

Regenerative endodontic therapy for managing immature non-vital teeth: a national survey of UK paediatric dental specialists and trainees

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Key points

Highlights and discusses the use of regenerative endodontic therapy.

Offers some guidance on how to overcome some important barriers to the use of this technique among specialist and practitioners.

Involves an update on the latest recommendation for regenerative endodontic treatment of non-vital immature teeth.

Background Several guidelines have been published advocating the use of regenerative endodontic therapy (RET) in managing non-vital immature permanent teeth. It is unclear, however, how many UK paediatric dental specialists routinely use this technique and their opinion of its outcomes, and barriers to its use. **Aim** To assess the knowledge, experience and the opinion of UK based paediatric dental specialists/trainees (UKPDS/T) and practitioners working in the capacity of paediatric dental specialists on the use of RET. **Design** A cross-sectional study using a 22-item questionnaire was developed using the Bristol Online Survey tool and circulated electronically to members of the British Society of Paediatric Dentistry between August and November 2016. **Results** Ninety-eight UKPDS/T completed the survey. A quarter of respondents (N = 24, 24.5%) reported using RET. Reasons cited for not using RET included lack of: training (N = 48, 45%), materials (N = 28, 26%), evidence (N = 17, 16%) and suitable cases (N = 6, 6%). Different protocols in terms of disinfection, medicaments, scaffolds, and obturation material were identified. **Conclusions** This survey highlights a low uptake of RET by current UKPDS and trainees with several barriers identified. Deviations from the current RET guidelines were identified. Recommendations addressing the use of RET in light of the findings of this survey were made.

Introduction

The management of necrotic immature permanent teeth in children has always been a challenge in paediatric dentistry due to the compromised crown root ratio, thin root dentine walls and wide-open apices. Traditionally, calcium hydroxide apexification or MTA apical plug techniques have been the treatment of choice for these teeth. However, it is well known that not only do these traditional methods fail to qualitatively improve root dentinal wall dimensions, teeth are further weakened by the materials used in such techniques.¹⁻³ Studies have shown that

despite receiving endodontic treatment, over 50% of such teeth are lost in the first 5–10 years following injury,³⁻⁵ thus leaving the child with a treatment burden for the rest of their life.

In order to overcome these problems, regenerative endodontic therapy (RET) has been advocated as an alternative treatment option, for treating necrotic immature permanent teeth. The paradigm shift towards management of necrotic immature permanent teeth using RET is not a novel concept in pulp biology, and has previously been discussed in the dental scientific literature by Nygaard-Østby as early as 1961.⁶ Currently, RET has received significant attention in the scientific community, with numerous studies and guidelines of various specialist organisations advocating its use as the foremost approach for treatment of non-vital immature permanent teeth.⁷⁻⁹ Although, healing of periapical pathology is a prerequisite of any successful technique, the main aim of RET is to facilitate an increase in root length and promote thickening of dentinal walls, which is essential in preventing long-term root fractures.⁴

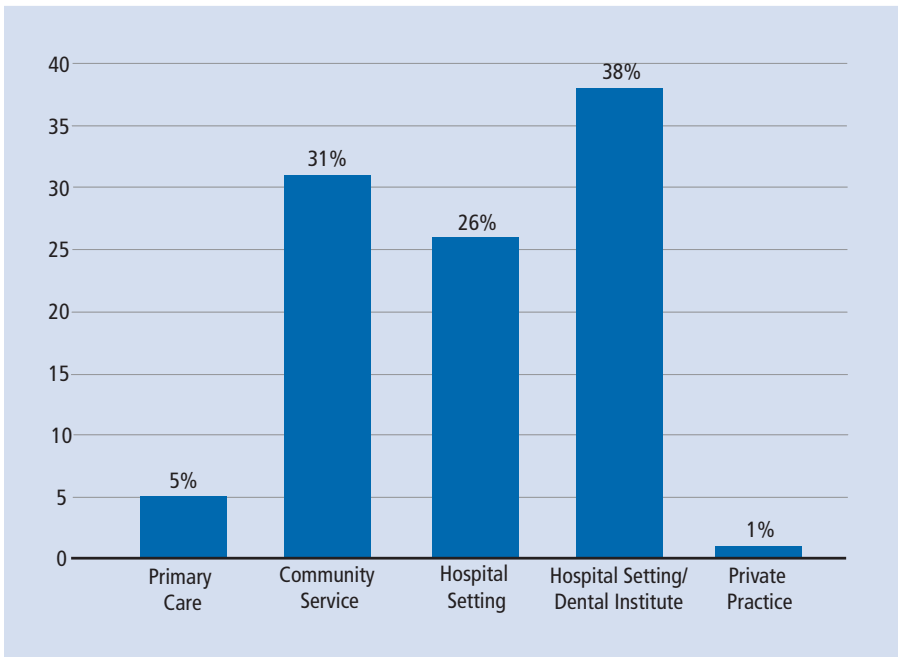
Several prospective studies, describing different techniques of RET, have been published in the last decade.¹⁰ However, the analysis of treatment outcomes have revealed conflicting results,¹¹ with the majority showing clinical signs of soft tissue healing and radiographic resolution of periapical pathology, but without the desired increase in root length, apex closure or dentinal wall thickening.¹²

Assessment of the available data suggests that these conflicting results possibly stem from the use of different RET techniques, and the significant lack of data differentiating between traumatised and non-traumatised teeth, thus resulting in difficulties comparing outcomes across studies.^{13,14} The removal of ischemic damaged Hertwig epithelial root sheaths (HERS) of autotransplanted teeth in monkeys have been found to lead to compromised or arrested root formation with subsequent invasion of bone, periodontal ligament (PDL) and cementoblasts into the pulp canal.¹⁵ Therefore, it is possible that, depending on the type of traumatic injury sustained, there may be different degrees of irreversible damage

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Fig. 1 Respondent demographics represented using a bar chart showing respondents' primary type of practice



to HERS in traumatised non-vital immature teeth, which in turn may influence the outcome of RET treatment resulting in some cases showing favourable results while others fail to regenerate.

In the UK, the majority of young individuals below the age of 16 are referred to paediatric dental specialists for management of dental conditions such as non-vital immature teeth. These patients are also treated by paediatric dental speciality trainees under the supervision of paediatric dental specialists or practitioners with advanced training in paediatric dentistry working in the capacity of paediatric dental specialists.

As RET gains popularity as an alternative treatment option for management of this condition in young individuals, it is timely that information about paediatric dental specialists' and speciality trainees' experiences and opinions on performing RET be evaluated. Therefore, this study aimed to

Fig. 2 Respondent demographics represented using a bar chart showing respondents' region of work

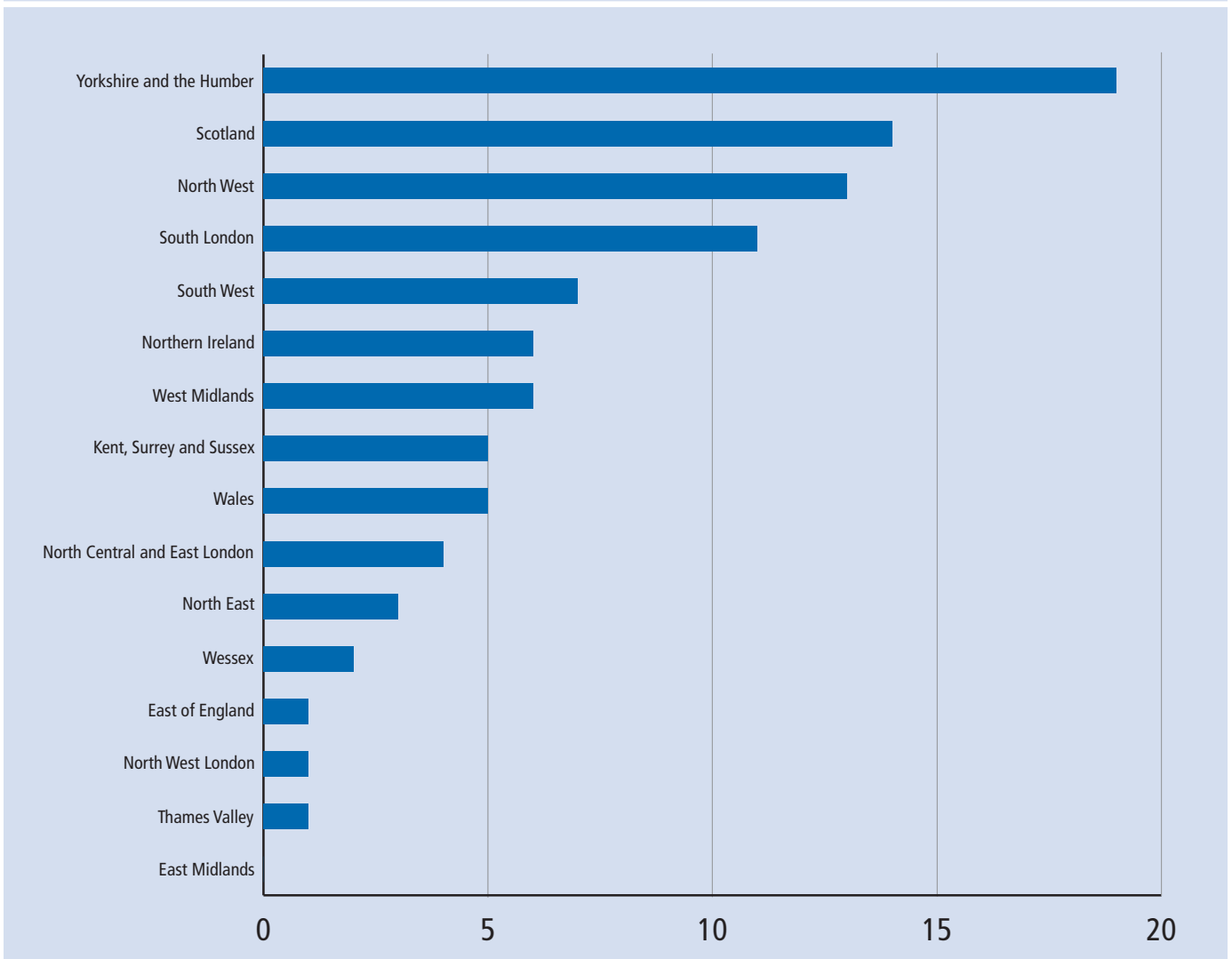
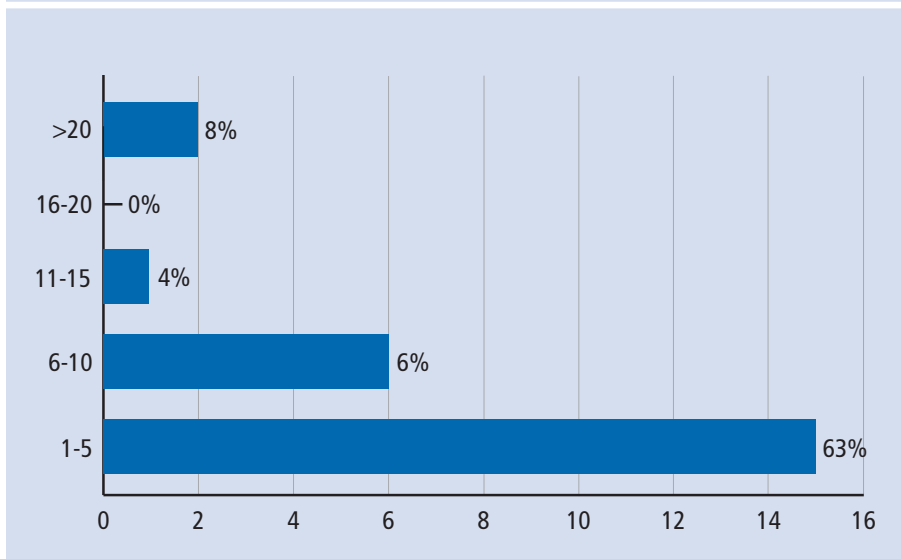


Fig. 3 Bar chart showing respondents' experience in using RET



assess the knowledge, experience and the opinion of UK paediatric dental specialists and speciality trainees on the use of RET for the treatment of immature non-vital teeth in children and adolescents.

Methods

This was a cross sectional study, with a 22-item questionnaire used to evaluate UK paediatric dental specialists' and trainees' experiences of using RET for the management of non-vital immature teeth. Institutional ethical approval was obtained from the University of Leeds Research Ethics Committee before commencement of the study (220,216/HN/190). The questionnaire was developed using the Bristol Online Survey tool and piloted on a small group of specialist dentists, for ease of understanding and reduction of ambiguity of questions, before administration. An invitation email explaining the survey and the questionnaire was circulated electronically to members of the British Society of Paediatric Dentistry (BSPD) between 16 August and 9 November 2016 with a reminder email sent on 30 October 2016. Individual follow-up with non-respondents was not carried out due to the anonymity of the survey.

Information collected in the questionnaire included the following:

1. Demographics – data on positions held, dentists' type of practice (primary care, community service etc), and region of work
2. Whether respondents use RET and/or alternative methods for managing non-vital immature teeth
3. Perceived barriers for the use of RET
4. Experience in using RET for treatment of

non-vital immature teeth

5. RET technique used: disinfection technique, intracanal medicament, type of scaffold, and coronal seal material used
6. Their opinions of what they considered as a successful outcome for RET in terms of continuation of root development, and periapical healing
7. Factors affecting RET success and any post-treatment sequelae encountered in their own cases.

Data were coded and analysed using the Bristol Online Survey tool. Descriptive statistics analysing participants' responses were computed.

Results

Participants

A total of 111 participants completed the survey, of which 13 responses were excluded as the respondents were neither UK General Dental Council (GDC) registered, UK-based paediatric dental speciality trainees, nor working in the capacity of a UK specialist in paediatric dentistry. A total of 98 responses were included in the final analysis. These consisted of UK paediatric dental specialists or trainees (UKPDS/T), of which 61 were UK based specialists (GDC registered specialists working in a UK based specialist post), 21 were UK based paediatric dental speciality trainees and 16 were dental practitioners working in the capacity of paediatric dental specialists. The responses of UK-based paediatric dental speciality trainees were included in this survey as they carry out paediatric dental specialist level work under the direct supervision of UK GDC registered paediatric dental specialists. The responses of dental practitioners working in the capacity of a paediatric dental specialist, such as staff grade

Fig. 4 Bar chart showing barriers preventing participants from using RET in managing non-vital immature teeth

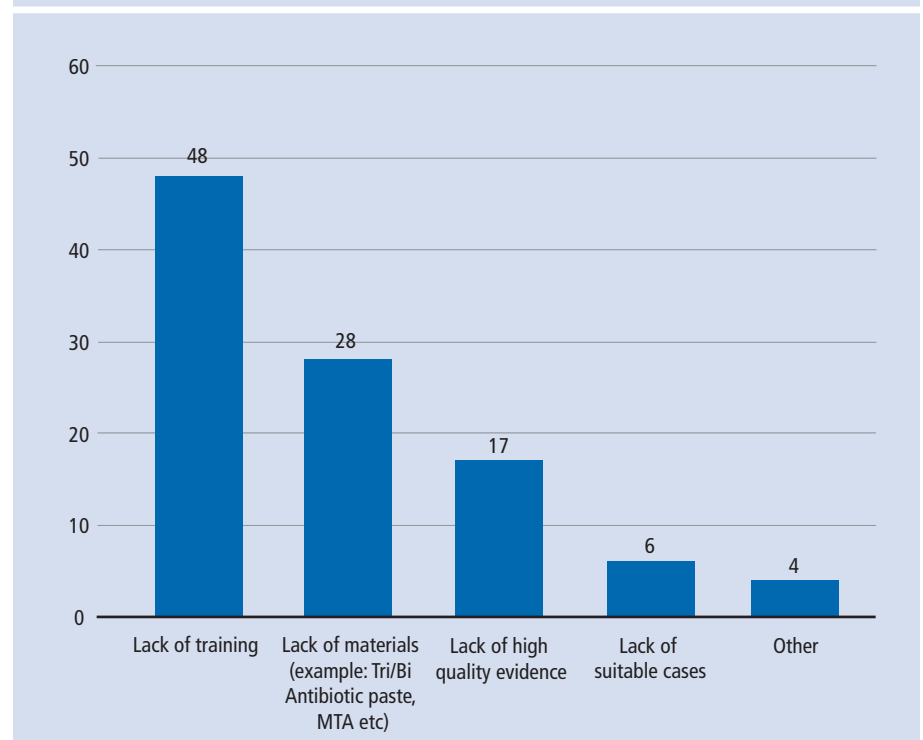
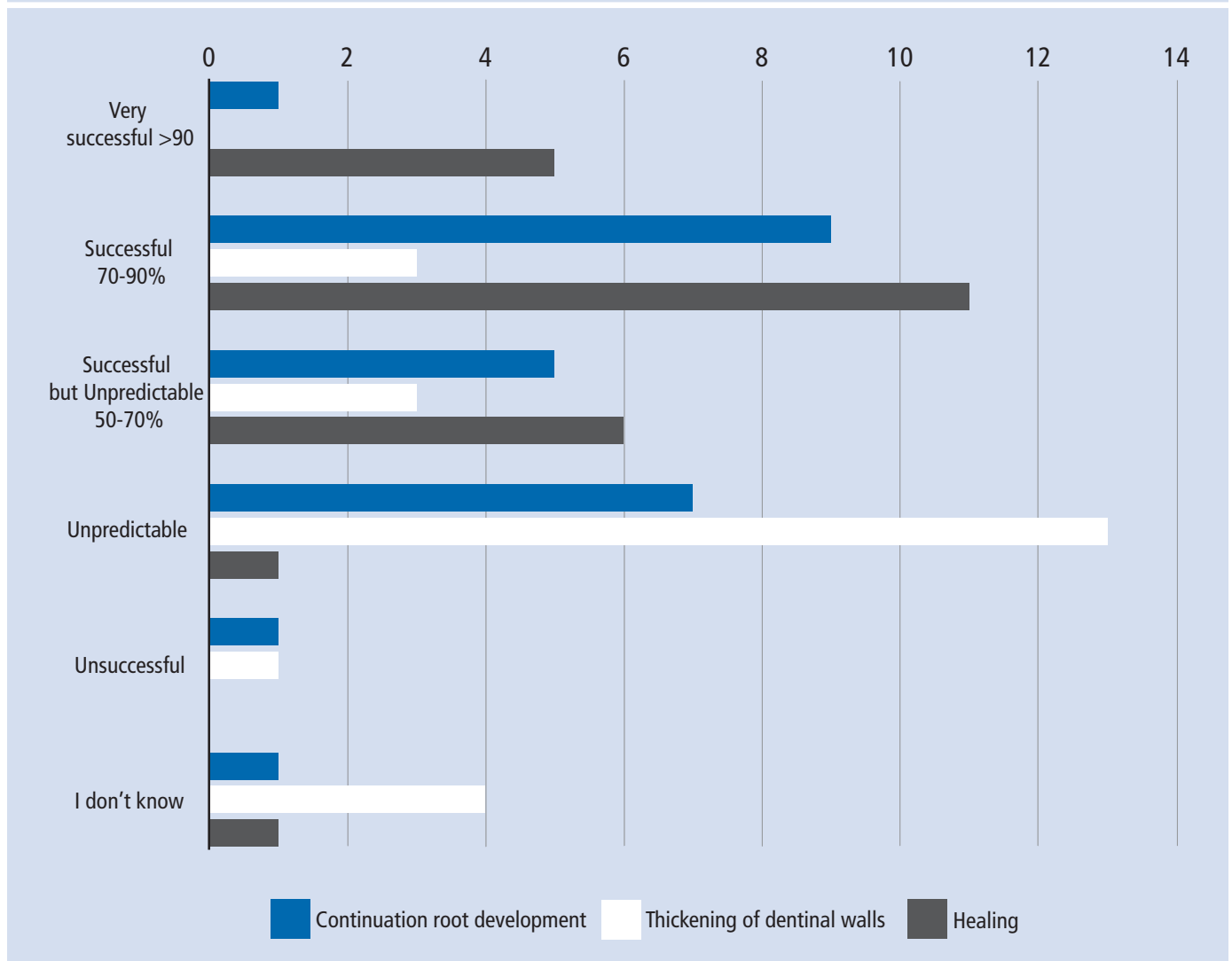


Fig. 5 Bar chart showing participants' experience with RET success in terms of continuation of root development, thickening of root dentinal wall and healing



paediatric dentists, were also included as such positions require higher education/training in paediatric dentistry delivered by approved training posts.

The majority of respondents worked at university-based dental institutes (N = 37, 37.7%) with an almost equal number working in community services and hospitals (Fig. 1). There was a good distribution of UKPDS/T representation across the country (Fig. 2).

Techniques used for the management of non-vital immature teeth

Close to a quarter of respondents (N = 24, 24.5%) reported using RET in the management of non-vital immature teeth. Of these, only two respondents reported having treated more than 20 cases in the last five years, with the majority (N = 15; 62.5%) reported treating between 1-5 cases in a 5-year period (Fig. 3).

Other respondents reported the use of calcium hydroxide apexification (N = 54, 48.6%) or mineral trioxide aggregate (MTA) apical plug technique (N = 47, 42.3%) as the more commonly used techniques in management of non-vital immature teeth. Furthermore, ten participants (9%) reported using Biodentine apical plug technique.

Different barriers to the use of RET have been reported by respondents as summarised in Figure 4.

Use of RET in the management of non-vital immature teeth

Respondents who reported using RET in the management of non-vital immature teeth (N = 24), were also required to respond to questions on case selection, RET technique/protocol used, perceived factors affecting RET success, and any post-operative complications following RET.

Case selection

Most participants reported using RET for immature permanent teeth which had become non-vital as a result of dental trauma (N = 22, 54%), followed by dental anomalies (N = 14, 34%) and dental caries (N = 5, 12%). With regards to the effect of trauma on success of RET, more than half of respondents were unsure as to its effect (N = 13, 54%). Seven respondents (29%), reported that they felt RET treatment on traumatised teeth was less successful than other teeth treated with RET, whereas two other respondents (9%) reported the opposite effect.

In response to the question regarding whether participants thought that the success of RET was affected by the aetiology for the loss of vitality, the majority of respondents (N = 12; 50%) reported being unaware of such relationship.

RET technique/protocol used

Canal disinfection

Most participants reported using sodium hypochlorite (NaOCl) as the primary disinfectant solution (N = 19, 89.2%) with an almost equal number of participants (one third) using concentrations of <1.5% (N = 8) and 1.6–6% (N = 9). Only two participants (8.3%) reported using a concentration of 1.5% NaOCl, while five (20.8%) did not use NaOCl in disinfection. Chlorhexidine use on the other hand was much less prevalent with only five (20.8%) participants using it as the sole disinfection solution, while two other respondents (8.3%) reported using it in combination with sodium hypochlorite. With regards to EDTA use, 16 participants (66.7%) reported using 17% EDTA in their RET protocol.

Intra-canal medicament

The majority of respondents reported using calcium hydroxide paste as intra-canal medicament (N = 10, 41.7%), followed by bi-antibiotic paste (ciprofloxacin and metronidazole) (N = 9, 37.9%) and tri-antibiotic paste (N = 5, 20.8%).

Scaffold and coronal seal

Eighteen participants (75%) reported using a blood clot as a scaffold with the remaining participants not using any other scaffold system.

Coronal seal

MTA was reported as the most commonly used coronal seal materials over the blood clot (N = 14, 58.3%), followed by Biodentine (N = 5, 20.8%), glass ionomer (N = 4, 16.7%) and composite (N = 1, 4.2%).

Success of RET

A successful outcome (>70% success rate) was reported by 66.6% (N = 16) of participants, whereas seven participants (29.2%) reported the technique to be successful (50–70% success rate) and/or unpredictable in terms of healing (Fig. 5).

In terms of promoting continuation of root development, slightly more than one third (N = 10, 41.6%) reported the technique to be successful in the majority (>70%) of their cases. Twelve participants reported the technique to be unpredictable while one participant reported the technique to be unsuccessful (Fig. 5).

With regards to promoting thickening of dentinal walls, more than half (N = 16, 66%) reported the technique to be unpredictable, with only three participants (12.5%) reporting the technique to be successful in 70–90% of cases (Fig. 5).

Respondents were largely undecided, with a 50% split in opinion, when asked whether they felt that healing of periapical pathology with absence of continuation of root development and thickening of dentinal walls was considered a successful outcome of RET.

Factors affecting success of RET

Participants were also asked whether stage of root development, aetiology of loss of vitality, and degree of infection had any impact on the success of RET. In general, a large number of participants were not aware of such effect, especially in relation to root development stage (N = 16, 66.7%) and reason for loss of vitality (N = 12, 50%). Some participants reported that teeth with more immature roots (N = 5, 20.8%)

and those non-traumatised (N = 9, 29.2%) appeared to have better outcomes.

RET post-operative complications

With regards to post-operative RET complications, most respondents reported post-operative discolouration of teeth (N = 21, 78%) (Fig. 6). Other complications such as root fractures and ankylosis as a result of RET were much less common (Fig. 6).

Discussion

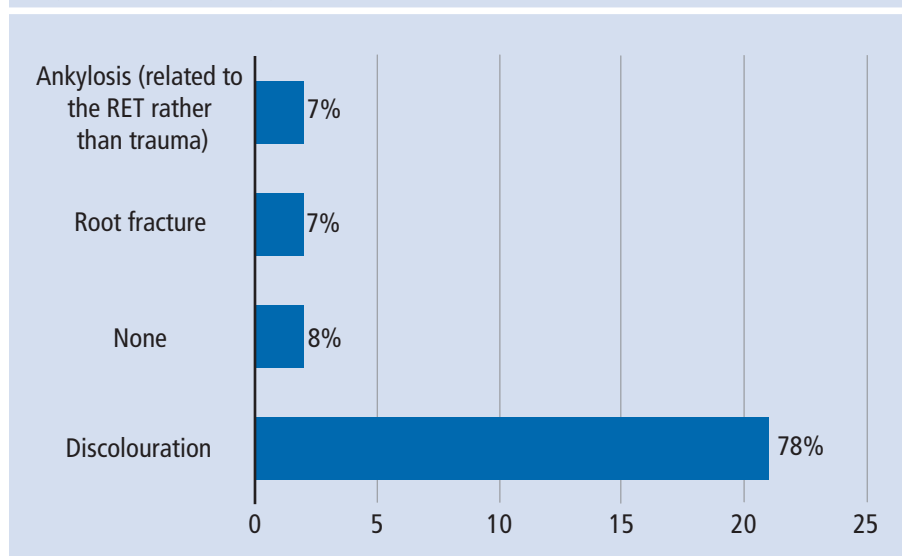
The distribution of the questionnaire survey was through the BSPD electronic mailing list, which includes most UK registered paediatric dental specialists and speciality trainees in paediatric dentistry. However, the authors acknowledge that it is possible that few UK-based specialists are non BSPD members. In addition, the mailing list also includes non-UK based members, which resulted in the need to discard some data sets. Nevertheless, the results included participation of a large number of UK-based specialists/trainees and practitioners working in the capacity of paediatric dental specialists, with an acceptable representation of paediatric dental specialists across the country.

Management of non-vital immature teeth remains a challenge in paediatric dentistry with different endodontic management techniques available. This survey showed different techniques used by UKPDS/T in managing non-vital immature teeth including calcium hydroxide apexification, apical plug technique using MTA/Biodentine and RET.

Although calcium hydroxide has been used for several decades in apexification, long term use of calcium hydroxide as intra-canal medicament has been shown to reduce dentinal fracture resistance, therefore, contributing to long-term cervical tooth fractures.^{2–4} Consequently, the prolonged use of calcium hydroxide in apexification has been discouraged as a first line management technique in non-vital immature teeth.^{8,9,13}

The use of MTA apical plug technique is currently considered the standard technique in managing non-vital immature teeth with a similar success rate to that of calcium hydroxide apexification.^{16,17} The most recent systematic review and meta-analysis comparing success rates between calcium hydroxide apexification and MTA apical plug technique, reported a high success rate for both techniques of 91% and 93%, respectively.¹⁷ The follow-up

Fig. 6 Bar chart showing post-operative RET complications



period, however, was only 34.8 ± 4.4 months. The high level of cervical fractures following calcium hydroxide apexification of 28–77% was reported after four-year follow-up.⁴ More recently, MTA has been shown to reduce dentinal fracture resistance^{1,18,19} which raises concerns regarding the long-term success and survival of MTA root treated teeth. This effect is, however, controversial, as other researchers have shown an opposite effect.^{20–22}

Consequently, promoting qualitative and quantitative increase in root dimensions through pulpal regeneration is ultimately the desired outcome hence the need for RET. Unfortunately, despite the plethora of published studies including randomised controlled trials the outcomes of this treatment modality remain unpredictable at best.^{11–13}

A recent systematic review and meta-analysis has recommended the use of MTA apical plug technique over RET and calcium hydroxide apexification.²³ However, MTA apical plug technique is not suitable in immature teeth with very short roots as such teeth have very compromised crown root ratios, therefore, poor long-term prognosis. Therefore, despite the unpredictability of the outcomes of the RET currently used, this treatment modality is a viable option of management in those teeth where MTA apical plug is judged to be unsuitable.⁹

In the UK, unlike many other countries, UKPDS/T usually manage non-vital immature permanent teeth with the management of such teeth being taught in all paediatric dentistry programmes across the country. It is, therefore, important to evaluate whether the adoption of a newer technique, such as RET, has been utilised by this group of practitioners. Despite the current recommendations that RET should be considered as one of the options for management of non-vital immature teeth, only 24.5% of respondents reported using RET in managing these teeth. The main perceived barrier reported included lack of training, lack of suitable case indications, and lack of evidence supporting the technique. Other reported barriers included work-related limitations, for example, lack of necessary medicaments, limited budget for RET and inability to obtain institution approval to perform RET. It is understandable that clinicians might feel cautious about using a new technique, especially one that they were not trained to use. However, this technique is currently well recognised as one of the treatment modalities in the management of

certain non-vital immature teeth and should be considered when managing these teeth as recommended by the American Association of Endodontics (AAE), the European Society of Endodontology (ESE) and the European Academy of Paediatric Dentistry (EAPD).^{7–9} The authors, therefore, would like to highlight that an evidence-based, free access, step by step description of the recommended RET protocol is published by the AAE and could be accessed electronically on the AAE website (http://www.aae.org/uploadedfiles/publications_and_research/research/currentregenerativeendodonticconsiderations.pdf).⁷ This should help improve clinicians' confidence in performing this technique and gain institutional approval in their places of work.

With regards to the necessary antibiotic mixture, obtaining the required antibiotic mixture (metronidazole [100 mg] and ciprofloxacin [100 mg]) is one of the barriers reported in this survey as access to TriBiodent (Royal Victoria Infirmary, Newcastle, UK), supplied as three capsules of metronidazole [100 mg], ciprofloxacin [100 mg] and minocycline [100 mg]) can be challenging. The use of calcium hydroxide paste rather than an antibiotics mixture has been suggested by the AAE and recommended by the ESE and EAPD.^{8,24–26} This recommendation is based on one study showing similar success rates when using calcium hydroxide to that of antibiotic mixtures,²⁷ laboratory studies showing less effect of calcium hydroxide on stem cell survival in comparison to the antibiotic mixtures,^{28,29} and difficulties in removing the antibiotic mixture from root canal systems in comparison to calcium hydroxide.³⁰

Tooth discolorations have been linked to the use of tetracycline group antibiotics, which has been cited as one of the undesirable effects of RET and certainly consistent with the results reported in this survey. The use of calcium hydroxide is unlikely to cause any significant discolouration.

Most participants reported using sodium hypochlorite in canal chemical disinfection while the recommended 1.5% concentration⁷ was only used by two participants. Sodium hypochlorite is the most commonly used irrigant in RET studies, with concentrations ranging from 0.5–6%. Decreasing NaOCl concentration reduces its stem cell toxicity, antibacterial effect and tissue dissolving abilities, while increasing its volume or temperature potentiates its effectiveness³¹ and stem cell toxicity. The recommendation of using

1.5% hypochlorite is based on the work of Martin *et al.* (2014)³² who assessed the effect of different sodium hypochlorite concentrations (0.5, 1.5, 3, and 6%) followed by either 17% EDTA or normal saline and reported negative effects of high concentration of sodium hypochlorite on the survival and differentiation of stem cells of the apical papilla (SCAP). They recommended the use of 1.5% sodium hypochlorite followed by 17% EDTA. Only 16 participants (66.7%), however, reported using 17% EDTA in their RET protocol. The use of EDTA following irrigation with sodium hypochlorite is now widely recommended.^{7–9} The effect of different combinations of irrigants on SCAP viability has been reported showing the best outcome, in terms of cell survival, when using 17% EDTA following the use of sodium hypochlorite. Therefore, the use of 1.5% sodium hypochlorite followed by 17% EDTA is currently the recommended irrigation protocol in RET and should be implemented.

The use of chlorhexidine as the sole disinfection irrigant was reported by a fifth of respondents, while another 8% reported using this in conjunction with other solutions such as sodium hypochlorite. The use of chlorhexidine has been shown to be toxic to the survival of SCAP cells.³³ Furthermore, chlorhexidine combined with either EDTA or NaOCl has been found to be antagonistic causing precipitations that increase the risk of tooth discoloration, as well as potential leaching of unidentified chemicals into the periradicular tissues³⁴ hence precluding the use of chlorhexidine as an irrigant in RET protocols.

Interestingly, a quarter of respondents did not induce bleeding nor use any other scaffold system in their RET protocol although the use of a scaffold system is recommended in all RET published studies. Although a blood clot is not biologically the best scaffold and possibly results in repair rather than regeneration, in the absence of other viable clinically available scaffolds, inducing bleeding into the root canal remains the easiest way in allowing stem cell population of the root canal system while orienting themselves in a three dimensional manner. Therefore, although a clot is not the best tissue engineering scaffold, this remains the most commonly used method.^{10,13,23,35}

Other types of scaffolds, reported in the literature, include the use of platelet rich plasma (PRP), which has been shown to result in similar outcomes to those reported with blood clots.^{12,36} This scaffold involves obtaining patient's intravenous blood,

therefore, requiring patient cooperation as well as additional equipment, such as a centrifuge machine, precluding its availability for routine chair-side treatment.

The use of MTA in creating a coronal seal has been reported as the most commonly used material in RETs. The use of this material is linked to crown discolouration as a result of MTA's bismuth oxide content. To circumvent this, other material including Portland cement has been shown to have similar properties to MTA with much less discolouration effect due to the lack of bismuth oxide³⁷ and currently being used in some RET protocols.¹³ Other recommended coronal seal materials include bioceramics or tricalcium silicate cements such as Biodentine.⁷

Several participants questioned the success of this technique in terms of root development and felt it was unpredictable. This was consistent with what is reported in the literature as although the predictability of periapical healing remains high,⁹ continuation of root development and thickening of dentinal walls, remain unpredictable.^{27,36,38,39}

Conclusions

This survey highlights a low uptake of RET by current UKPDS/T with several barriers identified. Deviations from the current evidence-based RET guidelines were identified. Recommendations addressing the management of immature non-vital teeth especially related to the use of RET in light of the findings of this survey were made as follows:

1. The prolonged use of calcium hydroxide in apexification techniques has been discouraged as a first line management technique in non-vital immature teeth^{8,9,13}
2. The use of MTA apical plug technique is currently considered the standard technique in managing non-vital immature teeth. However, MTA apical plug technique is not suitable in immature teeth with very short roots as such teeth have very compromised crown root ratios
3. Despite the unpredictability of RET outcomes especially in promoting continuation of root development and thickening of dentinal walls, this treatment modality is a viable option of management in teeth with wide open apices where MTA apical plug is judged to be unsuitable⁹
4. Several international guidelines have recently been published by AAE, ESE and EAPD in support of RET as one of the

viable management options of immature non-vital teeth. These guidelines should help clinicians gain institutional approval in their places of work, therefore, overcoming one of the barriers reported in this survey

5. The recent recommendation of using calcium hydroxide in root canal disinfection instead of antibiotic mixtures may help overcome the barrier of antibiotic availability, therefore facilitating a wider use of RET by UKPDS/T
6. The use of chlorhexidine as a root canal irrigant in current RET protocols is not recommended. Instead the use of 1.5% sodium hypochlorite followed by 17% EDTA is in line with current recommendations.
7. Although not the best tissue engineering scaffold, creation of a blood clot in the root canals remains the most commonly used method.^{10,13,23,35} The development of a scaffold system with specific signalling molecules targeted at promoting stem cell differentiation into the desired odontoblasts is currently ongoing⁴⁰
8. Creation of a UK national RET database similar to that established by the AAE is crucial in gathering data with regards to different RETs used, share best practices, and facilitating future research.

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Erratum

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In the original article one of the authors' names was given as 'A. Sarraf Shiraz'. The correct name is 'A. Sarraf Shirazi'.

The author information correctly reads as follows:

A. Bagherian and A. Sarraf Shirazi

We apologise for any confusion caused.