

REVIEW

A scoping review of root canal revascularization: relevant aspects for clinical success and tissue formation

M. C. M. Conde¹, L. A. Chisini¹, R. Sarkis-Onofre¹, H. S. Schuch², J. E. Nör³ & F. F. Demarco^{1,4}

¹Post-Graduate Program in Dentistry, School of Dentistry, Federal University of Pelotas, Pelotas, Brazil; ²Australian Research Centre for Population Oral Health (ARCPHO), School of Dentistry, The University of Adelaide, Adelaide, Australia; ³Department of Cariology, Restorative Sciences and Endodontics, School of Dentistry, University of Michigan, Ann Arbor, MI, USA; and ⁴Post-Graduate Program in Epidemiology, Federal University of Pelotas, Pelotas, Brazil

Abstract

Conde MCM, Chisini LA, Sarkis-Onofre R, Schuch HS, Nör JE, Demarco FF. A scoping review of root canal revascularization: relevant aspects for clinical success and tissue formation. *International Endodontic Journal*, **50**, 860–874, 2017.

The aim of this scoping study was to evaluate the survival rate and nature of tissue formed inside root canals of human immature permanent teeth with necrotic pulps (NIPT) under root canal revascularization (RCR). The search was performed in SciVerse Scopus®, PubMed/MEDLINE, Web of Science®, BIREME and in the grey literature up to November 2015. The keywords were selected using MeSH terms and DECs. Two independent reviewers scrutinized the records obtained considering specific inclusion criteria. The included studies were evaluated in accordance with a modified Arksey and O' Malley's framework. From 375 studies that were evaluated, 75 were included. A total of 367 NIPT were submitted to RCR, from which only 21 needed further endodontic treatment. The weighted mean follow-up

time was 17.6 months. The data were derived mainly from case reports (69%) or small case series (15%). NaOCl [0.5–6%] was applied as the disinfecting solution in almost all studies. Triple antibiotic paste was as effective as Ca(OH)₂ as an intracanal medicament. *De novo* tissue was cementum and poorly mineralized bone positive to bone sialoprotein (BSP) but negative to dentine sialoprotein (DSP). Failures were associated mainly with reinfection of the root canal. The majority of included studies reported a significant increase in both root length and width. However, as most of these data came from case reports, they must be interpreted with care, as most were focused on treatment successes (not failures). Therefore, well-designed randomized controlled trials comparing RCR with available apexification treatments are needed to address this gap in the literature.

Keywords: dental pulp necrosis, immature permanent teeth, root canal revascularization, scoping review, scoping study.

Received 16 May 2016; accepted 19 October 2016

Introduction

Immature permanent teeth with necrotic pulps (NIPT) have thin root walls associated with incomplete root

apices, characterized by a wide apical foramen (Wigler *et al.* 2013). Such characteristics are challenging to treat (Andreasen & Bakland 2012). Traditionally, NIPT were treated by apexification involving the insertion of Ca(OH)₂-based medicaments inside the root canal to establish favourable conditions for subsequent conventional root canal treatment (Rafter 2005). Even though in these cases traditional root canal treatment has a success rate of 74% (Kleier & Barr 1991, Cvek 1992, Andreasen *et al.* 2002), the

Correspondence: Flávio F. Demarco, Federal University of Pelotas, School of Dentistry, Post-Graduate Program of Dentistry and Epidemiology, 457, Gonçalves Chaves St. 5th floor, Pelotas, RS 96015-560, Brazil (Tel.: +55 5381112528, e-mail: ffdemarco@gmail.com).

need for multiple treatment appointments, as well as increased brittleness of root dentine (Andreasen *et al.* 2002), raises the risk of tooth fracture (Cvek 1992). Placing an apical plug of MTA has been reported as an alternative treatment option, but it does not regenerate the physiology of the pulp–dentine complex (Jeeruphan *et al.* 2012, Simon & Goldberg 2014), nor does it allow for further root formation.

Root canal revascularization (Wigler *et al.* 2013) was proposed to overcome the obstacles related to the clinical management of NIPT (Iwaya *et al.* 2001, Banchs & Trope 2004). RCR aims to fill the root

canal with pulp-like tissue after the induction of a blood clot inside the root canal system, which will serve as an anchorage site for cells from the apical region (Fig. 1). Since then, evidence regarding stimulating ingrowth of tissues into the root canal system following RCR has been provided (Murray *et al.* 2007, Nosrat *et al.* 2011, Garcia-Godoy & Murray 2012). In addition, the application of blood venous derivatives, such as platelet-rich plasma (PRP) and platelet-rich fibrin (PRF), could be performed in specific cases aiming to accelerate tissue formation (Mittal & Narang 2012).

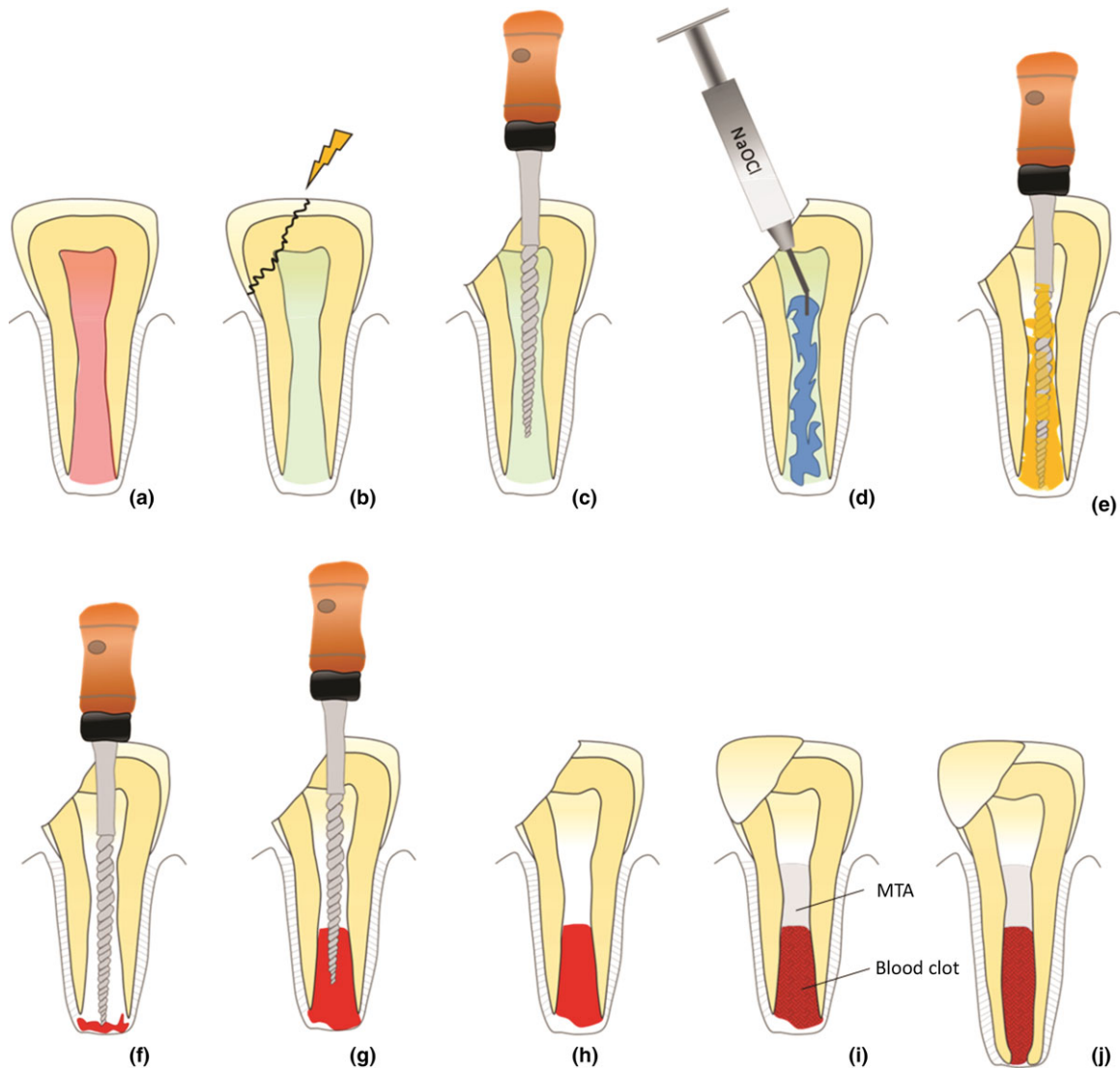


Figure 1 Schematic principle of maturogenesis in immature permanent teeth with necrotic pulps. (a) Immature permanent tooth; (b) immature permanent teeth with necrotic pulps; (c) pulp removal; (d) disinfection agent, (e) triple antibiotic paste; (f) irritating periapical tissue; (g) initial bleeding; (h) blood clot formation; (i) MTA; (j) continued root development.

Disinfection of the root canal system is a crucial step in RCR as mechanical instrumentation is contraindicated due to the thin walls, which could increase further the risk of root fracture (Andreasen & Bakland 2012). Rather, disinfection solutions, such as NaOCl, and a triple antibiotic paste (TAP) containing ciprofloxacin, metronidazole and minocycline (Hoshino *et al.* 1996) are applied.

Despite the promising results observed in several published case series, RCR is not a well-established therapy (Wigler *et al.* 2013) due to the lack of well-designed clinical trials evaluating its prognosis. Furthermore, little is known about the exact nature of the tissue growing into the canal after RCR is performed in humans. Taking these aspects in consideration, the aim of this study was to carry out a scoping review evaluating the performance of human NIPT submitted to RCR as well as the nature of tissue formed inside the root canal system of such teeth.

Material and methods

Conceptual definition

The American Association of Endodontists Guide to Current Dental Terminology (AAE 2013) describes a biological-based procedure named 'Pulpal regeneration', which aims to replace damaged tooth structures in NIPT. The process is based on root canal disinfection and subsequent induction of periapical tissue bleeding (AAE 2013). The first report describing the term 'revascularization' for NIPT (Iwaya *et al.* 2001) used a case study on the application of Hoshino's TAP (Hoshino *et al.* 1996) inside a root canal to treat an abscess (Iwaya *et al.* 2001). However, the term revascularization is not well accepted (Wigler *et al.* 2013); some authors claim that revascularization is more applicable to events related to dental trauma (Huang & Lin 2008). In such a context, the term 'maturogenesis' has been reported to better describe the clinical and radiographic data depicting the apical maturation in NIPT (Weisleder & Benitez 2003). As mentioned by Wigler *et al.* (2013), 'procedures designed to promote continued root development in NIPT should be described as maturogenesis, rather than revascularization'. The present authors believe that 'Maturogenesis' is a general term for the promotion of root development by different treatments and is not limited to vital pulp therapy. Therefore, the term 'Root Canal Revascularization – RCR' was applied by researchers for protocols aiming to treat apical periodontitis, to induce radiographic

evidence of apical root closure, and to promote root development, after the induction of a blood clot.

The clinical definition of the success of RCR varies between studies and methodologies. In general, the most frequently used method is the evaluation of root lengthening and root wall thickening, as well as the absence of pain or sinus tract, resulting in periapical healing. Aside from this, the follow-up periods vary largely in the published studies, making it difficult to define parameters to compare all cases. As a result, the ultimate goal of RCR is to increase tooth survival in the mouth with minimal intervention. In this scoping review, the clinical success of RCR was considered when there was no report indicating extraction or conventional root canal treatment for the treated tooth.

Exploratory search

An exploratory search was performed in PubMed/MEDLINE up to August 2015. To construct the search strategy, the terms 'root canal revascularization', 'maturogenesis', 'dental pulp necrosis', 'dental pulp regeneration' and 'infected teeth' were applied. The initial search resulted in 1297 initial records corresponding to 517 studies. Such an exploratory search was relevant to identify that the first studies relating to the importance of the blood clot over the healing of periapical tissues (Torneck & Smith 1970). A remarkable methodological heterogeneity amongst studies was observed; most of the data obtained were derived from case reports or relatively small case series. A systematic review is a key element to produce evidence-based clinical protocols, but based on the resultant evidence, a systematic review was not considered appropriate. Therefore, a scoping study (SS) was designed under a modified five-stage framework proposed by Arksey & O'Malley (2005) (Daudt *et al.* 2013). According to the applied framework (Daudt *et al.* 2013), 'A scoping review, or scoping study, is a form of knowledge synthesis that addresses an exploratory research question aimed at mapping key concepts, types of evidence and gaps in research related to a defined area or field by systematically searching, selecting and synthesizing existing knowledge'.

Information sources, literature search and inclusion criteria

A structured search was performed in SciVerse ScopusTM, PubMed/MEDLINE, ISI Web of ScienceTM and

BIREME up to November 2015. The keywords were selected based on the two pre-specified questions:

1. What is the performance of immature permanent teeth with necrotic pulps under RCR?
2. What is the nature of tissue formed inside the root canal of immature permanent teeth with necrotic pulps?

The relevant MeSH terms were considered, as well as the relevant entry terms (Table 1), and then combined (Table 2) to search the studies. The retrieved records were uploaded into EndNote™ software (Thomson Reuters, Rochester, New York, NY, USA), aiming to delete duplicates and to build up a virtual library (VL). Two independent reviewers (MCMC and LAC) read the titles and abstracts of all reports, under the following inclusion criteria:

- Studies: clinical studies, without language restriction
- Subjects: NIPT from humans
- Diagnosis: any classification of pulp necrosis
- Regenerative procedures carried out: induced bleeding from periapical region (classical RCR); application of blood venous derivatives (PRF and/or PRP); application of scaffolds over the clot formed after the induced bleeding of periapical region
- Clinical follow-up: any follow-up period

To confirm whether the selected studies met the inclusion criteria, the same reviewers independently

Table 1 Structured search strategy carried out in MEDLINE/ PubMed database^a

Search Syntaxes	
PubMed	#1 ('Immature Permanent Teeth' OR 'Immature Permanent Tooth' OR 'Young Permanent Teeth' OR 'Young Permanent Tooth')
	#2 ('Root Canal Revascularization' OR Revascularization OR Maturogenesis)
	#3 ('Dental pulp necrosis' [Mesh] OR 'Dental Pulp Necroses' OR 'Necroses, Dental Pulp' OR 'Pulp Necroses, Dental' OR 'Pulp Necrosis, Dental' OR 'Pulp Necroses' OR 'Pulp Necrosis' OR 'Necrosis, Pulp' OR 'Necroses, Pulp' OR 'Necrosis, Dental Pulp' OR 'Gangrene, Dental Pulp' OR 'Dental Pulp Autolysis' OR 'Autolyses, Dental Pulp' OR 'Dental Pulp Autolyses' OR 'Pulp Autolyses, Dental' OR 'Pulp Autolysis, Dental' OR 'Autolysis, Dental Pulp' OR 'Infected Teeth')
	#4 ('Platelet-Rich AND Fibrin')
	#5 ('Platelet-Rich Plasma' [Mesh] OR 'Plasma, Platelet-Rich' OR 'Platelet-Rich AND Plasma')

^aSearches in SciVerse Scopus™ (SS), ISI web of a science™ and BVS were adapted according to the database.

Table 2 Keywords combination and records recovered in each database

Key words applied to develop the search strategy	Records found			
	PubMed™	Scopus™	ISI web of science™	BVS™
#1 and #2 and #3	25	37	31	20
#1 and #2	64	107	107	52
#1 and #4	7	18	2	5
#1 and #5	8	6	41	5
#2 and #4	11	93	10	5
#2 and #5	38	188	84	34

judged their full text. If any disagreement was found, the reviewers attempted to reach a consensus through discussions. Persistent disagreements were resolved by intervention from the third reviewer (FFD). After that, MCMC and LAC evaluated manually all references reported in each selected studies. Twenty per cent of the studies were randomly selected, and the data were again checked.

The grey literature in the annals of International Association for Dental Research (IADR), European Society of Endodontology and AAE were searched. To identify registered clinical trials, the following databases were consulted: International Clinical Trials Registry Platform (ICTRP), Clinical trials.gov, Clinical Trials Registry-India (CTRI), EU Clinical Trials Register, Australian Clinical Trials, Pan African Clinical Trials Registration and Brazilian Clinical Trials Registration (*Registros Brasileiros de Ensaios Clínicos*) using the following free terms: 'root canal revascularization', 'maturogenesis' and 'dental pulp necrosis'.

Strategy for data synthesis

The selected studies were charted in accordance with the fourth and fifth stages of the applied framework (Daudt *et al.* 2013). Data analysis was carried out at the level of an individual tooth. The Kaplan–Meier was built simply to illustrate an overview of the evaluated follow-up time (Fig. 3). Each tooth submitted to RCR was inserted individually in the test with their respective follow-up. Initial failures due to impossibility of establishing bleeding or control infection were not submitted to the Kaplan–Meier analysis. Moreover, due to the impossibility of accessing the follow-up period for each tooth, studies reporting only the mean follow-up time were not included. Thus, 326 teeth were included in the Kaplan–Meier survival curve. The follow-up time was calculated by weighted average, considering weights proportional to the study size.

Results

The search resulted in 998 initial records, but only 375 of them were considered unique studies. After evaluation of titles and abstracts, 84 studies were selected for full-text assessment, from which 75 were included (Fig. 2). The reasons for exclusion are outlined in Table 3. In total, 367 teeth were submitted to RCR, from which 21 failed. The evaluated teeth had a weighted (according to study's follow-up time) mean follow-up time of 17.6 months. The Kaplan–Meier curve was built to illustrate the follow-up times reported by the selected studies (Fig. 3).

Studies

The oldest included publication dates from 2004 (Banchs & Trope 2004); the majority of the included studies were published from 2012 up to November 2015 (Fig. 4). Most studies were case reports (69%) or relatively small case series (15%). Stronger evidence was provided by three pilot randomized clinical studies (4%), four prospective clinical studies (5%) and two retrospective studies (Table 4).

Table 3 Excluded studies and reasons for exclusion

Reason	Studies
Periapical bleeding was not induced; neither PRF or PRP was applied	Iwaya <i>et al.</i> 2001, Chueh & Huang 2006, Akgun <i>et al.</i> 2009, Iwaya <i>et al.</i> 2011, Fujita & Maki 2013, Kumar <i>et al.</i> 2014, Saeki <i>et al.</i> 2014
Follow-up was not reported or carried out	Nagata <i>et al.</i> 2014

Grey literature

Four abstracts about RCR were found, and only one had been published (Bezgin *et al.* 2015). Seven clinical trials registration were found, two reporting status as completed (NCT00881491 and NCT00881907) and five as 'recruiting participants' (NCT01827098, NCT01976065, NCT01799187, NCT01817413, CTRI/2012/11/003086).

Disinfection solutions

NaOCl (0.5–6%) was applied as the disinfecting solution in almost all cases (Table 4), often associated mainly with chlorhexidine (CHX) – 0.12–2% (Banchs & Trope 2004,

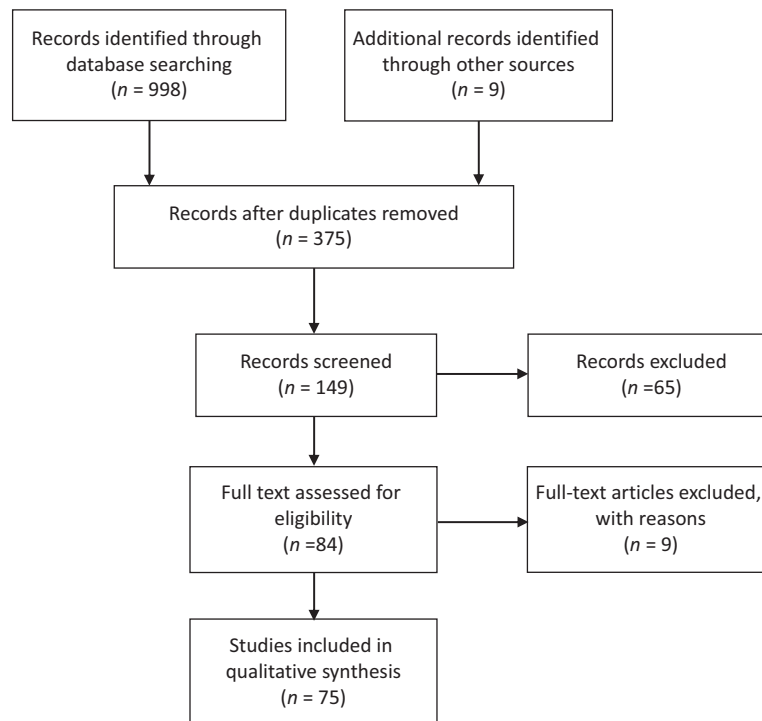


Figure 2 Flow chart depicting the search strategy applied.

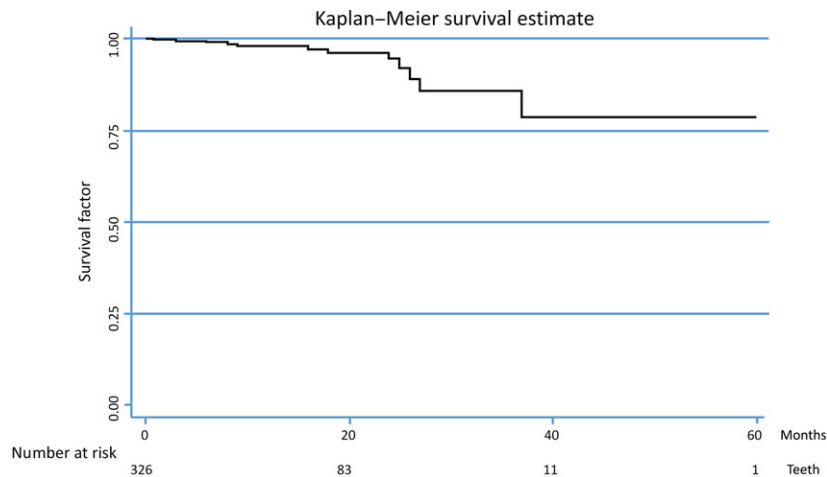


Figure 3 Kaplan–Meier survival estimate.

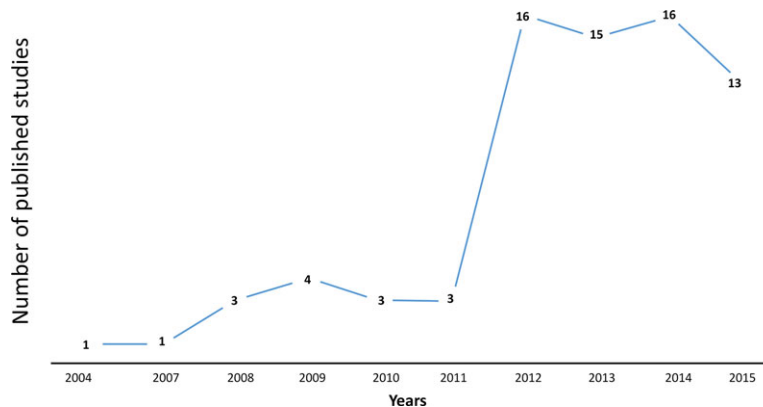


Figure 4 Studies grouped by year of publication.

Reynolds *et al.* 2009, Shin *et al.* 2009, Petrino *et al.* 2010, Shivashankar *et al.* 2012, Chen *et al.* 2013, McTi-gue *et al.* 2013, Becerra *et al.* 2014, Bezgin *et al.* 2014, 2015, Kaya-Buyukbayram *et al.* 2014, Nagata *et al.* 2014, Saoud *et al.* 2014a, Nevins & Cymerman 2015, Solomon *et al.* 2015) and hydrogen peroxide (Cotti *et al.* 2008, Shah *et al.* 2008, Santiago *et al.* 2015).

Intracanal medication

Hoshino's TAP, and its modifications (Table 4), were applied as the intracanal medicament in 86% of the studies whilst Ca(OH)_2 was registered in 13.5% (Cotti *et al.* 2008, Aggarwal *et al.* 2012, Cehreli *et al.* 2012, Chen *et al.* 2012, Rudagi & Rudagi 2012, Shimizu *et al.* 2012, 2013, Paryani & Kim 2013, Soares *et al.*

2013, Alobaid *et al.* 2014, Kaya-Buyukbayram *et al.* 2014, Lin *et al.* 2014, Nagata *et al.* 2014, Yadav *et al.* 2015). Two cases performed RCR in one-single appointment and so did not apply TAP or Ca(OH)_2 ; rather, systemic antibiotics (Shin *et al.* 2009) or NaOCl was used as the sole disinfectant (McCabe 2015). A microbiological analysis revealed that TAP, as well Ca(OH)_2 , did not reduce significantly the number of microorganisms after the application of disinfecting solutions (Nagata *et al.* 2014).

Histological features of the newly formed tissue inside root canals

Studies carrying out histological analysis (Torabinejad & Faras 2012, Martin *et al.* 2013, Shimizu *et al.*

Table 4 Characteristics of included studies

Study	Type of Study	Teeth/ Success	Follow-up (months)	Disinfection Agent [%] Intracanal Medication	Blood Derivatives
Banchs & Trope (2004)	Case Report	1/1	24	NaOCl [5.25]+Peridex™ TAP	–
Thibodeau & Trope (2007)	Case Report	1/1	24	NaOCl [1.5] TAP(CEF)	–
Cotti <i>et al.</i> (2008)	Case Report	1/1	30	NaOCl [5.25] + H ₂ O ₂ [3] Ca(OH) ₂	–
Jung <i>et al.</i> (2008)	Small Case Series	4/4	33	NaOCl [2.25] TAP	–
Shah <i>et al.</i> (2008)	Small Case Series	11/11	19	NaOCl [2.25] and H ₂ O ₂ [3] –	–
Ding <i>et al.</i> (2009)	Small Case Series	9/3	16	NaOCl [5.25] TAP	–
Reynolds <i>et al.</i> (2009)	Case Report	2/2	18	NaOCl [6] and CHX [2] TAP Hoshino	–
Shin <i>et al.</i> (2009)	Case Report	1/1	19	NaOCl [5.25] and CHX [2] Systemic AB	–
Thibodeau (2009)	Case Report	1/1	41	NaOCl [1.25] TAP(CEF)	–
Kim <i>et al.</i> (2010)	Case Report	1/1	8	NaOCl [3] TAP	–
Petrino <i>et al.</i> (2010)	Small Case Series	6/6	11	NaOCl [5.25] and CHX [0.2] TAP	–
Thomson & Kahler (2010)	Case Report	1/1	18	NaOCl [1] TAP(AMXI)	–
Cehreli <i>et al.</i> (2011)	Small Case Series	6/6	9.5	NaOCl [2.25] Ca(OH) ₂	–
Nosrat <i>et al.</i> (2011)	Case Report	2/2	16.5	NaOCl [5.25] TAP	–
Torabinejad & Turman (2011) ^a	Case Report	1/1 ^a	5.5	NaOCl [5.25] TAP	–
Aggarwal <i>et al.</i> (2012)	Case Report	1/1	24	NaOCl [5.25] TAP	–
Cehreli <i>et al.</i> (2012)	Case Report	1/1	18	NaOCl [2.5] Ca(OH) ₂	–
Chen <i>et al.</i> (2012)	Large Case Series	20/20	11.45	NaOCl [5.25] Ca(OH) ₂	–
Dabbagh <i>et al.</i> (2012)	Large Case Series	18/18	24	NaOCl [5] TAP	–
Gelman & Park (2012)	Case Report	1/1	11	NaOCl [6] TAP	–
Jadhav <i>et al.</i> (2012)	Randomized Clinical Study	20/20	12	NaOCl [2.25] TAP(DOXI)	–
Jeeruphan <i>et al.</i> (2012)	Retrospective Study	20/20	21.15	NaOCl [2.5] TAP	–
Kottoor & Velmurugan (2012)	Case Report	1/1	60	NaOCl [5.25] TAP	–
Kim <i>et al.</i> (2012)	Small Case Series	3/3	38	NaOCl [3] TAP(CEF)	–
Lenzi & Trope (2012)	Case Report	2/2	21	NaOCl [2.5] TAP	–
Narayana <i>et al.</i> (2012)	Case Report	1/1	12	NaOCl [5.25] TAP	–
Nosrat <i>et al.</i> (2012)	Case Report	2/2	72	NaOCl [5.25] TAP	–
Rudagi & Rudagi (2012)	Case Report	1/1	12	NaOCl [1] Ca(OH) ₂	PRF

Table 4 Continued

Study	Type of Study	Teeth/ Success	Follow-up (months)	Disinfection Agent [%] Intracanal Medication	Blood Derivatives
Shimizu <i>et al.</i> (2012)	Case Report	1/0	0.75	NaOCl [5.25] Ca(OH) ₂	–
Shivashankar <i>et al.</i> (2012)	Case Report	1/1	12	NaOCl [5.25] and CHX [0.12] TAP	PRF
Torabinejad & Faras (2012) ^a	Case Report	1/0	14	NaOCl [5.25] TAP	PRP
Chen <i>et al.</i> (2013)	Case Report	1/1	12	NaOCl [3] and CHX [DNR] TAP	–
Farsi <i>et al.</i> (2013)	Small Case Series	3/3	18	NaOCl [2.5] TAP	–
Forghani <i>et al.</i> (2013)	Case Report	1/1	18	NaOCl [5] TAP	–
Jadhav <i>et al.</i> (2013)	Small Case Series	6/6	12	NaOCl [2.5] TAP	PRP
Kalaskar & Kalaskar (2013)	Case Report	1/1	15	NaOCl [0.5] TAP	–
Keswani & Pandey (2013)	Case Report	1/1	15	NaOCl [5.25] TAP	PRF
McTigue <i>et al.</i> (2013)	Large Case Series	32/32	51	NaOCl [3] and CHX [2] TAP(CLIN)	–
Martin <i>et al.</i> (2013)	Case Report	1/0	25	NaOCl [5.25] TAP	–
Mishra <i>et al.</i> (2013)	Case Report	1/1	12	NaOCl [2.5] TAP	PRF
Paryani & Kim (2013)	Case Report	2/2	20	NaOCl [5.25] Ca(OH) ₂	–
Shimizu <i>et al.</i> (2013)	Case Report	1/0	26	NaOCl 2.6% Ca(OH) ₂	–
Soares <i>et al.</i> (2013)	Case Report	1/1	24	CHX [2] Ca(OH) ₂ and CHX	–
Sonmez <i>et al.</i> (2013)	Small Case Series	3/3	24	NaOCl [5.25] TAP	–
Wang <i>et al.</i> (2013)	Case Report	2/2	18	NaOCl [3] TAP	–
Yang <i>et al.</i> (2013)	Case Report	1/1	24	NaOCl [5.25] TAP	–
Abduljabbar <i>et al.</i> (2014)	Case Report	1/1	36	NaOCl [5.25] TAP	–
Alobaid <i>et al.</i> (2014)	Retrospective Study	19/15	17	¥NaOCl and CHX TAP versus DAP (ciprofloxacin, metronidazole) versus Ca(OH) ₂	–
Amit <i>et al.</i> (2014)	Case Report	1/1	18	NaOCl [5.25] TAP(CEF)	–
Becerra <i>et al.</i> (2014)	Case Report	1/1	24	NaOCl [5.25] and CHX [2] TAP	–
Bezgin <i>et al.</i> (2014)	Case Report	1/1	12	NaOCl [2.5] and CHX [0.12] TAP(CEF)	PRP
Chandran <i>et al.</i> (2014)	Case Report	1/1	12	NaOCl [5.25] TAP	–
Jadhav <i>et al.</i> (2014)	Case Report	1/1	12	NaOCl [2.5] TAP	PRP
Kahler <i>et al.</i> (2014)	Prospective Clinical Studies	16/16	18	NaOCl [1] TAP(AMXI)	–
Kaya-Buyukbayram <i>et al.</i> (2014)	Case Report	1/1	20	NaOCl [2.5] Ca(OH) ₂ and TAP	–
Lin <i>et al.</i> (2014)	Case Report	1/0	16	NaOCl [5.25]; Ca(OH) ₂ and TAP	–

Table 4 Continued

Study	Type of Study	Teeth/ Success	Follow-up (months)	Disinfection Agent [%] Intracanal Medication	Blood Derivatives
Nagata <i>et al.</i> (2014)	Prospective Clinical Studies	23/22	15	NaOCl [6] and CHX [2] TAP versus Ca(OH) ₂ ; Endogel™ (1:1)	–
Nagy <i>et al.</i> (2014)	Prospective Clinical Studies	20/17	18	NaOCl [2.6] TAP(DOXI)	–
Güven Polat <i>et al.</i> (2014)	Case Report	1/1	24	NaOCl [5] TAP(TETRA)	PRP
Raju <i>et al.</i> (2014)	Case Report	1/1	12	NaOCl [2.25] TAP(DOXI)	–
Saoud <i>et al.</i> (2014b)	Case Report	2/2	12	NaOCl [2.5] TAP	–
Saoud <i>et al.</i> (2014a)	Prospective Clinical Studies	20/20	12	NaOCl [2.5] TAP	–
Bezgin <i>et al.</i> (2015)	Randomized Clinical Study	20/19	18	NaOCl [2.5] and CHX [0.12%] TAP(CEF)	PRP
Jadhav <i>et al.</i> (2015)	Case Report	1/1	18	NaOCl [2.5] TAP	PRF
Lei <i>et al.</i> (2015)	Case Report	1/1	24	NaOCl [1] TAP(CEF)	–
McCabe (2015)	Case Report	1/1	18	NaOCl [5.25] –	–
Nagata <i>et al.</i> (2015)	Case Report	1/1	16	NaOCl [6] Ca(OH) ₂ ;Endogel™ (1:1)	–
Nagaveni <i>et al.</i> (2015)	Case Report	1/1	12	NaOCl [5.25] TAP	PRF
Narang <i>et al.</i> (2015)	Randomized Clinical Study	15/15	18	NaOCl [2.5] TAP	PRP versus PRF
Nevins & Cymerman (2015)	Small Case Series	5/5	10.5	NaOCl [6] DAP	–
Ray <i>et al.</i> (2015)	Case Report	1/1	36	NaOCl [0.5] DAP	PRF
Santiago <i>et al.</i> (2015)	Small Case Series	6/4	21	NaOCl [2.5/5.25%]; H ₂ O ₂ [3]; CHX[2] TAP	–
Solomon <i>et al.</i> (2015)	Case Report	1/1	18	NaOCl [0.25] and CHX [2] TAP	PRF
Wang <i>et al.</i> (2015)	Case Report	2/2	30	NaOCl [2.5] TAP	PRP
Yadav <i>et al.</i> (2015)	Case Report	1/0	24	NaOCl [2.5] Ca(OH) ₂	PRF

^aBoth studies represent the same clinical case. The follow-up from Torabinejad & Turman (2011) was considered to calculate the clinical success.

¥, data from retrospective study; AB, antibiotic; Ca(OH)₂, calcium Hydroxide; CHX, chlorhexidine; DAP, double antibiotic paste containing ciprofloxacin and metronidazole; H₂O₂, hydrogen peroxide; NaOCl, sodium hypochlorite; TAP, triple antibiotic paste developed by (1996); TAP(AMXI), triple antibiotic paste containing amoxicillin instead minocycline; TAP(CEF), triple antibiotic paste containing cefaclor instead minocycline; TAP(CLIN), triple antibiotic paste containing clindamycin instead minocycline; TAP(DOXI), triple antibiotic paste containing doxycycline instead minocycline; TAP(TETRA), triple antibiotic paste containing tetracycline instead minocycline; ™, trade mark. The follow-up time has been calculated by weighted average with weights proportional to the study size.

2013, Becerra *et al.* 2014, Lin *et al.* 2014, Lei *et al.* 2015) did not report the presence of both polarized cells resembling odontoblasts or pulp-like tissue. Continued root development was provided, mostly, by cellular/acellular cementum and poor mineralized bone

(Shimizu *et al.* 2013, Becerra *et al.* 2014). Immunohistochemical analysis showed that the tissue formed inside the root canal was positive to bone sialoprotein (BSP) but negative to dentine sialoprotein (DSP) (Shimizu *et al.* 2013).

Alternative strategies to improve the RCR

From the selected studies, 17 (22%) applied alternative strategies in an attempt to improve RCR. Thereby, blood venous derivatives, such as PRP (Jadhav *et al.* 2012, 2013, 2014, Guven Polat *et al.* 2014, Bezgin *et al.* 2015, Nagaveni *et al.* 2015, Narang *et al.* 2015, Wang *et al.* 2015) and PRF (Torabinejad & Turman 2011, Rudagi & Rudagi 2012, Shivashankar *et al.* 2012, Keswani & Pandey 2013, Mishra *et al.* 2013, Bezgin *et al.* 2014, Jadhav *et al.* 2015, Nagaveni *et al.* 2015, Narang *et al.* 2015, Ray *et al.* 2015, Solomon *et al.* 2015, Yadav *et al.* 2015), were the most commonly applied. It was reported that PRP slightly improved the results of periapical healing, dentinal walls thickening, root lengthening (Jadhav *et al.* 2013, Narang *et al.* 2015) and apical closure (Jadhav *et al.* 2013).

Failures and adverse events

Failures were associated mainly with reinfection of the root canal system (Alobaid *et al.* 2014, Lin *et al.* 2014), root resorption (Nagata *et al.* 2014, Santiago *et al.* 2015) and failure to induce periapical bleeding (Ding *et al.* 2009, Bezgin *et al.* 2015). Critical crown fractures occurred in cases considered successful (Shimizu *et al.* 2012, 2013, Martin *et al.* 2013). Inadequate removal of biofilm, the presence of bacteria in dentinal tubules or defective restoration were also related to failures (Torabinejad & Turman 2011, Torabinejad & Faras 2012, Yadav *et al.* 2015).

Discussion

The studies included in this scoping review reported a high success rate for the 367 teeth under RCR. The survival of teeth under RCR was based on an increase in root length and width (apical closure), resolution of apical periodontitis and the absence of clinical signs and symptoms. Comparing radiographic outcomes in NIPT submitted to Ca(OH)₂ apexification, MTA apical plugs, and RCR (Jeeruphan *et al.* 2012), those treated with RCR showed an average increase of 28.2% in root width and 14.9% in root length, whilst those receiving an MTA plug increased only 6% in root length (Chen *et al.* 2012, Jadhav *et al.* 2012). The survival rate in the revascularized group was 100%, against MTA (95%) and Ca(OH)₂ apexification (77.2%).

The main objective of RCR is to generate pulp-like tissue to reduce the risk of tooth loss (Wigler *et al.*

2013). Knowledge regarding the nature of tissue formed inside the root canal is fundamental in forecasting tooth survival as well as treatment prognosis (Conde *et al.* 2016). However, there is a lack of histological and biomolecular data on the tissues responsible for apical closure, canal narrowing and even the recovery of pulp sensibility. Selected studies (Martin *et al.* 2013, Shimizu *et al.* 2013, Becerra *et al.* 2014, Lin *et al.* 2014, Lei *et al.* 2015) reported that continued root development was provided, mainly by cellular/acellular cementum and poorly mineralized bone. Tissues formed after PRP application were histologically similar to those without PRP, deprived of odontoblast-like polarized cells (Martin *et al.* 2013). Furthermore, a fibrous nonmineralized connective tissue with different degrees of inflammation and dystrophic calcifications was observed (Becerra *et al.* 2014). The evaluated teeth had closed apices in radiographic evaluation; meanwhile, cone-beam analysis, together with the morphological and histological findings, depicted that root elongation was achieved only in the lingual portion. This observation highlights the difficulty in establishing parameters to confirm clinical success after RCR.

To perform RCR, decontamination is carried out by applying disinfecting solutions without conventional mechanical instrumentation (Wigler *et al.* 2013). In the present scoping review, almost 100% of the included studies applied NaOCl. However, an histological/bacteriological analysis related the presence of necrotic debris, comprising a thick bacterial biofilm, in the apical portion of NIPT. In addition, bacterial clusters were found on root walls and in dentinal tubules (Lin *et al.* 2014). Alobaid *et al.* (2014) suggested that passive disinfection with NaOCl may not be sufficient to reduce/eliminate contamination. However, a greater bacterial reduction was observed after the irrigation of root canal systems with NaOCl compared to TAP or Ca(OH)₂ placement (Nagata *et al.* 2014). Due to its extended residual antimicrobial properties, CHX has been successfully associated with NaOCl as a disinfecting agent (Reynolds *et al.* 2009, Shin *et al.* 2009, Petrino *et al.* 2010, Shivashankar *et al.* 2012, Chen *et al.* 2013, McTigue *et al.* 2013) and with Ca(OH)₂ as intracanal medicaments (Soares *et al.* 2013, Nagata *et al.* 2014).

When RCR was performed in traumatized teeth, TAP was as effective as Ca(OH)₂ in reducing spontaneous and induced pain as well as in repairing periapical lesions (Nagata *et al.* 2014). However, a high incidence of crown discoloration (83%) was associated

with TAP (Gelman & Park 2012, Nagata *et al.* 2014). In fact, the main concern related to TAP is the potential for tooth discoloration, derived from the contact between minocycline and the root walls during the time needed to eradicate the infection in RCR (Kim *et al.* 2010). Attempts to substitute minocycline by amoxicillin (Petrino *et al.* 2010, Thomson & Kahler 2010, Kahler *et al.* 2014), doxycycline (Jadhav *et al.* 2012, Nagy *et al.* 2014, Raju *et al.* 2014), clindamycin (McTigue *et al.* 2013, Kumar *et al.* 2014), tetracycline (Guven Polat *et al.* 2014) or cefaclor (Thibodeau & Trope 2007, Thibodeau 2009, Kim *et al.* 2012, Amit *et al.* 2014, Bezgin *et al.* 2014, 2015) have been reported. No discoloration was observed after the application of TAP containing cefaclor in a randomized clinical trial following-up 20 teeth for 18 months (Bezgin *et al.* 2015). Unaesthetic results were also associated with MTA, with crown discoloration being observed in 12 of 20 cases (60%) (Bezgin *et al.* 2015). Nevertheless, RCR was considered successful by the authors as the teeth were suitable for root canal treatment and the patient referred to prosthodontists for tooth restoration.

Root canal revascularization relies on the mechanical irritation of the periapical tissues to initiate bleeding into the canal to produce a blood clot, which is expected to act as a matrix where the migrating responsive cells will possibly adhere and differentiate to reestablish the physiological activities of the pulp–dentine complex (AAE 2013, Wigler *et al.* 2013). The impossibility of inducing initial bleeding comprises one of the main causes of failure of RCR (Ding *et al.* 2009). In multirooted teeth, after observing an inadequate level of haemorrhage in some canals, transferring blood between canals comprised an effective strategy (Cehreli *et al.* 2011). Bleeding and fibrin clot formation are the initial stage of wound healing after tissue injury. Fibrin is a biopolymer critical for haemostasis and wound healing (Mittal & Narang 2012), and it is responsible for blood clot formation and stabilization, acting as a ‘trap’ to retain the unknown cells enrolled in healing (Lovelace *et al.* 2011).

Based on tissue engineering principles (Langer & Vacanti 1993), a range of strategies has been proposed by incorporating artificial scaffolds, after the initial bleeding. The application of a gelatin hydrogel charged with basic fibroblast growth factor (bFGF) over the blood clot (Nagy *et al.* 2014) or injection of PRP into the apical third of the canal (Martin *et al.* 2013) did not appear to improve healing as both pulp-like tissue and odontoblastic cells were not observed in the

revascularized teeth. However, when a collagen sponge soaked with PRP was applied over the blood, a slight improvement in periapical healing, apical closure, root wall thickening and root lengthening was observed (Jadhav *et al.* 2013, Conde *et al.* 2016). The utilization of PRP and PRF has been reported more frequently in recent years (2012–2015), and they were feasible adjuncts to obtain clinical success over more than 30 months follow-up (Ray *et al.* 2015, Wang *et al.* 2015). PRP and PRF possess important differences regarding their properties to deliver growth factors (Mittal & Narang 2012). The releasing peak of growth factors from PRP takes place in the first day, decreasing significantly in the third day, whilst the releasing-GF peak of PRF, mainly for TGF- β 1 and alkaline phosphatase, ensues on the 14th day (He *et al.* 2009). These properties can justify the better response of periapical healing, root lengthening and root wall thickening of PRF over PRP and conventional blood clots observed in studies comparing these techniques (Narang *et al.* 2015). The main disadvantages of PRP and PRF are related to the need for centrifugation, mainly to obtain the PRP (Mittal & Narang 2012), and the need to collect venous blood from young patients. One reported failure occurred after application of blood venous derivatives (Yadav *et al.* 2015).

The periapical region of NIPT possesses a population of MSC, named stem cells of the apical papilla – SCAPs – (Sonoyama *et al.* 2008), which are odontoblastic-progenitor cell thought to be enrolled in healing during RCR (Wigler *et al.* 2013). However, histological and immunohistochemical analysis performed after RCR identified structures staining positively for bone sialoprotein (BSP) but negatively for dentine sialoprotein (DSP), which are a protein enrolled in dentinogenesis (Martin *et al.* 2013, Shimizu *et al.* 2013, Becerra *et al.* 2014, Lin *et al.* 2014, Lei *et al.* 2015). It has been speculated that both the inherent bacterial contents of necrosed pulps and the application of Ca(OH)₂ as a temporary filling could be harmful for these cells (Nagata *et al.* 2014). In such a context, EDTA has been suggested to be applied in RCR as it can solubilize the growth factors fossilized in the dentine matrix (Graham *et al.* 2006), which seems to be essential for pulp regeneration (Conde *et al.* 2016). However, only 14 from the selected studies applied EDTA during RCR (Paryani & Kim 2013, Soares *et al.* 2013, Alobaid *et al.* 2014, Amit *et al.* 2014, Jadhav *et al.* 2014, 2015, Nagata *et al.* 2014, 2015, Bezgin *et al.* 2015, Lei *et al.* 2015, McCabe 2015, Nevins & Cymerman 2015, Ray *et al.* 2015).

Conclusion

Most of the cases reported a significant gain in root length and width in NIPT. Histological analysis revealed cementum-like tissue inside the root canal suggesting that RCR in NIPT provides repair instead regeneration. NaOCl and TAP were the most frequently used intracanal medicaments. However, such results must be carefully interpreted as most of them are derived from case reports and uncontrolled clinical trials. Besides, it is unclear whether the motivation to submit and publish cases of RCR failure is as high as the motivation to publish RCR successes. Therefore, the results of this analysis are likely to overestimate the actual success rate of RCR. Thus, well-designed randomized controlled trials comparing RCR with available apexification treatments are needed to address this important gap knowledge.

Conflict of Interest

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

References

- AAE (2013) Endodontists' 2013 Guide to CTD. [WWW document]. <http://www.nxtbook.com/nxtbooks/aae/2013guidetocdt/#/18> URL [accessed on November 2015].
- Abduljabbar F, Bakhsh A, Abed H (2014) Revascularization procedure induced maturogenesis of upper permanent incisor. *Journal of Oral Health and Dental Management* **13**, 831–4.
- Aggarwal V, Miglani S, Singla M (2012) Conventional apexification and revascularization induced maturogenesis of two non-vital, immature teeth in same patient: 24 months follow up of a case. *Journal of Conservative Dentistry* **15**, 68–72.
- Akgun OM, Altun C, Guven G (2009) Use of triple antibiotic paste as a disinfectant for a traumatized immature tooth with a periapical lesion: a case report. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics* **108**, e62–5.
- Alobaid AS, Cortes LM, Lo J et al. (2014) Radiographic and clinical outcomes of the treatment of immature permanent teeth by revascularization or apexification: a pilot retrospective cohort study. *Journal of Endodontics* **40**, 1063–70.
- Amit V, Jain A, Nayak UA, Bhat M (2014) Maturogenesis by revascularization in an infected immature permanent tooth. *Journal of Indian Society of Pedodontics and Preventive Dentistry* **32**, 172–5.
- Andreasen JO, Bakland LK (2012) Pulp regeneration after non-infected and infected necrosis, what type of tissue do we want? A review. *Dental Traumatology* **28**, 13–8.
- Andreasen JO, Farik B, Munksgaard EC (2002) Long-term calcium hydroxide as a root canal dressing may increase risk of root fracture. *Dental Traumatology* **18**, 134–7.
- Arksey H, O'Malley L (2005) Scoping studies: towards a methodological framework. *International Journal of Social Research Methodology* **8**, 19–32.
- Banchs F, Trope M (2004) Revascularization of immature permanent teeth with apical periodontitis: new treatment protocol? *Journal of Endodontics* **30**, 196–200.
- Becerra P, Ricucci D, Loghin S, Gibbs JL, Lin LM (2014) Histologic study of a human immature permanent premolar with chronic apical abscess after revascularization/revitalization. *Journal of Endodontics* **40**, 133–9.
- Bezgin T, Yilmaz AD, Çelik BN, Sönmez H (2014) Concentrated platelet-rich plasma used in root canal revascularization: 2 case reports. *International Endodontic Journal* **47**, 41–9.
- Bezgin T, Yilmaz AD, Celik BN, Kolsuz ME, Sonmez H (2015) Efficacy of platelet-rich plasma as a scaffold in regenerative endodontic treatment. *Journal of Endodontics* **41**, 36–44.
- Cehreli ZC, Isbitiren B, Sara S, Erbas G (2011) Regenerative endodontic treatment (revascularization) of immature necrotic molars medicated with calcium hydroxide: a case series. *Journal of Endodontics* **37**, 1327–30.
- Cehreli ZC, Sara S, Aksoy B (2012) Revascularization of immature permanent incisors after severe extrusive luxation injury. *Journal of the Canadian Dental Association* **78**, c4.
- Chandran V, Chacko V, Sivadas G (2014) Management of a nonvital young permanent tooth by pulp revascularization. *International Journal of Clinical Pediatric Dentistry* **7**, 213–6.
- Chen MYH, Chen KL, Chen CA, Tayebaty F, Rosenberg PA, Lin LM (2012) Responses of immature permanent teeth with infected necrotic pulp tissue and apical periodontitis/abscess to revascularization procedures. *International Endodontic Journal* **45**, 294–305.
- Chen K, Xiang HC, Huang YB, Liu CQ (2013) Comparative analysis of *in vitro* periodontal characteristics of stem cells from apical papilla (SCAP) and periodontal ligament stem cells (PDLSCs). *Archives of Oral Biology* **58**, 997–1006.
- Chueh LH, Huang GTJ (2006) Immature teeth with paradigms of periodontitis or abscess undergoing apexogenesis: a paradigm shift. *Journal of Endodontics* **32**, 1205–13.
- Conde MC, Chisini LA, Demarco FF, Nör JE, Casagrande L, Tarquinio SB (2016) Stem cell-based pulp tissue engineering: variables enrolled in translation from the bench to the bedside, a systematic review of literature. *International Endodontic Journal* **49**, 543–50.
- Cotti E, Mereu M, Lusso D (2008) Regenerative treatment of an immature, traumatized tooth with apical periodontitis: report of a case. *Journal of Endodontics* **34**, 611–6.
- Cvek M (1992) Prognosis of luxated non-vital maxillary incisors treated with calcium hydroxide and filled with gutta-

- percha. A retrospective clinical study. *Endodontics & Dental Traumatology* **8**, 45–55.
- Dabbagh B, Alvaro E, Vu DD, Rizkallah J, Schwartz S (2012) Clinical complications in the revascularization of immature necrotic permanent teeth. *Pediatric Dentistry* **34**, 414–7.
- Daudt HM, van Mossel C, Scott SJ (2013) Enhancing the scoping study methodology: a large, inter-professional team's experience with Arksey and O'Malley's framework. *BMC Medical Research Methodology* **13**, 48.
- Ding RY, Cheung GSP, Chen J, Yin XZ, Wang QQ, Zhang CF (2009) Pulp revascularization of immature teeth with apical periodontitis: a clinical study. *Journal of Endodontics* **35**, 745–9.
- Farsi N, Abuzeid S, El Ashiry E (2013) Revascularization of dental pulp in human necrotic permanent teeth with immature apex: three case reports. *Life Science Journal* **10**, 1516–21.
- Forghani M, Parisay I, Maghsoudlou A (2013) Apexogenesis and revascularization treatment procedures for two traumatized immature permanent maxillary incisors: a case report. *Restorative Dentistry & Endodontics* **38**, 178–81.
- Fujita Y, Maki K (2013) Single-visit revascularization treatment of an immature permanent tooth with apical periodontitis: a case report. *Pediatric Dental Journal* **23**, 57–61.
- Garcia-Godoy F, Murray PE (2012) Recommendations for using regenerative endodontic procedures in permanent immature traumatized teeth. *Dental Traumatology* **28**, 33–41.
- Gelman R, Park H (2012) Pulp revascularization in an immature necrotic tooth: a case report. *Pediatric Dentistry* **34**, 496–9.
- Graham L, Cooper PR, Cassidy N, Nor JE, Sloan AJ, Smith AJ (2006) The effect of calcium hydroxide on solubilisation of bio-active dentine matrix components. *Biomaterials* **27**, 2865–73.
- Güven Polat G, Yildirim C, Akgun OM, Altun C, Dincer D, Ozkan CK (2014) The use of platelet rich plasma in the treatment of immature tooth with periapical lesion: a case report. *Restorative Dentistry & Endodontics* **39**, 230–4.
- He L, Lin Y, Hu X, Zhang Y, Wu H (2009) A comparative study of platelet-rich fibrin (PRF) and platelet-rich plasma (PRP) on the effect of proliferation and differentiation of rat osteoblasts in vitro. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology* **108**, 707–13.
- Hoshino E, Kurihara-Ando N, Sato I et al. (1996) In-vitro antibacterial susceptibility of bacteria taken from infected root dentine to a mixture of ciprofloxacin, metronidazole and minocycline. *International Endodontic Journal* **29**, 125–30.
- Huang GT, Lin LM (2008) Letter to the editor: comments on the use of the term “revascularization” to describe root regeneration. *Journal of Endodontics* **34**, 511–2.
- Iwaya SI, Ikawa M, Kubota M (2001) Revascularization of an immature permanent tooth with apical periodontitis and sinus tract. *Dental Traumatology* **17**, 185–7.
- Iwaya S, Ikawa M, Kubota M (2011) Revascularization of an immature permanent tooth with periradicular abscess after luxation. *Dental Traumatology* **27**, 55–8.
- Jadhav G, Shah N, Logani A (2012) Revascularization with and without platelet-rich plasma in nonvital, immature, anterior teeth: a pilot clinical study. *Journal of Endodontics* **38**, 1581–7.
- Jadhav G, Shah N, Logani A (2013) Comparative outcome of revascularization in bilateral, non-vital, immature maxillary anterior teeth supplemented with or without platelet rich plasma: a case series. *Journal of Conservative Dentistry* **16**, 568–72.
- Jadhav GR, Shah N, Logani A (2014) Platelet-rich plasma supplemented revascularization of an immature tooth associated with a periapical lesion in a 40-year-old man. *Case Reports in Dentistry* **2014**, 1–4.
- Jadhav GR, Shah D, Raghvendra SS (2015) Autologous Platelet Rich Fibrin aided Revascularization of an immature, non-vital permanent tooth with apical periodontitis: a case report. *Journal of Natural Science, Biology and Medicine* **6**, 224–5.
- Jeeruphan T, Jantararat J, Yanpiset K, Suwannapan L, Khew-sawai P, Hargreaves KM (2012) Mahidol study 1: comparison of radiographic and survival outcomes of immature teeth treated with either regenerative endodontic or apexification methods: a retrospective study. *Journal of Endodontics* **38**, 1330–6.
- Jung IY, Lee SJ, Hargreaves KM (2008) Biologically based treatment of immature permanent teeth with pulpal necrosis: a case series. *Journal of Endodontics* **34**, 876–87.
- Kahler B, Mistry S, Moule A et al. (2014) Revascularization outcomes: a prospective analysis of 16 consecutive cases. *Journal of Endodontics* **40**, 333–8.
- Kalaskar RR, Kalaskar AR (2013) Maturogenesis of non-vital immature permanent teeth. *Contemporary Clinical Dentistry* **4**, 268–70.
- Kaya-Buyukbayram I, Ozalp S, Aytugur E, Aydemir S (2014) Regenerative endodontic treatment of an infected immature dens invaginatus with the aid of cone-beam computed tomography. *Case Reports in Dentistry* **2014**, 403–5.
- Keswani D, Pandey RK (2013) Revascularization of an immature tooth with a necrotic pulp using platelet-rich fibrin: a case report. *International Endodontic Journal* **46**, 1096–104.
- Kim JH, Kim Y, Shin SJ, Park JW, Jung IY (2010) Tooth discoloration of immature permanent incisor associated with triple antibiotic therapy: a case report. *Journal of Endodontics* **36**, 1086–91.
- Kim DS, Park HJ, Yeom JH et al. (2012) Long-term follow-ups of revascularized immature necrotic teeth: three case reports. *International Journal of Oral Science* **4**, 109–13.
- Kleier DJ, Barr ES (1991) A study of endodontically apexified teeth. *Endodontics & Dental Traumatology* **7**, 112–7.
- Kotthoor J, Velmurugan N (2012) Revascularization for a necrotic immature permanent lateral incisor: a case report

- and literature review. *International Journal of Paediatric Dentistry* **23**, 310–6.
- Kumar H, Al-Ali M, Parashos P, Manton DJ (2014) Management of 2 teeth diagnosed with dens invaginatus with regenerative endodontics and apexification in the same patient: a case report and review. *Journal of Endodontics* **40**, 725–31.
- Langer R, Vacanti JP (1993) Tissue engineering. *Science* **260**, 920–6.
- Lei LS, Chen YM, Zhou RH, Huang XJ, Cai ZY (2015) Histologic and immunohistochemical findings of a human immature permanent tooth with apical periodontitis after regenerative endodontic treatment. *Journal of Endodontics* **41**, 1172–9.
- Lenzi R, Trope M (2012) Revitalization procedures in two traumatized incisors with different biological outcomes. *Journal of Endodontics* **38**, 411–4.
- Lin LM, Shimizu E, Gibbs JL, Loghin S, Ricucci D (2014) Histologic and histobacteriologic observations of failed revascularization/revitalization therapy: a case report. *Journal of Endodontics* **40**, 291–5.
- Lovelace TW, Henry MA, Hargreaves KM, Diogenes A (2011) Evaluation of the delivery of mesenchymal stem cells into the root canal space of necrotic immature teeth after clinical regenerative endodontic procedure. *Journal of Endodontics* **37**, 133–8.
- Martin G, Ricucci D, Gibbs JL, Lin LM (2013) Histological findings of revascularized/revitalized immature permanent molar with apical periodontitis using platelet-rich plasma. *Journal of Endodontics* **39**, 138–44.
- McCabe P (2015) Revascularization of an immature tooth with apical periodontitis using a single visit protocol: a case report. *International Endodontic Journal* **48**, 484–97.
- McTigue DJ, Subramanian K, Kumar A (2013) Management of immature permanent teeth with pulpal necrosis: a case series. *Pediatric Dentistry* **35**, 55–60.
- Mishra N, Narang I, Mittal N (2013) Platelet-rich fibrin-mediated revitalization of immature necrotic tooth. *Contemporary Clinical Dentistry* **4**, 412–5.
- Mittal N, Narang I (2012) Revascularisation of immature necrotic teeth: platelet rich fibrin an edge over platelet rich plasma. *Dental Hypotheses* **3**, 29–38.
- Murray PE, Garcia-Godoy F, Hargreaves KM (2007) Regenerative endodontics: a review of current status and a call for action. *Journal of Endodontics* **33**, 377–90.
- Nagata JY, De Almeida F, Gomes BP et al. (2014) Traumatized immature teeth treated with 2 protocols of pulp revascularization. *Journal of Endodontics* **40**, 606–12.
- Nagata JY, Rocha-Lima TF, Gomes BP et al. (2015) Pulp revascularization for immature replanted teeth: a case report. *Australian Dental Journal* **60**, 416–20.
- Nagaveni NB, Poornima P, Joshi JS, Pathak S, Nandini DB (2015) Revascularization of immature, nonvital permanent tooth using platelet-rich fibrin in children. *Pediatric Dentistry* **37**, 1–6.
- Nagy MM, Tawfik HE, Hashem AAR, Abu-Seida AM (2014) Regenerative potential of immature permanent teeth with necrotic pulps after different regenerative protocols. *Journal of Endodontics* **40**, 192–8.
- Narang I, Mittal N, Mishra N (2015) A comparative evaluation of the blood clot, platelet-rich plasma, and platelet-rich fibrin in regeneration of necrotic immature permanent teeth: a clinical study. *Contemporary Clinical Dentistry* **6**, 63–8.
- Narayana P, Hartwell GR, Wallace R, Nair UP (2012) Endodontic clinical management of a dens invaginatus case by using a unique treatment approach: a case report. *Journal of Endodontics* **38**, 1145–8.
- Nevins AJ, Cymerman JJ (2015) Revitalization of open apex teeth with apical periodontitis using a collagen-hydroxyapatite scaffold. *Journal of Endodontics* **41**, 966–73.
- Nosrat A, Seifi A, Asgary S (2011) Regenerative endodontic treatment (revascularization) for necrotic immature permanent molars: a review and report of two cases with a new biomaterial. *Journal of Endodontics* **37**, 562–7.
- Nosrat A, Homayounfar N, Oloomi K (2012) Drawbacks and unfavorable outcomes of regenerative endodontic treatments of necrotic immature teeth: a literature review and report of a case. *Journal of Endodontics* **38**, 1428–34.
- Paryani K, Kim SG (2013) Regenerative endodontic treatment of permanent teeth after completion of root development: a report of 2 cases. *Journal of Endodontics* **39**, 929–34.
- Petrino JA, Boda KK, Shambarger S, Bowles WR, McClanahan SB (2010) Challenges in regenerative endodontics: a case series. *Journal of Endodontics* **36**, 536–41.
- Rafter M (2005) Apexification: a review. *Dental Traumatology* **21**, 1–8.
- Raju SM, Singhyadav S, Ramakumar M (2014) Revascularization of immature mandibular premolar with pulpal necrosis – a case report. *Journal of Clinical and Diagnostic Research* **8**, ZD29–31.
- Ray HL Jr, Marcelino J, Braga R, Horwat R, Lisien M, Khaliq S (2015) Long-term follow up of revascularization using platelet-rich fibrin. *Dental Traumatology* **32**, 80–4.
- Reynolds K, Johnson JD, Cohenca N (2009) Pulp revascularization of necrotic bilateral bicuspid using a modified novel technique to eliminate potential coronal discoloration: a case report. *International Endodontic Journal* **42**, 84–92.
- Rudagi KB, Rudagi BM (2012) One-step apexification in immature tooth using grey mineral trioxide aggregate as an apical barrier and autologous platelet rich fibrin membrane as an internal matrix. *Journal of Conservative Dentistry* **15**, 196–9.
- Saeki K, Fujita Y, Shiono Y, Morimoto Y, Maki K (2014) Pulp revascularization in immature permanent tooth with apical periodontitis using mineral trioxide aggregate. Case reports in medicine, [WWW document]. <https://>

- www.hindawi.com/journals/crim/2014/564908/
[Accessed on 9 November 2016].
- Santiago CN, Pinto SS, Sassone LM, Hirata R, Fidel SR (2015) Revascularization technique for the treatment of external inflammatory root resorption: a report of 3 cases. *Journal of Endodontics* **41**, 1560–4.
- Saoud TM, Zaazou A, Nabil A, Moussa S, Lin LM, Gibbs JL (2014a) Clinical and radiographic outcomes of traumatized immature permanent necrotic teeth after revascularization/revitalization therapy. *Journal of Endodontics* **40**, 1946–52.
- Saoud TMA, Sigurdsson A, Rosenberg PA, Lin LM, Ricucci D (2014b) Treatment of a large cystlike inflammatory periapical lesion associated with mature necrotic teeth using regenerative endodontic therapy. *Journal of Endodontics* **40**, 2081–6.
- Shah N, Logani A, Bbaskar U, Aggarwal V (2008) Efficacy of revascularization to induce apexification/apexogenesis in infected, nonvital, immature teeth: a pilot clinical study. *Journal of Endodontics* **34**, 919–25.
- Shimizu E, Jong G, Partridge N, Rosenberg PA, Lin LM (2012) Histologic observation of a human immature permanent tooth with irreversible pulpitis after revascularization/regeneration procedure. *Journal of Endodontics* **38**, 1293–7.
- Shimizu E, Ricucci D, Albert J et al. (2013) Clinical, radiographic, and histological observation of a human immature permanent tooth with chronic apical abscess after revitalization treatment. *Journal of Endodontics* **39**, 1078–83.
- Shin SY, Albert JS, Mortman RE (2009) One step pulp revascularization treatment of an immature permanent tooth with chronic apical abscess: a case report. *International Endodontic Journal* **42**, 1118–26.
- Shivashankar VY, Johns DA, Vidyantath S, Ramesh Kumar M (2012) Platelet Rich Fibrin in the revitalization of tooth with necrotic pulp and open apex. *Journal of Conservative Dentistry* **15**, 395–8.
- Simon S, Goldberg M (2014) Regenerative endodontics: regeneration or repair? *The Dental Pulp: Biology, Pathology, and Regenerative Therapies* **40**(4 Suppl), S70–5.
- Soares AD, Lins FF, Nagata JY et al. (2013) Pulp revascularization after root canal decontamination with calcium hydroxide and 2% chlorhexidine gel. *Journal of Endodontics* **39**, 417–20.
- Solomon RV, Faizuddin U, Guniganti SS, Waghay S (2015) Analysis of the rate of maturogenesis of a traumatized Cvek's stage 3 anterior tooth treated with platelet-rich fibrin as a regenerative tool using three-dimensional cone-beam computed tomography: an original case report. *Indian Journal of Dental Research* **26**, 90–5.
- Sonmez IS, Akbay Oba A, Erkmén Almaz M (2013) Revascularization/Regeneration performed in immature molars: case reports. *International Journal of Clinical Pediatric Dentistry* **37**, 231–4.
- Sonoyama W, Liu Y, Yamaza T et al. (2008) Characterization of the apical papilla and its residing stem cells from human immature permanent teeth: a pilot study. *Journal of Endodontics* **34**, 166–71.
- Thibodeau B (2009) Case report: pulp revascularization of a necrotic, infected, immature, permanent tooth. *Pediatric Dentistry* **31**, 145–8.
- Thibodeau B, Trope M (2007) Pulp revascularization of a necrotic infected immature permanent tooth: case report and review of the literature. *Pediatric Dentistry* **29**, 47–50.
- Thomson A, Kahler B (2010) Regenerative endodontics – Biologically-based treatment for immature permanent teeth: a case report and review of the literature. *Australian Dental Journal* **55**, 446–52.
- Torabinejad M, Faras H (2012) A clinical and histological report of a tooth with an open apex treated with regenerative endodontics using platelet-rich plasma. *Journal of Endodontics* **38**, 864–8.
- Torabinejad M, Turman M (2011) Revitalization of tooth with necrotic pulp and open apex by using platelet-rich plasma: a case report reply. *Journal of Endodontics* **37**, 743–4.
- Torneck CD, Smith J (1970) Biologic effects of endodontic procedures on developing incisor teeth. I. Effect of partial and total pulp removal. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology* **30**, 258–66.
- Wang HJ, Chen YHM, Chen KL (2013) Conservative treatment of immature teeth with apical periodontitis using triple antibiotic paste disinfection. *Journal of Dental Sciences* **11**, 196–201.
- Wang Y, Zhu XF, Zhang CF (2015) Pulp revascularization on permanent teeth with open apices in a middle-aged patient. *Journal of Endodontics* **41**, 1571–5.
- Weisleder R, Benitez CR (2003) Maturogenesis: is it a new concept? *Journal of Endodontics* **29**, 776–8.
- Wigler R, Kaufman AY, Lin S, Steinbock N, Hazan-Molina H, Torneck CD (2013) Revascularization: a treatment for permanent teeth with necrotic pulp and incomplete root development. *Journal of Endodontics* **39**, 319–26.
- Yadav P, Pruthi PJ, Naval RR, Talwar S, Verma M (2015) Novel use of platelet-rich fibrin matrix and MTA as an apical barrier in the management of a failed revascularization case. *Dental Traumatology* **31**, 328–31.
- Yang J, Zhao Y, Qin M, Ge L (2013) Pulp revascularization of immature dens invaginatus with periapical periodontitis. *Journal of Endodontics* **39**, 288–92.