PRF[tiab]) AND ("Cone-Beam Computed Tomography"[Mesh] OR "Tomography, X-Ray Computed"[Mesh] OR CBCT[tiab] OR cone beam computed tomography[tiab] OR cone-beam CT[tiab] OR three dimensional imaging[tiab])) AND ("Tooth Root"[Mesh] OR root development[tiab] OR root length[tiab] OR dentinal wall thickness[tiab] OR dentin thickness[tiab] OR apical closure[tiab] OR apical maturation[tiab] OR root maturation[tiab] OR continued root development[tiab]))	142
Embase	embase.com	('regenerative endodontics'/exp OR 'pulp regeneration'/exp OR 'pulp revascularization'/exp OR regenerative endodontic*:ti,ab OR pulp regeneration:ti,ab OR revitalization:ti,ab) AND ('cone beam computed tomography'/exp OR cbct:ti,ab OR cone beam computed tomography:ti,ab) AND ('tooth root'/exp OR root development:ti,ab OR root length:ti,ab OR dentinal wall thickness:ti, ab OR apical closure:ti,ab)	118
Scopus	scopus.com	(TITLE-ABS-KEY("regenerative endodontic*" OR "pulp regeneration" OR "pulp revascularization" OR revitalization OR "cell homing")) AND (TITLE-ABS-KEY("cone beam computed tomography" OR CBCT OR "cone-beam CT")) AND (TITLE-ABS-KEY("root development" OR "root length" OR "dentinal wall thickness" OR "apical closure" OR "root maturation"))	135
Web of Science	webofknowledge.com	Executable search expression not available. The previously reported Scopus-specific TITLE-ABS-KEY operator is not valid Web of Science syntax.	92
Google Scholar	scholar.google. com	"regenerative endodontics" AND ("CBCT" OR "cone beam computed tomography") AND ("root development" OR "root length")	8 *
ProQuest Dissertations & Theses*	proquest.com	Search terms were described as corresponding to the Google Scholar search; platform-specific execution details were not reported.	
OpenGrey*	opengrey.eu	Search terms were described as corresponding to the Google Scholar search; platform-specific execution details were not reported.	
SSRN*	ssrn.com	Search terms were described as corresponding to the Google Scholar search; platform-specific execution details were not reported.	
Supplementary methods*	—	Backward screening of the reference lists of all included studies and relevant reviews; forward citation tracking of key included studies in Scopus and Web of Science; direct contact with authors and experts in regenerative endodontics regarding unpublished or ongoing studies	

*tiab: Title/Abstract]; TITLE-ABS-KEY: Title/Abstract/Keyword; *Not reported separately; supplementary sources collectively contributed 8 additional records*

Study selection process

All references retrieved from the database and supplementary searches were imported into reference-management software (EndNote X9, Clarivate Analytics, Philadelphia, PA, USA). Duplicate records were removed using the program's automated function and subsequently verified manually to ensure accuracy. Two authors (AG and RD) independently screened the titles and abstracts of every unique record against the predefined eligibility criteria, following which the full texts of all potentially eligible records were retrieved. The same two authors then independently assessed each full-text article, and any disagreement at this stage was resolved through discussion or, where necessary, by adjudication by a third author (NC).

Data extraction process

A standardized extraction form was developed and piloted on three of the included studies to ensure the consistency and completeness of the abstracted information. Two authors (AG and RD) subsequently extracted data independently from every eligible study using this form, resolving discrepancies through discussion and, where required, by consultation with a third author (NC). Pilot testing confirmed that the form captured all relevant variables; only minor refinements to the wording of the outcome fields, together with the incorporation of a dedicated field for CBCT acquisition parameters, were necessary before full data extraction.

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Risk of bias assessment

Two authors (AG and RD) independently assessed the risk of bias for all included studies, with disagreements resolved through discussion or by a third author (NC). The Cochrane RoB 2 tool was applied to randomized controlled trials and the ROBINS-I tool to non-randomized studies of interventions. For the ROBINS-I assessment, the hypothetical target trial was defined as a randomized controlled trial comparing the scaffolds of interest in immature permanent teeth with pulp necrosis, incorporating random allocation to scaffold groups, standardized regenerative protocols, and blinded CBCT-based outcome assessment; each non-randomized study was appraised against this reference.

Data synthesis

Qualitative synthesis

A narrative synthesis was performed for all included studies, organized according to the following domains:

- **Study characteristics:** including study design, sample size, and study setting.
- **Participant characteristics:** including age, etiology of pulp necrosis, and tooth type.
- **Intervention characteristics:** including scaffold type and treatment protocol.
- **Outcome measures:** including root length change, dentinal wall thickness change, and apical closure.
- **Factors influencing outcomes:** including age, etiology, microbiological status, and size of periapical lesions.

The findings were presented in both narrative and tabular form, with studies grouped by scaffold type and outcome variable to facilitate comparison across interventions.

Quantitative synthesis

A quantitative meta-analysis was considered but not undertaken because the studies differed substantially in scaffold materials, comparator structures, CBCT outcome definitions, measurement scales and follow-up periods. In particular, within-arm changes and between-scaffold effects do not estimate the same quantity. Accordingly, results were synthesised narratively without post hoc statistical pooling.

Assessment of publication bias

Formal assessment of small-study effects or publication bias was not performed because there were insufficient sufficiently comparable studies for any clearly defined outcome and comparison. The possibility of selective publication and reporting cannot be excluded.

Certainty of evidence assessment

The certainty of evidence for each primary outcome, change in root length, dentinal wall thickness, and apical closure was evaluated using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework. Two authors (AG and RD) applied the GRADE approach independently, and any discrepancies were resolved through discussion.

Results

Study selection

The literature search encompassed four electronic databases-PubMed, Embase, Scopus, and Web of Science, spanning the period January 2000 to January 2026 and yielded 487 records in total: 142 from PubMed, 118 from Embase, 135 from Scopus, and 92 from Web of Science. An additional 8 records were identified through supplementary sources, namely manual screening of reference lists, consultation with experts in regenerative endodontics, and grey-literature repositories such as ProQuest Dissertations & Theses, OpenGrey, and the Social Science Research Network (SSRN).

Following the removal of duplicates, 339 unique records proceeded to title and abstract screening. Two reviewers (AG and RD) screened these independently against the predefined eligibility criteria, with disagreements resolved by a third reviewer (NC). At this stage, 287 records were excluded for failing to meet the criteria, principally review articles (n=78), case reports of fewer than five cases (n=64), in vitro studies (n=52), animal studies (n=41), studies of primary teeth (n=23), and reports unrelated to regenerative endodontics or CBCT imaging (n=29).

The full texts of the remaining 52 articles were retrieved and independently assessed by two reviewers, following which 40 were excluded. The reasons comprised the absence of CBCT-based root-development outcomes (n=18), case reports or series of fewer than five cases (n=9), inclusion of mature teeth with closed apices (n=6), insufficient outcome data for extraction (n=4), and duplicate reporting of identical cohorts (n=3).

Twelve studies ultimately fulfilled all eligibility criteria and were incorporated into the qualitative synthesis, as illustrated in the flow diagram (Fig. 1).

Study characteristics

A customized data-extraction table was employed to abstract the requisite information from each study that satisfied the inclusion criteria (Table 3).

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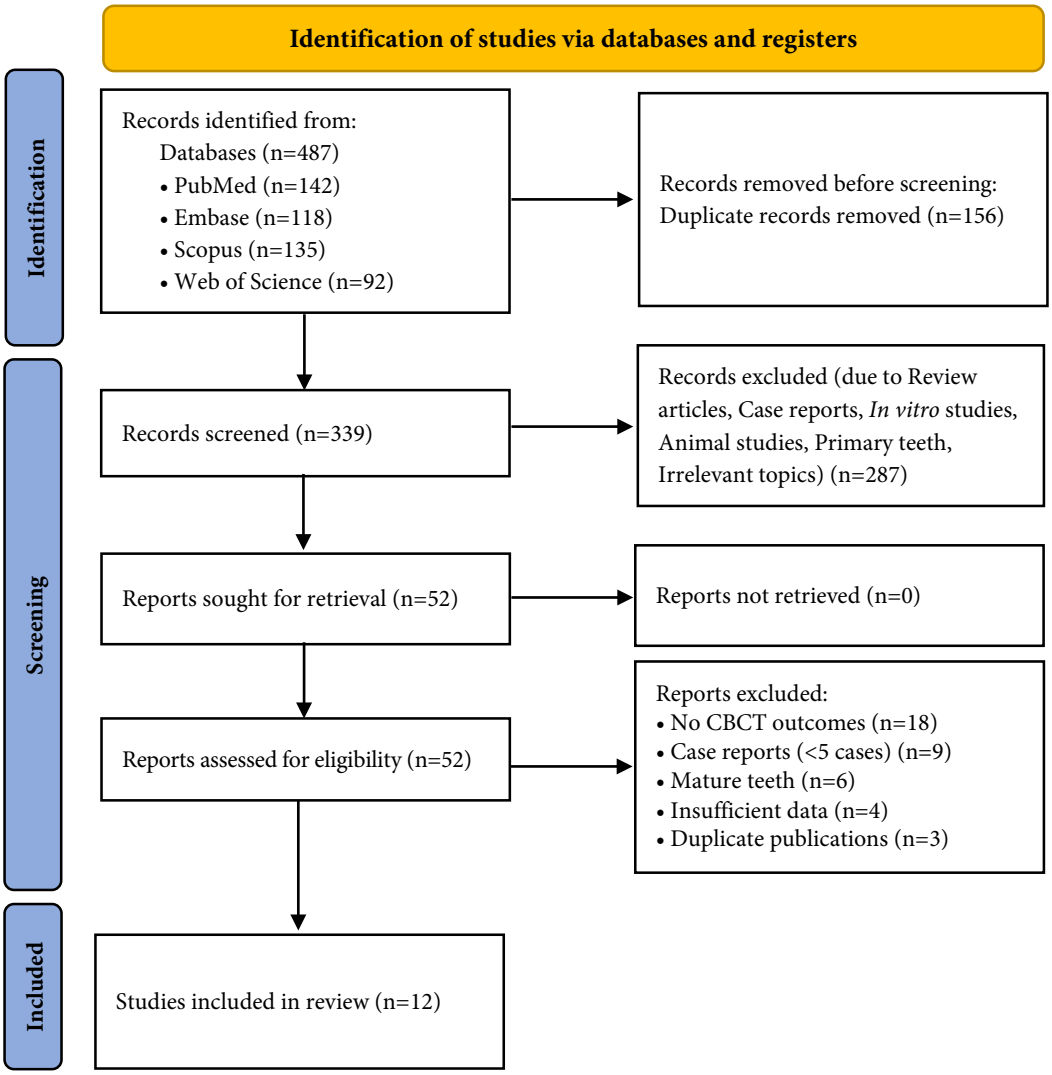


Figure 1. PRISMA flowchart of study selection from database and additional source searches

Published between 2017 and 2025, the 12 included studies [1, 4, 7, 8, 13, 18-24] reflect a growing research emphasis on CBCT-based assessment of regenerative endodontic procedures, with the majority (*n*=9) appearing within the most recent four-year interval of 2021 to 2025.**S**

Sample characteristics

The 12 studies collectively comprised approximately 466 teeth obtained from paediatric, adolescent, and young-adult patients. The sample size of individual studies ranged from 10 to 103 teeth (median 35), and participant ages ranged from 6 to 40 years, with mean ages predominantly reported between 8 and 16 years. The aetiology of pulp necrosis was documented in every study: dental trauma was the most frequent cause (10 studies), followed by dental caries (6 studies), whereas dens evaginatus and dens invaginatus were each reported in 2 studies. Unless otherwise specified, sample sizes denote the number of teeth; where the number of patients was additionally reported, patient-level counts were generally lower than tooth-level counts, as some studies included more than one tooth per patient. Tooth-level and patient-level sample sizes are therefore distinguished throughout the text and tables.

Risk of bias assessment

Assessment of randomized controlled trials

The seven randomized controlled trials were appraised using the Cochrane Risk of Bias tool (RoB-2). The study by Alagl *et al.* [18], which employed a split-mouth design, was assessed using adapted RoB-2 criteria (Fig. 2).

Assessment of non-randomized studies

The five non-randomized studies were assessed using the ROBINS-I tool (Fig. 3).

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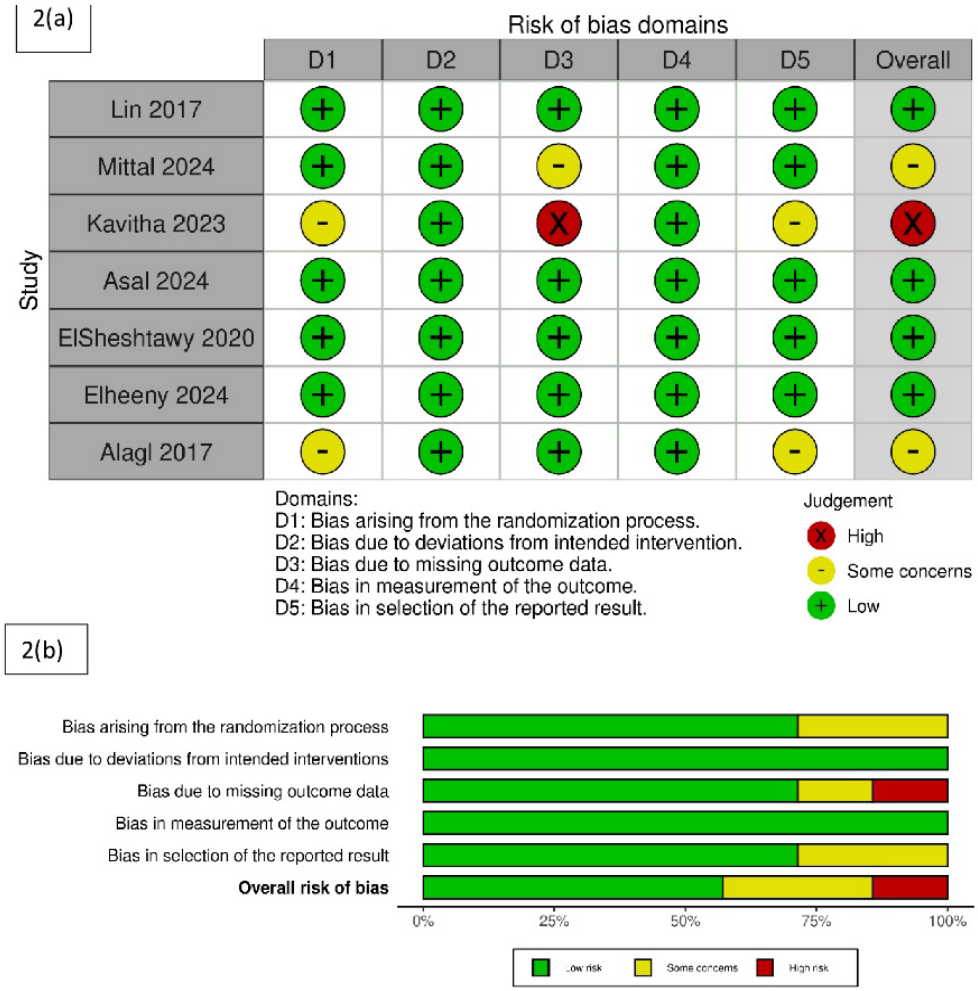


Figure 2. *A*): Risk of bias summary for randomized controlled trials assessed using the Cochrane RoB-2 tool; *B*): Risk of bias graph showing the proportion of studies with low risk, some concerns, and high risk across the RoB-2 domains for the included randomized controlled trials

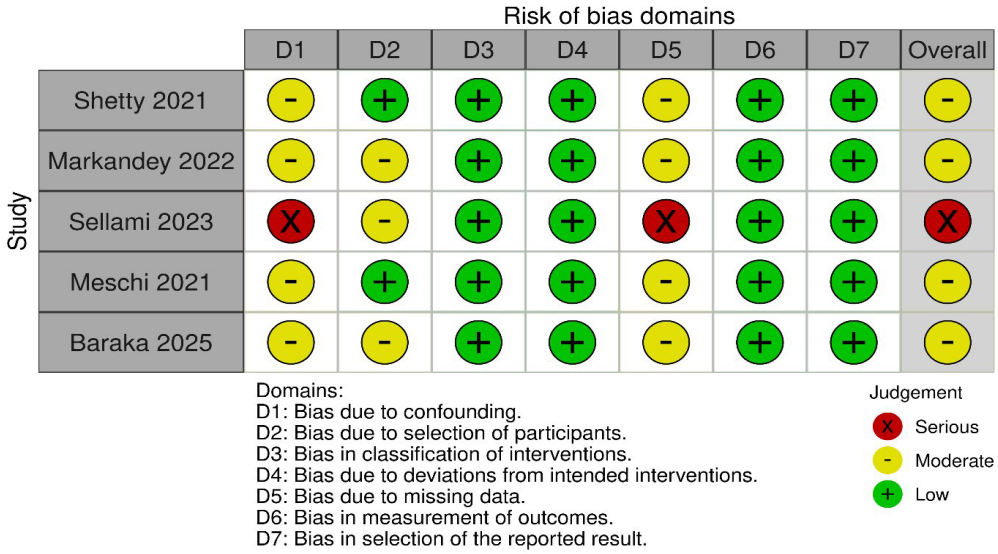


Figure 3. Risk of bias summary for the included non-randomized studies assessed using the ROBINS-I tool across seven bias domains

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Synthesis of results: Root length change

All 12 studies reported CBCT-based changes in root length following regenerative endodontic therapy, as summarized in Supplementary Table S1. The mode of reporting nonetheless varied across studies: some expressed the change as absolute values in millimeters, others as percentages, and a small number relied on score-based systems or qualitative descriptions of root development.

Synthesis of results: Dentinal wall thickness change

Eleven studies reported changes in dentinal wall thickness or related parameters (root hard-tissue thickness, pulp-space diameter, or dentinal-wall volumetric change) determined by CBCT (Supplementary Table S1).

Synthesis of results: Apical closure

Ten studies reported apical closure or related parameters (closure of the apical foramen, reduction in apical diameter, or decrease in apical foramen width) following regenerative endodontic therapy (Supplementary Table S1).

Comparative outcomes by scaffold type

The comparisons collated in Table 4 are derived from individual studies characterized by small samples and heterogeneous designs, scaffold-preparation methods, and outcome definitions. They are therefore study-specific and do not constitute pooled or meta-analytic estimates; any statistically significant differences observed within a single trial should be interpreted with caution as hypothesis-generating findings rather than as confirmed evidence of scaffold superiority.

Factors influencing outcomes (Table 5)

CBCT parameters and measurement methods (Table 6)

Publication bias

No formal assessment of small-study effects or publication bias was undertaken. The included studies differed in scaffold type, comparator, follow-up and outcome measurement, preventing a meaningful common analysis. Potential selective publication and outcome reporting therefore remain limitations of the evidence base.

Certainty of evidence (grade assessment) (Table 7)

Summary of findings by scaffold type (Table 8)

Quality of evidence

Root length change was rated as low certainty of evidence. Commencing from a high baseline for the randomized evidence, the rating was downgraded by one level for risk of bias (deficiencies in randomization, blinding, and reporting across several trials) and by one level for imprecision (small samples and wide confidence intervals); although some inconsistency was evident, it did not warrant an additional downgrade given the broadly consistent and positive direction of effect.

Dentinal wall thickness change was rated as very low certainty of evidence, being downgraded for risk of bias, for substantial inconsistency (marked variability in measurement approaches, encompassing linear, volumetric, and score-based methods), and for imprecision arising from small, heterogeneous samples.

Apical closure was likewise rated as very low certainty of evidence, being downgraded for risk of bias, for marked inconsistency in outcome definition and measurement (percentage closure, apical-diameter reduction, ordinal scores, and qualitative description), and for imprecision. The detailed domain-by-domain judgements underlying these ratings are presented in Table 7.

Table 3. Detailed Characteristics of Included Studies

ID	Author	Study design	Sample size	Age range	Follow-up	Scaffold types	Imaging modality
1	Lin *et al.* [1]	Prospective RCT	103	8-16	12 months	Blood clot	Periapical radiograph and CBCT
2	Mittal *et al.* [4]	RCT	52	10-35	12 months	Chitosan hydrogel variants, PRF	Periapical radiograph and CBCT
3	Kavitha *et al.* [7]	RCT	10	15-35	18 months	PRF, CGF	Periapical radiograph and CBCT
4	Asal *et al.* [8]	RCT	24	7-11	15 months	PRF, Treated dentin matrix	Periapical radiograph and CBCT
5	Alagl *et al.* [18]	Split-mouth clinical	30	8-11	12 months	PRP, Blood clot	CBCT
6	ElSheshtawy *et al.* [19]	RCT	26	8-17	12 months	PRP, Blood clot	Periapical radiograph and CBCT
7	Shetty *et al.* [20]	Prospective cohort	37	9-38	18-48 months	Blood clot	CBCT
8	Markandey *et al.* [13]	Prospective	35	15-36	12-24 months	Blood clot, PRP, PRF	Periapical radiograph and CBCT
9	Sellami *et al.* [21]	Non-randomized controlled	14	7-16	3-36 months	L-PRF	Periapical radiograph and CBCT
10	Baraka *et al.* [22]	Retrospective cohort	46	8-40	12 months	Regenerative procedure	Periapical radiograph and CBCT
11	Meschi *et al.* [23]	Multicenter controlled	23	6-19	3-36 months	L-PRF, Blood clot	Periapical radiograph and CBCT
12	Elheeny *et al.* [24]	RCT	66	7-11	12 months	CGF, PRF	Periapical radiograph and CBCT

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Table 4. Head-to-head comparisons of scaffolds

Comparison	Studies	Root length	Dentinal wall thickness	Apical closure
PRF *vs* Blood clot	Markandey *et al.* [13]; Meschi *et al.* [23]	No significant difference (Markandey, *P*=0.79); No difference (Meschi, *P*=0.72)	No significant difference (Markandey, *P*=0.63); Blood clot superior (Meschi, *P*=0.003)	No significant difference (Markandey, *P*=0.10); L-PRF inferior (Meschi)
PRF *vs* PRP	Markandey *et al.* [13]	No significant difference (*P*=0.79)	No significant difference (*P*=0.63)	No significant difference (*P*=0.10)
PRF vs CGF	Kavitha *et a*l. [7]; Elheeny *et al.* [24]	CGF superior (Elheeny, *P*<0.001); No difference (Kavitha, 60% vs 60%)	No significant difference (Elheeny, NS)	Both 100% (Kavitha)
PRF *vs* Chitosan	Mittal *et al.* [4]	DA+Chitosan hydrogel superior (37.72% vs 20.95%)	DA+Chitosan hydrogel superior (27.86% *vs* 9.82%)	DA+Chitosan hydrogel superior (9.6% *vs* 2.83%)
PRF *vs* TDM	Asal *et al.* [8]	PRF superior (0.74 mm *vs* 0.60 mm, *P*<0.05)	Not directly compared	Not directly compared
PRP *vs* Blood clot	Alagl *et al.* [18]; ElSheshtawy *et al.* [19]	PRP superior (Alagl, *P*<0.05; ElSheshtawy, significant)	PRP superior (ElSheshtawy, +0.06 mm)	Comparable (Alagl, 73% overall)
CGF *vs* PRF	Elheeny *et al.* [24]	CGF superior (2.42 mm *vs* 1.16 mm, *P*<0.001)	No significant difference (5.99 mm *vs* 5.71 mm, NS)	Not reported

CGF, concentrated growth factor; DA, dopamine; L-PRF, leukocyte- and platelet-rich fibrin; NS, not statistically significant; P, probability value; PRF, platelet-rich fibrin; PRP, platelet-rich plasma; TDM, treated dentin matrix

Table 5. Factors influencing regenerative outcomes

Factor	Studies reporting	Effect on outcomes	Statistical significance
Age	Lin *et al.* [1]; Shetty *et al.* [20]; Meschi *et al.* [23]	Younger age associated with better outcomes	Not quantified in most studies
Etiology (Trauma *vs* Caries)	Shetty *et al.* [20]; Sellami *et al.* [21]	Trauma showed better outcomes than caries	Not quantified
Preoperative lesion size	Shetty *et al.* [20]	Larger lesions associated with reduced root development	*P*<0.05
Microbiology	Sellami *et al.* [21]	Presence of bacteria negatively impacted outcomes	-
Dens evaginatus	Lin *et al.* [1]	Premolars with dens evaginatus showed good response	-
Tooth type	Multiple studies	Incisors more commonly studied; premolars also show response	-

Table 6. CBCT Parameters across studies

ID	Study	Voxel Size (mm)	Field of View	Measurement Method	Reliability Reported (ICC)
1	Lin *et al.* [1]	0.125	6x6 cm	Manual	ICC>0.85
2	Mittal *et al.* [4]	Not specified	Not specified	Manual	Not reported
3	Kavitha *et al.* [7]	Not specified	Not specified	Manual	Not reported
4	Asal *et al.* [8]	0.1	4×4 cm	Manual	ICC>0.90
5	Alagl *et al.* [18]	0.2	8×8 cm	Manual	Not reported
6	ElSheshtawy *et al.* [19]	0.125	5×5 cm	Manual	ICC>0.90
7	Shetty *et al.* [20]	0.075	4×4 cm	Semi-automated	ICC>0.90
8	Markandey *et al.* [13]	Not specified	Not specified	Manual	Not reported
9	Sellami *et al.* [21]	0.125	5×5 cm	Manual	Not reported
10	Baraka *et al.* [22]	0.1	4×4 cm	Automated (3D U-NET)	ICC>0.95
11	Meschi *et al.* [23]	0.125	5×5 cm	Manual	ICC>0.85
12	Elheeny *et al.* [24]	0.1	4×4 cm	Manual	ICC>0.90

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Table 7. GRADE assessment of certainty of evidence, by body of evidence and question

Part A. Within-arm question: change from pre-treatment baseline in teeth undergoing regenerative endodontic treatment

Outcome and body of evidence	Studies (teeth)	Starting certainty	Risk of bias	Inconsistency	Indirectness	Imprecision	Certainty
Root length change, randomized	7 (311)	High	Serious *a*	Not serious *b*	Not serious	Serious *c*	⨁⨁◯◯ LOW
Root length change, non-randomized	5 (155)	Low	Serious *d*	Not serious *b*	Not serious	Serious *c*	⨁◯◯◯ VERY LOW
Dentinal wall thickness , randomized	6 (281)	High	Serious *a*	Very serious *e*	Not serious	Serious *c*	⨁◯◯◯ VERY LOW
Dentinal wall thickness, non-randomized	5 (155)	Low	Serious *d*	Very serious *e*	Not serious	Serious *c*	⨁◯◯◯ VERY LOW
Apical closure, randomized	6 (245)	High	Serious *a*	Very serious *f*	Not serious	Serious *c*	⨁◯◯◯ VERY LOW
Apical closure, non-randomized	3 (72)	Low	Serious *d*	Very serious *f*	Not serious	Serious *c*	⨁◯◯◯ VERY LOW

Part B. *Comparative question: one scaffold material versus another, or versus the conventional blood clot*

Comparison	Studies (teeth)	Outcomes rated	Principal limitations	Certainty
PRF *vs* blood clot	Markandey *et al.* [13]	Root length; dentinal wall thickness; apical closure	Single non-randomized study at moderate risk of bias; ordinal 0–3 scoring only, with no quantitative estimate; no significant difference for any outcome	⨁◯◯◯ VERY LOW
PRP *vs* blood clot	Alagl *et al.* [18]; ElSheshtawy *et al.* [19]	Root length; dentinal wall thickness; apical closure	Two small trials, one a split-mouth design assessed with adapted RoB-2 and raising some concerns; differences of 0.06–0.56 mm with wide uncertainty; a third study found no difference	⨁◯◯◯ VERY LOW
L-PRF *vs* blood clot	Sellami *et al.* [21]; Meschi *et al.* [23]	Root length; dentinal wall thickness; apical closure	Both non-randomized, one at serious risk of bias for confounding and missing data; case-wise reporting without summary statistics in one	⨁◯◯◯ VERY LOW
CGF *vs* PRF	Kavitha *et al.* [7]; Elheeny *et al.* [24]	Root length; dentinal wall thickness; apical closure	One trial at high risk of bias reporting proportions only; discordant findings between the two trials for root length	⨁◯◯◯ VERY LOW
PRF *vs* PRP	Markandey *et al.* [13]	Root length; dentinal wall thickness; apical closure	Single non-randomized study; ordinal scoring; no quantitative estimate	⨁◯◯◯ VERY LOW
PRF *vs* chitosan hydrogel	Mittal *et al.* [4]	Root length; dentinal wall thickness; apical closure	Single trial raising some concerns for missing outcome data; percentage change only; four arms with small per-arm samples; no replication	⨁◯◯◯ VERY LOW
PRF *vs* treated dentin matrix	Asal *et al.* [8]	Root length	Single small trial; dentinal wall thickness and apical closure not directly compared	⨁◯◯◯ VERY LOW

a Of the seven randomized trials, one was at high risk of bias overall (Kavitha et al. [7]: high risk for missing outcome data, some concerns for randomization and for selection of the reported result); two raised some concerns (Mittal et al. [4], missing outcome data; Alagl et al. [18], randomization and selection of the reported result, assessed with adapted RoB-2 for its split-mouth design); and four were at low risk across all domains (Lin et al. [1]; Asal et al. [8]; ElSheshtawy et al. [19]; Elheeny et al. [24]). b Not downgraded: although reporting formats varied (millimetres, percentages, ordinal scores and qualitative descriptions), the direction of effect was positive and broadly consistent across every study and scaffold. c Sample sizes ranged from 10 to 103 teeth (median 35); no study reported a sample-size calculation for a comparative outcome, and several comparisons rest on a single study. d Under ROBINS-I, one study was at serious risk of bias (Sellami et al. [21], serious for confounding and for missing data) and four at moderate risk (Shetty et al. [20]; Markandey et al. [13]; Meschi et al. [23]; Baraka et al. [22]), principally for confounding and missing data. e Extreme variability in measurement method: absolute thickness in millimetres, percentage change, pulp-space diameter, root hard-tissue volume, dentinal-wall volumetric change and ordinal score. f Variability in definition and measurement: percentage closure, ordinal score, qualitative description and apical-foramen width. Certainty symbols: ⨁⨁◯◯ low; ⨁◯◯◯ very low. Sample sizes denote teeth, not patients. Alagl et al. [18] did not report dentinal wall thickness; Shetty et al. [20], Baraka et al. [22] and Elheeny et al. [24] did not report apical closure.

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Table 8. Summary of findings by scaffold type

Scaffold type	Root length	Dentinal wall thickness	Apical closure	Studies (n)	Studies with positive outcomes	Studies with negative or neutral outcomes	Consistency of reported findings
Blood clot	0.50–1.64 mm; 5–21%	0.24 mm increase; 33% decrease in pulp space	65–73%	7	Lin *et al.* [1]; Shetty *et al.* [20]; Alagl *et al.* [18]	Markandey *et al.* [13] (neutral *vs* others)	Findings consistent in direction across studies
PRF	0.74–1.16 mm; 21% (increase in up to 60% of teeth)	9.8% increase; variable	2.8–100% (variable definition)	7	Kavitha *et al.* [7]; Asal *et al.* [8]; Elheeny *et al.* [24]	Markandey *et al.* [13] (neutral); Mittal *et al.* [19] (inferior to chitosan)	Findings inconsistent across studies
PRP	0.21–1.06 mm	0.06 mm increase	73% (combined with blood clot)	3	Alagl *et al.* [18]; ElSheshtawy *et al.* [19]	Markandey *et al.* [13] (neutral)	Findings inconsistent; few studies
CGF	2.42 mm; increase in 60% of teeth	5.99 mm (final thickness)	100%	2	Kavitha *et al.* [7]; Elheeny *et al.* [24]	None	Favourable findings; two studies only
Chitosan hydrogel + antibiotics	37.7% increase	27.9% increase	9.6% (specific measure)	1	Mittal *et al.* [4]	None	Favourable findings; single study
L-PRF	No improvement over control	Inferior to blood clot	55.6% showed no closure	2	None	Sellami *et al.* [21]; Meschi *et al.* [23]	No benefit over blood clot in the two reporting studies
Treated dentin matrix	0.60 mm	Not directly reported	Not directly reported	1	Asal *et al.* [8]	None	Single study

Discussion

This review synthesized the CBCT-based evidence on root development after regenerative endodontic therapy and compared the performance of the scaffold materials used. Overall, the included studies indicate that RET reliably supports continued root maturation, with three-dimensional imaging documenting gains in root length, thickening of the dentinal walls, and progressive apical closure. Across the seven randomized controlled trials [1, 4, 7, 8, 18, 19, 24], root length increased by roughly 0.5 to 1.6 mm and apical closure occurred in 65% to 73% of treated teeth. Consistent with this, the blood clot in the conventional revascularization scaffold produced modest but dependable improvements that reaffirm its clinical predictability and align with earlier observations [25]; mechanistically, the fibrin network formed within the clot is thought to guide stem-cell migration and support subsequent.

When the alternative scaffolds were examined against this reference, their comparative performance was less consistent. PRP enhanced root development in some trials [18, 19] yet offered no measurable advantage in others [13], and PRF followed a similar pattern, appearing beneficial in several reports [7, 8, 24] but not in others [4, 13]. This variability most plausibly reflects differences in preparation protocols and in the temporal release of growth factors between platelet derivatives [26]. CGF yielded encouraging results in the few studies that evaluated it, including larger root-length increases and complete apical closure [7, 24], an effect attributable to its dense fibrin scaffold and prolonged growth-factor release [27], although the evidence base remains small. An antibiotic-loaded chitosan hydrogel achieved the greatest percentage gains in root length and dentinal wall thickness in a single trial [4]; because this derives from one small study, it should be interpreted as preliminary and does not demonstrate clinical superiority over the blood clot. By contrast, L-PRF failed to improve outcomes and may be less effective than the blood clot [21, 23] possibly owing to leukocyte-related inflammation or scaffold degradation while treated dentin matrix produced only a modest root-length gain comparable to PRF in a single study [8]. Taken together, these findings show that although several newer scaffolds are biologically promising, none has yet been shown to outperform the conventional blood clot, and the current data are insufficient to establish clear clinical superiority for any single material.

By contrast, L-PRF did not improve outcomes relative to the blood clot in the two studies reporting it [21, 23]; the reasons for this were not investigated in either study. Treated dentin matrix produced a modest root-length gain comparable to that of PRF in a single study [8].

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Several prognostic variables were associated with these outcomes. Younger age was associated with more favourable outcomes [1, 20, 23], and trauma-related cases showed better outcomes than caries-related ones [20, 21]; neither stem-cell activity nor microbial load was measured in any included study, and the mechanisms underlying these associations were not examined and remain hypothetical. Smaller periapical lesions and thorough canal disinfection were similarly associated with more favourable results [5, 28].

A defining strength of this review is its exclusive reliance on CBCT-derived outcomes, which directly reflects the study aim and title. Three-dimensional imaging permits an accurate appraisal of root development that two-dimensional radiography cannot provide, avoiding the geometric distortion and anatomical superimposition inherent to periapical films. Across the included studies, voxel sizes ranged from 0.075 to 0.2 mm, and most reported high intra- and inter-examiner agreement (intraclass correlation coefficient>0.85), supporting the reproducibility of the reported measurements [12, 22, 29]. To our knowledge, this is the first systematic review to restrict its synthesis solely to CBCT-assessed regenerative outcomes, distinguishing it from earlier reviews that combined two- and three-dimensional data and thereby enabling a more precise comparison of scaffold performance.

Because the review is predicated specifically on CBCT outcomes, several imaging-related factors warrant consideration. Voxel size governs spatial resolution and the accuracy of both linear and volumetric measurement, with finer voxels affording greater precision at the cost of higher radiation exposure. Differences between studies in acquisition settings, field of view, and reconstruction protocols added to the heterogeneity and limited direct comparison, while beam-hardening and metallic artefacts from intracanal medicaments, coronal restorations, or calcium-silicate/MTA barriers can degrade image quality and impair reproducible measurement near the apex. Although measurement reliability was generally high, the absence of standardised acquisition and measurement protocols remains an important source of variability. Finally, given the higher radiation dose of CBCT relative to conventional radiography, adherence to the as low as reasonably achievable (ALARA) principle is essential, particularly because most patients undergoing regenerative treatment are children or adolescents.

The clinical relevance of these imaging findings merits explicit consideration. Root-length gains of approximately 0.5–1.6 mm together with measurable increases in dentinal wall thickness would be expected to improve the crown-to-root ratio and root fracture resistance, reducing the long-term risk of cervical root fracture that characterizes thin-walled immature teeth, while apical closure creates a more favourable setting for periapical healing and for any future endodontic intervention. Because these observations stem from studies of low to very low certainty and were rarely linked directly to long-term tooth survival, however, their translation into improved prognosis should be regarded as biologically plausible but not yet firmly established.

Consistent with this, the certainty of evidence ranged from low to very low, reflecting small sample sizes, methodological heterogeneity, and risk of bias, with limitations in randomization, blinding, and reporting evident even among the randomized trials. Most studies enrolled few teeth (range 10–103; median 35), which curtailed statistical power and widened the uncertainty around individual estimates; consequently, some apparent differences between scaffolds may represent underpowered comparisons and random variation rather than genuine biological superiority, an interpretation captured by the imprecision downgrades applied in the GRADE assessment.

A further limitation concerned inconsistent outcome reporting. Several studies presented individual case data, ordinal scores, or incomplete quantitative results; specifically, Markandey *et al.* [13] used an ordinal 0–3 scale, Sellami *et al.* [21] reported case-wise change values without summary statistics, and Kavitha *et al.* [7] expressed outcomes as the proportion of teeth showing improvement rather than as absolute measurements. As the synthesis was narrative, a formal quantitative exclusion analysis was not feasible; instead, a qualitative sensitivity appraisal was performed in which these studies were provisionally set aside and the synthesis re-examined (Supplementary Table S2). The overall direction of the evidence that RET promotes continued root development and that the blood clot remains predictable while newer materials are promising but unconfirmed was unchanged, indicating that the principal conclusions are not driven by the less completely reported studies. Even so, this reliance on qualitative or ordinal reporting contributed to the inconsistency and imprecision that lowered the GRADE ratings and remains a key constraint of the current evidence. Future work should therefore adopt standardised CBCT outcome measures, particularly reporting root length and dentinal wall thickness in millimeters, and pursue adequately powered randomized trials with uniform imaging protocols, since the integration of advanced imaging with automated analysis is likely to further improve measurement accuracy and reproducibility.

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Limitations

A principal limitation was the heterogeneity of outcome reporting and imaging methods, which precluded meaningful quantitative synthesis. Several studies presented case-level data, ordinal scores or incomplete quantitative outcomes. A qualitative sensitivity appraisal excluding less completely reported studies did not materially alter the narrative conclusions, although the certainty of evidence remains limited. An additional methodological limitation concerns search reproducibility: the reported Web of Science strategy used TITLE-ABS-KEY, a Scopus-specific operator rather than native Web of Science syntax. Consequently, the Web of Science search cannot be verified as executed, and studies indexed exclusively in that database may have been missed. Furthermore, the January search dates in Table 2 conflict with a previous account of February searches, including CENTRAL; absent original logs and a CENTRAL-specific record count, completeness of the reported search and PRISMA accounting cannot be confirmed. These uncertainties may affect the comprehensiveness of the evidence base and should be resolved using original search histories or a documented updated search.

Conclusion

Low- to very-low-certainty evidence suggests that continued root development occurs following regenerative endodontic treatment, with increases observed in root length and, less consistently, in dentinal wall thickness and apical closure on CBCT. The comparative superiority of individual scaffold materials over the conventional blood clot remains uncertain, and findings should be interpreted with caution pending adequately powered, methodologically standardized trials.

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Conflict of Interest

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Author Contributions

Conceptualization: NDC/RR; Methodology: NDC/ABG/AC; Formal Analysis and Investigation: NDC/RHD; Writing-Original draft preparation: NDC/ABG/RHD/RR/AC; Writing-review and editing: NDC/ABG; Supervision: ABG. All authors read and approved the final manuscript.

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Supplementary Table S1. Individual study-level CBCT outcomes by study and scaffold type.

ID	Study	Scaffold type	Root length change	Dentinal wall thickness change	Apical closure	Statistical significance
1	Lin *et al.* [1]	Blood clot	1.64 ± 1.43 mm (*vs* apexification 0.60 ± 1.06 mm)	0.24 ± 0.25 mm (*vs* 0.08 ± 0.21 mm)	65.21% achieved closure (*vs* apexification 82.35%)	*P*<0.001 (root length; wall thickness)
2	Mittal *et al.* [4]	PRF	20.95 ± 13.33%	9.82 ± 9.49%	2.83 ± 2.55%	Significant (inferior to DA+chitosan)
2	Mittal *et al.* [4]	DA+chitosan hydrogel	37.72±9.23%	27.86±13.03%	9.61±5.60%	Significant (superior to all groups)
2	Mittal *et al.* [4]	DA-hydrogel	27.20±15.62%	20.43±21.98%	4.47±3.20%	—
2	Mittal *et al.* [4]	Chitosan hydrogel	20.98±11.90%	11.17±10.27%	4.35±4.19%	—
3	Kavitha *et al.* [7]	PRF	Increase in 60% of teeth	Not reported quantitatively	100% apical closure	Not significant (*vs* CGF)
3	Kavitha *et al.* [7]	CGF	Increase in 60% of teeth	Not reported quantitatively	100% apical closure	Not significant (*vs* PRF)
4	Asal *et al.* [8]	PRF	0.74±0.28 mm	Not directly reported (radiographic root area)	Apical diameter reduction measured	*P*<0.05 (PRF>TDM, root length)
4	Asal *et al.* [8]	TDM	0.60±0.17 mm	Not directly reported	Apical diameter reduction measured	—
5	Alagl *et al.* [18]	PRP	1.06±0.62 mm	Not reported	73% root development/closure (both groups combined)	*P* < 0.05 (PRP > blood clot, root length)
5	Alagl *et al.* [18]	Blood clot	0.50±0.42 mm	Not reported	73% (combined)	—
6	ElSheshtawy *et al.* [19]	PRP	+0.21 mm	+0.06 mm	Apical foramen width −0.07 mm	Significant (PRP>blood clot)
6	ElSheshtawy *et al.* [19]	Blood clot	Inferior to PRP	Inferior to PRP	Inferior to PRP	—
7	Shetty *et al.* [20]	Blood clot	5.65±4.08% increase	Pulp space diameter decrease (apical 33.33 ± 20.92%)	Not reported	Significant (pre–post)
8	Markandey *et al.* [13]	Blood clot	Score-based (0–3): no significant difference	Score-based: no significant difference	Score-based: no significant difference	Root length *P*=0.79; wall thickness *P*=0.63; closure *P*=0.10
8	Markandey *et al.* [13]	PRP	Score-based (0–3): no significant difference	Score-based: no significant difference	Score-based: no significant difference	(as above)
8	Markandey *et al.* [13]	PRF	Score-based (0–3): no significant difference	Score-based: no significant difference	Score-based: no significant difference	(as above)
9	Sellami *et al.* [21]	L-PRF	ΔRL (%) reported case-wise; no mean	ΔRHTV (%) reported case-wise	Evaluated by PBH and healing type	No improvement over control
10	Baraka *et al.* [22]	REP (immature)	0.33 mm (*vs* contralateral 0.19 mm)	No significant volumetric difference	Not reported	Not significant
11	Meschi *et al.* [23]	L-PRF	No significant difference (*P*=0.72)	Root hard tissue thickness increased more in control group (*P*=0.003)	~55.6% showed no development/closure	Blood clot superior (wall thickness)
12	Elheeny *et al.* [24]	CGF	2.42±0.98 mm	5.99±1.02 mm (final)	Not reported	*P*<0.001 (CGF>PRF, root length)
12	Elheeny *et al.* [24]	PRF	1.16±0.83 mm	5.71±0.82 mm (final)	Not reported	Not significant (wall thickness)

BC, blood clot; CGF, concentrated growth factor; DA, double antibiotic; L-PRF, leukocyte–platelet-rich fibrin; PRF, platelet-rich fibrin; PRP, platelet-rich plasma; REP, regenerative endodontic procedure; TDM, treated dentin matrix; ΔRHTV, change in root hard-tissue volume; ΔRL, change in root length; PBH, periapical bone healing.

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Supplementary Table S2. Qualitative sensitivity analysis excluding studies with incomplete or non-quantitative outcome reporting.
Because the review used a narrative synthesis, sensitivity analysis was performed qualitatively by provisionally excluding the three studies that reported outcomes using ordinal scores, case-wise values, or proportions (Markandey 2022, Sellami 2023, Kavitha 2022) and re-examining the direction and certainty of the evidence.

CBCT outcome	Studies in primary synthesis	Studies excluded (incomplete/qualitative reporting)	Studies retained	Conclusion primary synthesis	Conclusion after exclusion	Conclusion changed?
Root length change	12	Markandey *et al.* [13] (ordinal 0–3); Sellami 2023 (case-wise, no mean); Kavitha *et al.* [7] (proportion of teeth)	9	RET consistently increased root length; blood clot predictable (0.50–1.64 mm); PRP/PRF/CGF favourable but inconsistent	Direction and magnitude unchanged; quantitative mm-based gains for blood clot, PRP, PRF and CGF retained	No
Dentinal wall thickness change	11	Markandey *et al.* [13] (ordinal); Sellami *et al.* [21] (case-wise)	9	Increases across scaffolds; blood clot superior to L-PRF (Meschi 2021)	Unchanged; blood-clot/L-PRF comparison and quantitative increases retained	No
Apical closure	10	Markandey *et al.* [13] (ordinal); Sellami *et al.* [21] (healing-type only)	8	Variable closure (65–100%); definitions heterogeneous	Unchanged; overall pattern of progressive closure retained	No

GRADE certainty ratings were unaffected by exclusion and remained low (root length) to very low (dentinal wall thickness, apical closure). The principal conclusions of the review are therefore not driven by the less completely reported studies

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