

REVIEW ARTICLE

Vital pulp treatment for traumatized permanent teeth: A systematic review

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Abstract

Background: Traumatic dental injuries involving the pulp are quite common and there is a need to evaluate the quality of evidence on the success of vital pulp treatment (VPT) interventions in traumatised permanent teeth.

Objectives: The aim of this systematic review was to assess the success of VPT in the management of traumatised human vital permanent teeth diagnosed with complicated crown or crown-root fractures.

Methods: An electronic search of the following databases: Web of Science, Scopus, PubMed, MEDLINE, EMBASE, LILACS, Clinical Trial Registries and the grey literature was performed until 25th/8/2021. Controlled clinical trials, cohort studies, case-control studies, case series with at least five cases and a minimum of 12-months follow-up were included. Non-English language literature was excluded. Two independent assessors performed study selection, data extraction and quality assessment using the National Institutes of Health's quality assessment tool. Disagreements were resolved through consensus/with a third assessor.

Results: A total of 14-studies (2-controlled clinical trials, 1-case-control, and 11-case series) published between 1978–2020, with a total of 1081 permanent teeth and an age range between 6–42 years-old were included. Bias analysis ranged considerably from 'good' to 'poor'. Meta-analysis was not performed due to data heterogeneity, unclear reporting, and limited number of controlled clinical studies. Partial pulpotomy was the main reported clinical procedure with an overall success rate between 82.9–100%. Complete pulpotomy and direct pulp capping were associated with lower success rates of 79.4–85.7% and 19.5%, respectively. Calcium hydroxide was the main pulp capping material with favourable clinical and radiographic success (79.4–100%). Biodentine[®], mineral trioxide aggregate and IRoot[®] BP were also associated with a high clinical and radiographic success, 80–91%, 80–100%, and 90–100%, respectively, *albeit* in fewer studies.

Discussion: Although a high success rate has been reported when using VPT in managing pulpally involved traumatised teeth, the results of this systematic review clearly highlighted a paucity and low quality of the available evidence.

Conclusions: Overall high success of VPT in the management of traumatised vital permanent teeth were reported, although based on limited evidence of well-conducted clinical studies.

Registration: PROSPERO database (CRD42020205213).

KEYWORDS

complicated crown fracture, dental trauma, pulp exposure, systematic review, traumatized teeth, vital pulp treatment

INTRODUCTION

Traumatic dental injuries (TDIs) account for approximately 5% of all injuries, with high prevalence in children and young adults (Andersson, 2013). In the permanent dentition, crown fractures are more prevalent than luxation injuries, of which, complicated crown and crown-root fractures are commonly seen (DiAngelis et al., 2016). Several complications such as tooth discolouration, mobility, malocclusion, pulp necrosis and eventually tooth loss might occur following TDIs. Hence, prompt and accurate management of TDIs improves the overall prognosis and reduces the risk of future complications (Krstl, Weiger, Ebeleseder, et al., 2021).

Loss of pulpal vitality, especially in immature teeth, can significantly reduce the long-term prognosis of injured teeth (Nazzal & Duggal, 2017). Furthermore, shortcomings in the initial management of TDIs can potentially lead to a lifelong treatment cycle with an inherent increase in treatment costs (Andersson, 2013). Therefore, preservation of pulp vitality through the use of available vital pulp treatment (VPT) interventions is a key component in the management of traumatized teeth (Cohenca et al., 2013; da Rosa, Piva, et al., 2018).

Clinically, various VPT interventions are well documented and aim to maintain the vitality of pulp tissue that has been previously compromised (Kodonas et al., 2021). Direct pulp capping involves the placement of a protective pulp capping material directly over the exposure site and is mainly indicated in a recent and pinpoint-sized exposed vital pulp (Duncan et al., 2019). Partial (Cvek) pulpotomy, involves partial removal of the coronal pulp, achieving haemostasis followed by placement of a pulp capping material. Furthermore, full (complete) pulpotomy involves removal of the entire coronal pulp to the level of pulp stumps, achieving haemostasis followed by placement of a pulp capping material (Duncan et al., 2019; Krstl, Weiger, Ebeleseder, et al., 2021).

Currently, available systematic reviews and meta-analyses assessing the success of VPT in permanent teeth have mainly focussed on carious exposed pulp

tissue (Aguilar & Linsuwanont, 2011; Cushley et al., 2021; Munir et al., 2020). More recently, a systematic review assessing VPT in permanent teeth due to multifactorial pulpal diagnosis (cariou and traumatic exposures) has been performed (Sabeti et al., 2021). However, to the authors' knowledge, no previous systematic reviews assessing VPT in relation to traumatized exposed pulp tissue have been reported. In contrast to microbial-driven dental caries exposures, which subjects the pulp to a low-grade chronic injury, pulp exposure as a result of TDIs generally involves a considerably lower microbial contamination and shorter exposure time. Consequently, pulpal exposures, as a result of dental trauma, are likely to have a better chance of healing (Bjørndal et al., 2010; Cohenca et al., 2013; da Rosa, Piva, et al., 2018). Therefore, the aim of this systematic review was to assess the success of VPT interventions in the management of traumatized human vital permanent teeth diagnosed with complicated crown or crown-root fractures.

MATERIALS AND METHODS

Protocol registration and review question

This systematic review was registered with the international prospective register of systematic reviews (PROSPERO; CRD42020205213) and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Moher et al., 2009). The research question was formulated using the PICOS framework: In traumatized human vital permanent (immature/mature) teeth diagnosed with complicated crown fracture or crown-root fracture (P), with or without concomitant injuries, do VPT interventions or medicaments (I & C) lead to clinical and radiographic success (O) as reported in randomized, non-randomized and quasirandomized clinical trials, cohort studies, case-control studies, case series of at least 5 cases and a minimum of 12-months follow-up period (S)? Detailed inclusion and exclusion criteria are listed in Table 1.

TABLE 1 Inclusion and exclusion criteria

Parameter	Inclusion criteria	Exclusion criteria
Population	<ul style="list-style-type: none"> • Traumatized vital permanent teeth 	<ul style="list-style-type: none"> • Traumatized vital primary (deciduous) teeth • Exposed pulp as a result of caries or developmental anomalies in the permanent/primary dentition • Studies reporting on pulp exposures of multiple aetiologies, of which data on traumatized teeth is not separate or cannot be clearly identified
Intervention and comparator	<ul style="list-style-type: none"> • Direct pulp capping • Partial (Cvek) pulpotomy • Full (complete) pulpotomy • Other techniques such laser and electrosurgery 	<ul style="list-style-type: none"> • Pulpectomy or root canal treatment
Outcome	<ul style="list-style-type: none"> • Studies reporting both clinical and radiographic success and/or survival of various vital pulp treatments • Studies reporting both clinical and radiographic success and/or survival of various medicaments used in vital pulp treatments such as calcium hydroxide, mineral trioxide aggregate, Biodentine or other calcium silicate-based materials • Results can be either stated in the publication or calculated from raw published data or following contact with corresponding authors 	<ul style="list-style-type: none"> • Studies reporting either clinical or radiographic success/survival data • Inability to obtain outcome results pertaining to traumatized teeth
Study design	<ul style="list-style-type: none"> • Randomized and nonrandomized clinical trials • Quasirandomized clinical trials • Case series with a minimum of 5 cases • Cohort studies • Case-control studies 	<ul style="list-style-type: none"> • Case reports • Case series of less than 5 cases • <i>In-vitro</i> studies • Animal studies
Duration of follow-up	<ul style="list-style-type: none"> • A minimum of 12 months 	<ul style="list-style-type: none"> • Less than 12 months
Language of publication	<ul style="list-style-type: none"> • English 	<ul style="list-style-type: none"> • Languages other than English
Date of publication	<ul style="list-style-type: none"> • No restriction was applied • Available in-print or online at the termination of the search on 25 August 2021 	

Information sources and search strategy

To identify all studies related to our research question, several databases were searched systematically. Clarivate Analytics' Web of Science [1980–2021], Scopus [1960–2021], PubMed [1964–2021], MEDLINE [1946–2021], EMBASE [1947–2021] and Latin American and Caribbean Health Sciences Library [LILACS; 1982–2021]. Clinical Trial Registries [Cochrane Central Register for Controlled Trials (CENTRAL) '<https://www.cochranelibrary.com/central>' and ClinicalTrials.gov '<https://clinicaltrials.gov/>'] were electronically searched and only published data were included. Furthermore, to identify unpublished manuscripts, conference papers, research reports and other grey literature through available digital repositories; OpenGrey (Europe), ProQuest Dissertations and Theses and Google Scholar (first 50 returns) were searched. All database searches were performed by one author (A.S.) with the

assistance of a librarian. Controlled indexing vocabulary (e.g. Medical Subject Headings – MeSH) and free-text or synonymous terms, were used in all search engines while following the syntax rules in each database. All combinations using (OR, AND, NOT) were used (if applicable) for refinement of the search results. The detailed electronic search strategy is presented in Table S1.

Furthermore, five endodontic and dental trauma specialized key journals namely: *Australian Endodontic Journal*, *Dental Traumatology*, *International Endodontic Journal*, *Journal of Endodontics*, and *Oral Surgery Oral Medicine Oral Pathology Oral Radiology and Endodontology*, were individually searched through their respective journal's website. The reference lists of all identified eligible studies and other published systematic reviews were hand-searched in order to identify further eligible studies. No time (i.e. year of publication) restrictions were applied and only English language literature

was included. The initial search was conducted on 5th October 2020 and an updated search up to 25th August 2021 was performed.

Study selection process

Following duplicates removal, the titles and abstracts of all identified manuscripts were screened independently in this stage by four trained and calibrated assessors (M.M, A.S, H.N, & H.J.T.) against a stipulated inclusion criterion using Rayyan application (<https://rayyan.qcri.org/welcome>) (Ouzzani et al., 2016). Full-text assessment of potential studies was independently performed by two of the assessors (M.M. and A.S.). Discrepancies and disagreements on study selection were resolved through consensus or discussion with two other assessors (H.N. and H.J.T.).

Data extraction

Data were entered into a standardized pretested electronic data collection form (modified checklist form provided in the Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0.). Data extraction of all the included studies was performed independently by two calibrated assessors (M.M. and A.S.) who were not blinded to the identity of the authors of the studies, their institutions or the results of their research. All extracted data were stored in a predeveloped Excel spreadsheet created using Microsoft Office software (Microsoft Inc.). If stated, the sources of funding, trial registration and publishing of the trial's protocol were also recorded. This information was used to aid the assessment of heterogeneity and the external validity of included studies. In case of missing data, attempts were made to contact the corresponding author. Disagreements were resolved through consensus or by discussing with two other assessors (H.N. and H.J.T.).

Quality assessment of included studies

The risk of bias in the included studies was performed by two independent and calibrated assessors (A.S. and M.M.) using the National Institutes of Health's (NIH) quality assessment tool. Developed in 2013 by National Heart, Lung, and Blood Institute, the NIH quality assessment tools enable the evaluation of various study designs via a set of tailored criteria that aim to assist the reviewer on key concepts focussing on a study's internal validity (<https://www.nhlbi.nih.gov/health-topics/study-quali>

ty-assessment-tools). The comprehensive evaluation criteria cover various aspects of study design and reporting, such as sample selection, comparability of the groups, dropout rates and outcome assessment. The overall quality rating of each study is classified as either 'good', 'fair' or 'poor' depending on the overall score percentage of 100–80%, 79–60 and <60%, respectively (George et al., 2019). The Scottish Intercollegiate Guidelines Network (SIGN) Grading System (SIGN 50, 2019) was also applied to grade the level of evidence (LOE). Disagreements were resolved by discussing with two other assessors (H.N. and H.J.T.). In case of clarification, the corresponding author was contacted by e-mail. A record of all decisions on study identification was kept.

RESULTS

Literature search and characteristics of the included studies

The literature search retrieved a total of 5255 records, of which 1298 duplicate records were removed and 3904 were excluded following initial title and abstract screening. A total of 53 studies underwent full-text assessment, of which 39 studies were excluded (Table S2). Consequently, a total of 14 studies were found to be eligible for inclusion in this systematic review (Figure 1). Upon further assessment, two studies were found to belong to the same study cohort in which the authors reported their results at different time points. However, as the sample size reduced from 63 to 40 participants in the second report, both studies are presented individually (Fuks et al., 1987, 1993).

The characteristics of the included studies are described in Table 2, where the following parameters have been summarized: Study design, pulp capping material, participants' age, stage of root development, irrigation/haemostatic agent, time to treatment; including trauma to pulp therapy and trauma to definitive coronal seal, definitive coronal seal, operator, follow-up period, dropout rates and both clinical and radiographic outcomes. The majority of studies were conducted in a university hospital setting, with the exception of two studies; one conducted in a governmental setting (de Blanco, 1996) and one in a private practice setting (Witherspoon et al., 2006).

The age range of the participants within the included studies varied from 6 to 42-years-old and involved a total of 1081 permanent teeth. The majority of the included studies specified the type of injured tooth/teeth, of which maxillary central incisors were the most common. Teeth with concomitant trauma were included in five studies

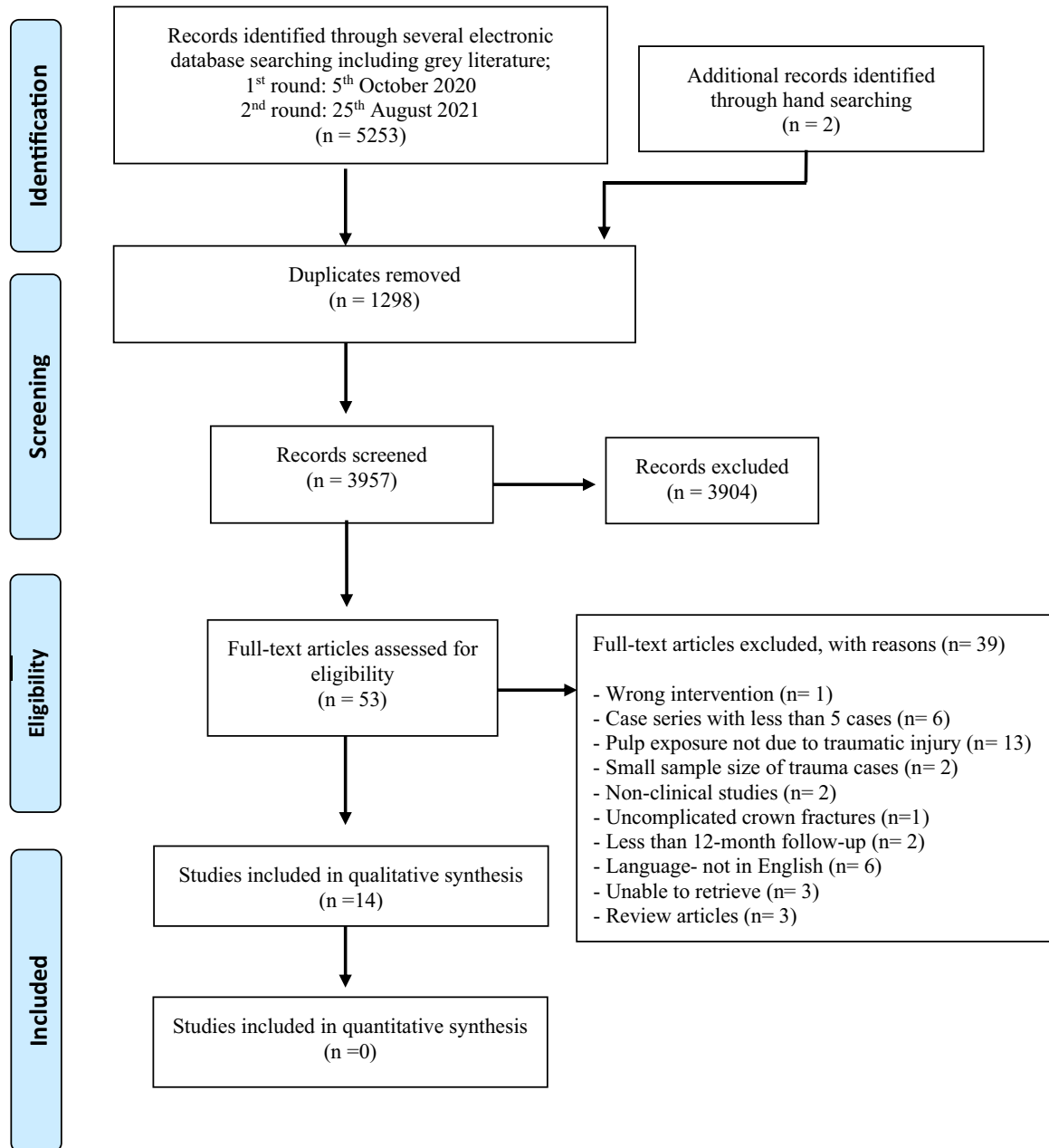


FIGURE 1 PRISMA flow diagram of the study search strategy and identification of relevant studies

(Fuks et al., 1987, 1993; Haikal et al., 2020; Klein et al., 1985; Maguire et al., 2000), whereas excluded in one study (Rao et al., 2020). The remaining seven studies did not report on the presence or absence of concomitant injury (Abuelniel et al., 2020; de Blanco, 1996; Cvek, 1978, 1993; Gelbier & Winter, 1988; Koyuncuoglu et al., 2013; Witherspoon et al., 2006; Yang et al., 2020).

Radiographic outcomes in the majority of studies were assessed with periapical radiographs, with only two studies performing additional root quantification measurements utilizing ImageJ software (Abuelniel et al., 2020; Yang et al., 2020). With regard to the definitive coronal seal, glass ionomer cement and/or composite resin were

the most commonly reported material used either placed at the first visit or subsequent visits. Stainless steel crowns were also utilized in cases of deep fractures; however, these were restricted mainly to studies performed in late 80s and early 90s (Fuks et al., 1987, 1993; Klein et al., 1985).

Only two studies declared sources of funding: A retrospective case-control conducted in China received grant support from the National Natural Science Foundation of China (Rao et al., 2020), while a prospective case series conducted in Canada acknowledged a pharmaceutical and medical device company (Septodont) for donating Biodentine® for their research (Haikal et al., 2020).

TABLE 2 Study characteristics and outcome measures of complicated crown fracture studies

Author (year)	Study design	Material (sample size)	Age range (years)	Stage of root development	Irrigation/haemostatic agent	Time to treatment	
						Trauma to pulp therapy	Trauma to definitive coronal seal
Procedure: Full pulpotomy							
Abuelniel et al. (2020)	Prospective superiority two-arm RCT	Biodentine® (25) ProRoot White MTA (25)	7.5–9	Immature	Saline-moist cotton pellet	Same day	First visit
Witherspoon et al. (2006)	Case series	ProRoot MTA (7)	8–16	NR	S2-ml 6% NaClO	NR	NR
Gelbier and Winter (1988)	Case series	Ca(OH) ₂ (175)	6.2–12.6	Immature	NR	Variable; 57% within 24 h	NR
Procedure: Partial pulpotomy							
Yang et al. (2020)	Prospective parallel group RCT	IRoot® BP Plus (55) Ca(OH) ₂ (55)	7–11	Immature	Sterile saline solution/ saline-moist cotton pellet	Less than 1 week	First visit
Rao et al. (2020)	Retrospective case-control study	IRoot® BP Plus (105) Ca(OH) ₂ (100)	7.8–10.4	Immature (77) Mature (128)	2-ml 0.5% NaClO and 5-ml saline solution/ saline-moist cotton pellet	2 h–1 m	First visit
Haikal et al. (2020) ^a	Prospective case series	Biodentine® (51)	8.4–13.2	Immature (29) Mature (22)	3% NaClO solution/ NaClO cotton-soaked pellet	4 h (median)	Either a temporary or definitive restoration was applied in first visit
Koyuncuoglu et al. (2013)	Case series	ProRoot White MTA (13)	7–10	Immature	NaClO solution	24–72 h	First visit
de Blanco (1996)	Case series	Ca(OH) ₂ powder (30)	7–42	Immature (10) Mature (20)	Sterile saline solution	1 h–9 days	Subsequent visit

Definitive coronal seal	Operator	Follow-up	Dropout (n)	Outcome measures	
				Clinical	Radiographic
GIC + Composite resin	One paediatric dentist	18 m	Biodentine® (2) ProRoot MTA (2)	<ul style="list-style-type: none"> • Pain • Swelling • Mobility • Discolouration 	<ul style="list-style-type: none"> • No intrapulpal or periapical pathosis • Continued root development of immature teeth
NR	Not specified, all treatment was performed in private practice/s limited to endodontics	12–25 m	(1)	<ul style="list-style-type: none"> • Pain assessment • Pulp sensibility tests • Percussion 	<ul style="list-style-type: none"> • Radiographic appearance of the tooth consistent with developmental age
NR	NR	Up to 24 m	(0)	<ul style="list-style-type: none"> • Pulp sensibility tests 	<ul style="list-style-type: none"> • Dentine bridge formation • Root resorption (internal, external/lateral, external/apical) • Pulpal calcification • Periapical radiolucency
Composite resin	Three paediatric dentists	24 m	IRoot® BP Plus (5) Ca(OH) ₂ (6)	<ul style="list-style-type: none"> • Pain assessment • Palpation and percussion • Mobility • Soft-tissue assessment (swelling/sinus tract) • Cold test • Discolouration 	<ul style="list-style-type: none"> • Dentine bridge thickness • Dentine wall thickness • Absence of radiographic pathosis • Continued root development of immature teeth
GIC + composite resin/ reattachment of fractured tooth fragment	NR	12– 24 m	(0)	<ul style="list-style-type: none"> • Pain assessment • Percussion • Soft-tissue assessment (swelling/sinus tract) • Mobility • Pulp sensibility tests 	<ul style="list-style-type: none"> • Dentine bridge formation • Absence of radiographic pathosis
NR	NR ^b	24 m	(6)	<ul style="list-style-type: none"> • Patient's symptoms • Tenderness to palpation and percussion • Probing depth • Mobility • Pulp sensibility tests • Discolouration 	<ul style="list-style-type: none"> • Dentine bridge formation • Continued root development of immature teeth
GIC + composite resin	NR	18 m	NA	<ul style="list-style-type: none"> • Patient's signs and symptoms • Pulp sensibility tests 	<ul style="list-style-type: none"> • Dentine bridge formation
GIC + composite resin	Single operator	1 –8 years	(0)	<ul style="list-style-type: none"> • Absence of signs and symptoms • Pulp sensibility tests 	<ul style="list-style-type: none"> • Dentine bridge formation • Absence of apical radiolucency • Continued root development of immature teeth

(Continues)

TABLE 2 (Continued)

Author (year)	Study design	Material (sample size)	Age range (years)	Stage of root development	Irrigation/ haemostatic agent	Time to treatment	
						Trauma to pulp therapy	Trauma to definitive coronal seal
Cvek (1993)	Case series	Ca(OH) ₂ (178)	6–17	Immature (90) Mature (88)	Sterile saline solution	1–984 h	Subsequent visit
Cvek (1978)	Case series	Ca(OH) ₂ (60)	7–16	Immature (28) Mature (32)	Sterile saline solution	1–2160 h	Subsequent visit
Fuks et al. (1993) ^c	Case series	Ca(OH) ₂ (40)	7–22	NR	Sterile saline solution/sterile cotton pellet	2 h–3 weeks	First visit
Fuks et al. (1987) ^c	Case series	Ca(OH) ₂ (63)	7–22	Immature (10) Mature (53)	Sterile saline solution/sterile cotton pellet	2 h–3 weeks	First visit
Klein et al. (1985)	Case series	Ca(OH) ₂ (34)	7–22	NR	Sterile saline solution	<2 h–3 weeks	First visit
Variable (Direct pulp capping and pulpotomy)							
Maguire et al. (2000)	Retrospective case series	Ca(OH) ₂ and other dressings (65) ^f	6–16	Immature (32) Mature (33)	NR	Variable; 75% within 48 h	Either a temporary or definitive restoration was applied in first visit

Abbreviations: Ca(OH)₂, calcium hydroxide; d, days; GIC, glass ionomer cement; h, hours; m, months; MTA, mineral trioxide aggregate; NaClO, sodium hypochlorite; NR, not reported; RCT, randomized control trial; SSBC, stainless steel basket crown; wks, weeks; yrs, years.

^aOut of the total 51 cases, 10 were complete pulpotomy and 41 were partial pulpotomy.

^bAll operators attended a training session before the beginning of the study and yearly to ensure that all examinations and treatments performed followed a standardized operating protocol.

^cSame study/population with an extended follow-up.

^dOriginal sample size was 63, of which 4 failed and 19 lost at follow-up.

^eTreatment performed in the Department of Pedodontics of the Hadassah Faculty of Dental Medicine, Jerusalem.

^fStudy included 96 teeth treated using different techniques out of which vital pulp treatment was performed on 65 teeth (46 direct pulp capping and 19 pulpotomy).

^gOperators in both primary and secondary care settings.

Clinical and radiographic success

The criteria for clinical and radiographic outcomes defining success are listed in Table 2. Clinical parameters such as pain assessment, pulp sensibility tests, soft tissue assessment, mobility, discolouration and radiographic

parameters, e.g. dentine bridge formation, absence of radiographic pathosis, continuation of root development in immature teeth, are reported in the majority of included studies. However, detailed quantification measurement of the continuation in root development of immature teeth was only assessed in 14.3% ($n = 2$) of included studies

Definitive coronal seal	Operator	Follow-up	Dropout (n)	Outcome measures	
				Clinical	Radiographic
Composite resin	32 dentists, training level not specified	3–15 years	(0)	<ul style="list-style-type: none"> • Absence of signs and symptoms • Evidence of continuous hard tissue barrier • Pulp sensibility tests 	<ul style="list-style-type: none"> • Dentine bridge formation • No intrapulpal or periapical pathosis - Continued root development of immature teeth
Composite resin	11 dentists, training level not specified	14–60 m	(0)	<ul style="list-style-type: none"> • Absence of signs and symptoms • Evidence of a continuous hard tissue barrier • Pulp sensibility tests 	<ul style="list-style-type: none"> • Dentine bridge formation • No intrapulpal or periapical pathosis • Continued root development of immature teeth
Composite resin/SSBC (deep fractures)	NR ^e	7 ½–11 years	(23 ^d)	<ul style="list-style-type: none"> • Absence of signs and symptoms • Pulp sensibility tests 	<ul style="list-style-type: none"> • Dentine bridge formation • No intrapulpal or periapical pathosis - Continued root development of immature teeth
Composite resin/SSBC (deep fractures)	NR ^e	½–4 years	(0)	<ul style="list-style-type: none"> • Absence of signs and symptoms • Pulp sensibility tests 	<ul style="list-style-type: none"> • Dentine bridge formation • No intrapulpal or periapical pathosis • Continued root development of immature teeth
Composite resin/SSBC (deep fractures)	NR ^e	7–36 m	(0)	<ul style="list-style-type: none"> • Absence of signs and symptoms • Pulp sensibility tests 	<ul style="list-style-type: none"> • Dentine bridge formation • No intrapulpal or periapical pathosis • Continued root development of immature teeth
Variable	Variable operators ^g	48 yrs	(0)	<ul style="list-style-type: none"> • Dental records were retrospectively assessed 	<ul style="list-style-type: none"> • Radiographic records were retrospectively assessed

(Abuelniel et al., 2020; Yang et al., 2020). In terms of coronal discolouration, only two studies assessed this outcome. In a randomized controlled trial (RCT), Abuelniel and colleagues reported a significantly higher discolouration following full pulpotomy in the MTA group (88%) compared with the Biodentine[®] group (0%) (Abuelniel

et al., 2020). On the contrary, in a case series design of 51 teeth, discolouration was observed in 17% of cases following Biodentine[®] partial pulpotomy (Haikal et al., 2020).

Detailed outcomes of all included studies are listed in Table 3. Overall, a high success rate of VPT interventions in the treatment of traumatized vital permanent teeth

TABLE 3 Reported outcomes of included studies

Author (year)	Clinical success	Radiographic success	Calific bridge formation	Continued root development in immature teeth
Procedure: Full pulpotomy				
Abuelmel et al. (2020)	Biodentine®: 20/25 (80%) ^a ProRoot White MTA: 20/25 (80%) ^a	Biodentine®: 20/25 (80%) ^a ProRoot MTA: 21/25 (84%) ^a	NR	Biodentine®: 19/25 (76%) MTA: 21/25 (84%)
Witherspoon et al. (2006)	MTA: 6/7 ^b (85.7%)		NR	6/7 (85.7%) ^c
Gilber and Winter (1988)	Ca(OH) ₂ : 139/175 ^b (79.4%)		95/108 (88%)	NR
Procedure: Partial pulpotomy				
Yang et al. (2020)	Ca(OH) ₂ : 40/49 ^b (82.9%) ^d IRoot® BP Plus: 45/50 ^b (90%) ^d ^a		Ca(OH) ₂ : 1.36 ± 0.12 mm IRoot® BP Plus: 0.97 ± 0.13 mm	Ca(OH) ₂ : 14.38 ± 1.43 mm IRoot® BP Plus: 14.46 ± 1.99 mm
Rao et al. (2020)	Ca(OH) ₂ : 94/100 (94%) ^e IRoot® BP Plus: 105/105 (100%) ^e	Ca(OH) ₂ : 93/100 (93%) ^e IRoot® BP Plus: 104/105 (99%) ^e	Ca(OH) ₂ : 90.3% IRoot® BP Plus: 92.3%	NR
Haikal et al. (2020)	Biodentine®: 41/45 ^b (91%)		42/45 (93%)	100%
Koyuncuoglu et al. (2013)	ProRoot White MTA: 13/13 ^b (100%)		8/13 (61.5%)	NR
de Blanco (1996)	Ca(OH) ₂ powder: 30/30 ^b (100%)		100%	NR
Cvek (1993)	Ca(OH) ₂ : 169/178 ^b (95%)		71%	NR
Cvek (1978)	Ca(OH) ₂ : 58/60 ^b (96%)		96%	NR
Fuks et al. (1993) ^f	Ca(OH) ₂ : 35/40 ^b (87.5%)		87.5%	NR
Fuks et al. (1993) ^f	Ca(OH) ₂ : 59/63 ^b (94%)		94%	NR
Klein et al. (1985)	Ca(OH) ₂ : 32/34 ^b (94.1%)		94.1%	NR
Variable (Direct pulp capping and pulpotomy)				
Maguire et al. (2000)	Direct pulp capping: 9/46 ^b (19.5%) Partial & full pulpotomy: 2/19 ^b (10.5%)		NR	NR

Abbreviations: Ca(OH)₂, calcium hydroxide; MTA, mineral trioxide aggregate; NR, not reported.^aNo statistically significant difference between groups.^bCombined clinical and radiographic success.^cRadiographic appearance of the tooth consistent with developmental age.^dThe survival rate for the pulp was used to revise the success frequency.^eStatistically significant difference between groups.^fSame study/population with an extended follow-up.

across the included studies was shown. Partial pulpotomy was the main reported clinical procedure accounting for approximately 71.4% ($n = 10$) of the studies, with an overall success rate between 82.9–100%. On the other hand, three studies reported full pulpotomy, and only one study reported direct pulp capping, with lower success rates of 79.4–85.7% and 19.5%, respectively. Calcium hydroxide was the most commonly used pulp capping material, with favourable clinical and radiographic success rates of between 79.4–100%. Other pulp capping materials such as Biodentine[®], MTA and IRoot[®] BP were also associated with high clinical and radiographic success, 80–91%, 80–100% and 90–100%, respectively, albeit in fewer studies.

Quality of included studies

Detailed assessment of the risk of bias utilizing the NIH quality assessment tool was performed (Table S3). The quality of the evidence of the included RCTs was scored as 'good' (Abuelniel et al., 2020) and 'fair' (Yang et al., 2020), with overall LOE = 1+. The quality assessment for the included retrospective case-control study was also scored as 'fair' (LOE = 2+). The lack of a sample size justification and/or power description was deemed to negatively affect the overall study quality. Out of the 11 case series, 8 were scored as 'good' (LOE = 3), (Cvek, 1978, 1993; Fuks et al., 1987, 1993; Haikal et al., 2020; Klein et al., 1985; Maguire et al., 2000; Witherspoon et al., 2006), two as 'fair' (LOE = 3) (Gelbier & Winter, 1988; Koyuncuoglu et al., 2013) and one as 'poor' (LOE = 3) (de Blanco, 1996).

DISCUSSION

Despite the common nature of TDIs, to the authors' knowledge, no systematic reviews looking into the clinical and radiographic success/survival of various VPT interventions in pulpal exposed traumatized permanent teeth have been reported. Due to the specific nature of TDIs, prospective controlled clinical trials are difficult to perform. Therefore, cohort, case-control and case series studies with a minimum of five cases were included in this review. Although of low evidence level, the decision to include case series was based on the number of factors. Firstly, there is a paucity of the literature on this topic. Also, many such studies are considered in the literature as longitudinal single-arm studies on which the current dental trauma guidelines are based (Bourguignon et al., 2020; Krastl et al., 2021). These studies also included a large number of cases, treated using standardized protocols, which is more valuable than a standard case series (with no standardized protocol). As an example, one study

reported 178 cases (Cvek, 1993), but because of the non-comparative nature of this study, for the purpose of our review, it was considered to be a case series according to the Algorithm suggested for classification of studies by National Institute for Health and Care Excellence (NICE, 2014).

The NIH quality assessment tool, one of the recommended tools by the National Institute for Health and Care Excellence (NICE, 2014), was utilized in the current review as it enables the assessment of various study designs using comprehensive evaluation criteria. A 14-criteria based tool is used for controlled intervention studies and observational cohort studies, while a 9-criteria based tool is used for case series studies covering all aspects of bias including selection, detection, performance, attrition and reporting bias.

In this review, a total of 14 studies were included with an overall quality ranging from 'good' to 'poor'. In the two clinical trials that were included, performance bias was high due to the lack of blinding of operators, which is quite clinically impractical due to the nature of the clinical intervention. Regarding detection bias, although blinding of assessors was claimed in some studies, it remained possible for the assessors to identify the treatment provided as a result of radiographic differences in material radio-opacities and crown discolouration associated with certain materials used. Additionally, both performance and reporting bias negatively affected the overall quality rating of the included retrospective case-control study. Despite the inherent limitations within uncontrolled clinical studies, the majority of these case series rated low bias. Unfortunately, based on the limited number of included RCTs, substantial heterogeneity in terms of clinical protocols, assessment criteria and outcome reporting among included studies a meta-analysis was not performed.

Additionally, several variables, including the VPT technique, haemostatic/irrigation agent used and the skill of the operator, pulp capping material, size of the pulpal exposure, time interval from trauma to VPT/ VPT to definitive coronal seal, the presence of a concomitant trauma, root development stage, pulp contamination appear to affect the prognosis of traumatized teeth with pulpal exposure. However, the evidence on some of these factors remains contradictory and will be briefly discussed in the context of this review.

Vital pulp treatments

In this review, partial pulpotomy was the main reported clinical procedure following traumatic pulpal exposure of vital permanent teeth, accounting for approximately

71.4% of the studies and the highest overall success rate (82.9–100%). On the contrary, full pulpotomy was reported in only 21.4% of studies with lower success rates (79.4–85.7%). With regard to direct pulp capping, a surprisingly low success rate of 19.5% was reported; however, these data cannot be generalized as data were extracted from a sole retrospective study design of a limited sample size. More recently, given the low reported success rates of direct pulp capping in comparison to partial pulpotomy its use in traumatized exposed pulps has been questioned (Krastl, Weiger, Ebeleseder, et al., 2021). Indeed, partial pulpotomy has been reported to provide better control of the exposure wound, hence enhancing the clinical stability of the pulp capping material (Cvek, 1978). Additionally, irrespective of the applied treatment, various clinical steps such as water cooling, irrigation solution, haemostatic agent, applied pressure and aseptic field could potentially affect the treatment outcome and should be considered in future studies. Although, the effect of different irrigation solutions/concentrations on the survival of stem cells from the apical papilla has been widely studied (Martin et al., 2014; Trevino et al., 2011), little is known about their effect on the superficial pulp tissue following traumatic pulp exposure. Furthermore, the skill of the (operator treatment provider) was under-reported in the majority of the included studies. Although, it is logical to assume that the skill of the operator directly affects the treatment outcome. Nevertheless, the effect of this factor on the success and survival of treated teeth has not been ascertained.

Pulp capping materials

Several pulp capping materials have been used with variable physio-mechanical properties such as sealing ability, wound healing, antimicrobial efficacy, biocompatibility and bioactivity properties when placed in contact with the inflamed pulp tissue (da Rosa, Cocco, et al., 2018). Calcium hydroxide is well-known as the standard pulp capping material with a long track record of clinical success mainly related to its excellent antimicrobial activity, biocompatibility and the ability to induce calcific bridge formation (Krastl et al., 2021; Mohammadi & Dummer, 2011). In the current review, Ca(OH)₂ was the main reported material in 10 out of the 14 included studies, with an overall high clinical and radiographic success (79.4–100%). Calcium hydroxide drawbacks such as mechanical instability, poor sealing ability and a ‘tunnel defect’ in the newly formed calcific bridge (Krastl et al., 2021; Mohammadi & Dummer, 2011) have been documented in the literature that led to further material innovation. Additionally, the occurrence of internal resorption has also been reported

with Ca(OH)₂ use as a pulp medicament in traumatized permanent teeth with pulp exposures (Akhlaghi & Khademi, 2015).

The use of MTA, a bioactive endodontic cement mainly comprised of calcium and silicate elements, introduced by Torabinejad and colleagues in the 1990s, is another well-known favourable pulp capping material (Torabinejad et al., 1993). Advantages of MTA, such as no or low solubility, high pH, excellent sealing and biocompatibility properties are well documented (Parirokh et al., 2018). However, difficult handling characteristics, prolonged setting time, high cost and tooth discolouration are known potential clinical drawbacks (Parirokh et al., 2018). Additionally, in spite of continuous material improvements, tooth discolouration remains an adverse clinical issue (Belobrov & Parashos, 2011; Sabeti et al., 2021). In the current review, ProRoot MTA was utilized in two case series and an RCT in comparison with Biodentine[®], with an overall high clinical and radiographic success (80–100%). Despite, previous systematic reviews reporting a comparable clinical success rate of ProRoot Grey MTA and Ca(OH)₂ as a pulp capping material for partial pulpotomy in permanent molars with deep carious lesions (Qudeimat et al., 2007), none of the included studies in this systematic review directly compared both these materials. It would not be prudent to compare the results from the use of such materials used for VPT in trauma and caries as the pathophysiology of the pulp is completely different in these two clinical scenarios. In carious exposures, the pulp is likely to be inflamed whereas in traumatic pulp exposures, it is more likely to be merely contaminated with perhaps inflammation in just the superficial part exposed to the oral environment, especially where treatments are performed quite soon after the injury (Cvek et al., 1982; Heide & Mjör, 1983).

To circumvent the limitations of MTA, a variety of new bioactive cements based on calcium silicate composition such as Biodentine[®] (Septodont) and IRoot[®] BP Plus (Innovative BioCeramix), have been developed. IRoot[®] BP Plus has been shown to enhance human dental pulp cells attachment, proliferation, migration, mineralization and dentine bridge formation (Mahgoub et al., 2019). This review found that in comparison with Ca(OH)₂, IRoot[®] BP Plus had a greater ability to increase calcific bridge thickness; however, overall similar clinical and radiographic success was reported. In line with these results, the cost-effectiveness of IRoot[®] BP Plus in comparison to Ca(OH)₂ will most likely hinder clinicians to select new and expensive materials of a similar clinical outcome to cheaper competitors.

Biodentine[®] as a ‘dentine replacement’ material has also gained significant clinical attention. Recent

RCTs assessing ProRoot white MTA and Biodentine® as a pulp capping material found no significant difference between clinical and radiographic success rates for both materials following full pulpotomy in carious (Abuelniel et al., 2021) and traumatized (Abuelniel et al., 2020) exposed pulp tissue. MTA has been commonly linked to coronal discolouration of teeth, which has been attributed to the presence of bismuth oxide content. Similarly, this review found a significantly higher coronal discolouration with MTA use as compared to Biodentine®, thus suggestive that Biodentine® may be considered a suitable alternative material with better aesthetic outcomes, which is especially significant when carrying out VPT in permanent anterior teeth. In addition, irrespective of material classification, other factors such as blood contamination (Chen et al., 2020; Lenherr et al., 2012), type of irrigant solution (Camilleri et al., 2020), the influence of light and environmental conditions (Vallés et al., 2013a, 2013b) should be carefully controlled and may negatively contribute to tooth discolouration.

Size of pulp exposure

The effect of the size of the pulpal exposure on the prognosis of traumatized teeth has been assessed in some studies. The size of the pulpal exposure ranging from 0.5 to 4.0 mm following Ca(OH)₂ partial pulpotomy in relation with traumatized teeth resulted in no influence on the frequency of healing (Cvek, 1978). Similarly, Fuks and colleagues also found that the size of pulp exposure, did not affect treatment outcome, as long as the remaining pulp tissue is vital (Fuks et al., 1987, 1993).

Time interval between trauma, VPT treatment and placement of definitive restoration

The time interval between trauma and VPT treatment has been reported with conflicting results. In three case series, the time interval from trauma to treatment did not affect treatment outcome, as long as the remaining pulp tissue is vital (Cvek, 1978; Fuks et al., 1987, 1993). Contrastingly, a study by Cvek of a 3–15-years follow-up found a statistically significant difference in the frequency of healing in teeth treated within 72 h after trauma in comparison to those treated after a longer time interval (Cvek, 1993). This is echoed by Gilber and Winter, who reported that only 12% of teeth treated within 24 h lost their vitality compared with 32% of teeth treated after 24 h following pulp exposure

(Gelbier & Winter, 1988). The time interval between the VPT treatment and placement of a definitive restoration varied, either at the first visit or subsequent visits, within the included studies. In a retrospective study design, the immediate placement of a bonded definitive coronal seal increased the mean survival time for vitality in both mature and immature teeth (Maguire et al., 2000). Indeed following VPT in a traumatized tooth, it is advisable that a definitive bonded restoration should be placed as soon as possible, ideally during the same visit, to prevent any unwanted coronal leakage and subsequent pulp infection (Krstl et al., 2021). Unfortunately, in several studies included in this review, a definitive bonded restoration was placed at a subsequent follow-up visit. The effects of this delay on the success and survival of treated teeth cannot be ascertained in the context of this review; however, it is highly encouraged that placement of a definitive bonded restoration at the initial treatment visit.

Concomitant trauma

The presence of concomitant injury, sustaining more than one injury, is reported to create a synergist effect, hence resulting in a more detrimental effect than a single injury (Bourguignon et al., 2020). In this review, Haikal et al. (2020) reported that the presence of concurrent luxation injury was the only independent variable that significantly affected the treatment outcome. In line with the above, a significant increase of pulp necrosis in mature teeth with crown fractures combined with concussion or subluxation injuries has been reported (Lauridsen et al., 2012). However, we must acknowledge that the healing scenario is complex and multifactorial related to patient, trauma or treatment factors (Lauridsen et al., 2012).

Stage of root development

The effects of stage of root development (immature, mature) on the clinical outcome following VPT has been debatable, with previous reports restricting VPT to only young patients with immature roots (Koyuncuoglu et al., 2013). However, several studies have shown that patients with ages ranging from 6 to 70-years-old have been treated successfully with VPT (Aguilar & Linsuwanont, 2011). This is in line with the results of the current systematic review. Indeed, it has been shown that the complete removal of the inflamed pulp is a critical clinical factor for pulp healing, rather than the stage of root development (Aguilar & Linsuwanont, 2011).

Pulpal diagnosis

The diagnosis of the injured pulp status is an important clinical factor; however, accurate diagnosis even to the experienced clinician is challenging, especially in young patients who may be uncooperative following a traumatic injury. Additionally, the commonly used pulp sensibility tests (electric and/or thermal stimulation) physiologically rely on a functional vascular supply. However, pulpal oedema following trauma results in a temporary loss of sensibility, limiting their diagnostic accuracy (Krstl et al., 2021).

Moreover, pulp sensibility testing especially in immature teeth remains a challenge, partly due to delay in the full development of the plexus of Rashkow, which has been shown to take place up to 5-years post tooth eruption (Johnsen, 1985). Furthermore, pulp sensibility testing in teeth, which have undergone VPT and have a thick layer of pulp capping material and restorative coronal seal material, such as those with deep coronal pulpotomy may impede responses to conventional cold and electric pulp tests, with clinicians depending mainly on radiographic evidence of continued root development as the most reliable sign of pulp vitality. Physiology aside, it should also be acknowledged that pulp sensibility testing in anxious young patients cannot always be substantiated and are often unreliable.

Other suggested forms of pulp testing that have shown to offer a more objective assessment and better diagnostic accuracy in evaluating the tooth's vascular supply include the use of Laser Doppler Flowmetry or pulse oximetry (Krstl et al., 2021). However, it should be noted that studies supporting its use were subject to a high level of bias (Ghouth et al., 2018). The use of such device was further challenged by the results of an RCT showing a subclinical accuracy of the Laser Doppler Flowmetry (Ghouth et al., 2019).

Strengths, limitations and future directions

Inherent strengths of this systematic review rely on the robust inclusion and exclusion criteria to maintain the focus of the review question. In addition to the risk of bias assessment, the LOE of the included studies was graded to reflect and compare the quality of evidence. However, this systematic review has the following limitations: the majority of included studies were uncontrolled clinical studies with inherent bias resulting from the lack of a control group, the presence of substantial heterogeneity in terms of clinical protocols, assessment criteria and outcome reporting among included studies, which prevented data synthesis, the exclusion of non-English language manuscripts as a result of lack of funding and access to professional translation services.

Further assessment of the effect of the VPT technique, pulp capping material, size of the pulpal exposure, time interval from trauma to VPT, time interval from VPT to definitive coronal seal, the presence of a concomitant trauma, root development stage, pulp contamination, haemostatic/irrigation agent used and the skill of the operator, is recommended in future studies using well designed controlled prospective clinical trials. In order to standardize future studies, the authors would like to recommend a list of minimum clinical and radiographic criteria for outcome assessment as outlined in Table 4. Such criteria would help improve study standardization and reduce heterogeneity between studies. Both clinical and radiographic success parameters should be clearly defined, assessed and reported. Additionally, all RCTs should register and strictly comply with the Consolidated Standards of Reporting Trials (CONSORT) guidelines.

TABLE 4 Recommended criteria for outcome evaluation

Criteria	Failed	Partial success	Complete success
Clinical	<ul style="list-style-type: none"> • Presence of pain, swelling or mobility 	<ul style="list-style-type: none"> • Absence of pain, swelling and mobility 	
Radiographic ^a	<ul style="list-style-type: none"> • Presence of radiographic pathosis • No further progression of root formation/development 	<ul style="list-style-type: none"> • Absence of radiographic pathosis • No continuation of root development (no increase in root length and/or thickening of root dentine and/or apical closure) • Formation of apical barrier 	<ul style="list-style-type: none"> • Root formation/development is evident radiographically and reached apical closure/apexogenesis

^aRadiographic success should be based on a combination of lack of apical radiolucency and continuation of root development in immature teeth. Radiographs should be standardized using radiographic holders with bite blocks and/or mathematically corrected using the TurboReg plug-in application (Biomedical Imaging Group, Swiss Federal Institute of Technology, Lausanne, Switzerland). Increase in root length, thickening of root dentinal walls and apical closure should be measured using ImageJ software (National Institutes of Health) or similar radiographic quantification software. The modified Nosrat et al. (2013) radiographic classification adopted by Abuelniel et al. (2020) is recommended for future studies standardization.

CONCLUSION

Despite the common occurrence of complicated TDIs, high-quality evidence-based studies are scarce. The present systematic review reports high clinical and radiographic success rates of VPT interventions in the treatment of traumatized vital permanent teeth, although based on limited clinical evidence of variable quality rating. Calcium hydroxide was the most studied pulp capping material with favourable clinical outcomes. The most recent evidence, although of limited studies, also suggests that alternative bioactive biomaterials (Biodentine[®], IRoot[®] BP and MTA) are associated with high clinical and radiographic success and are regarded as a suitable VPT biomaterial. Crown discolouration following the use of MTA limits its use in the management of traumatized anterior teeth in comparison to Ca(OH)₂ and other less discolouring calcium silicate material such as Biodentine[®] and non-bismuth oxide-containing MTA.

CONFLICT OF INTEREST

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

ETHICAL APPROVAL


Ethical approval was not necessary as this article is not a research study that involved any human or animal experiments.

AUTHOR CONTRIBUTION

All the authors have made substantial contributions to the manuscript. All the authors have read and approved the final version of the manuscript.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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