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THE EFFECT OF SMEAR LAYER REMOVAL ON ENDODONTIC OUTCOMES

by

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ABSTRACT

THE EFFECT OF SMEAR LAYER REMOVAL ON ENDODONTIC OUTCOMES

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Introduction: A double blinded randomized controlled clinical trial to assess the outcome of initial root canal therapy with or without smear layer removal.

Methods: Patients requiring initial non-surgical root canal treatment were eligible for enrollment. Consented subjects were randomly assigned into one of 2 groups differentiated by final irrigation protocol. All canals were prepared using a standardized instrumentation protocol and received a blinded irrigation of either 1ml/canal of 17% EDTA or 1ml/canal of 0.9% saline. Obturation was completed with zinc oxide eugenol sealer (Roth) using continuous wave compaction. A final radiograph was taken for use in the outcome assessment. Subjects were recalled after at least 12 months for clinical and radiographic evaluation. Radiographs were scored using a modified periapical index score of 1-5 by three board certified endodontists. Disagreement regarding the clinical outcome was resolved by forced consensus amongst the three evaluators. Chi-square and Fisher's exact tests ($\alpha < 0.05$) were used to perform all statistical comparisons of patient, treatment, and clinical characteristics by healed status at 12-months follow up.

Results: A recall rate of 81.2% was achieved for a total of 250 subjects included in the analysis. The overall percent healed was 68% (N = 82) for the saline group and 66% (N = 85) for the EDTA group with no significant differences between the 2 study groups ($p = 0.86$). The following variables were associated with lower percent healed regardless of canal irrigant utilized: Increased patient age ($p<0.04$), presence of a pre-operative sinus tract ($p=0.04$), pulpal necrosis ($p<0.01$), and pre-operative radiolucency ($p<0.001$).

Conclusions: Healing from nonsurgical endodontic treatment is not dependent on the use of EDTA and the theoretically removal of the smear layer. Increased patient age, presence of pre-operative sinus tract and/or periapical radiolucency, and/or a diagnosis of pulpal necrosis were all associated with lower percent healed.

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LIST OF ABBREVIATONS

EDTA	Ethylenediaminetetraacetic acid
mm	Millimeters
NPDS	Naval Postgraduate Dental School
NSRCT	Non-surgical root canal treatment
PAI	Periapical index

CHAPTER 1: Introduction

The primary objective of endodontic treatment is to eradicate bacteria, along with their byproducts and infected pulpal tissue, and to prevent them from re-entering the canal causing periradicular diseases.[1] The determination of root canal therapy success hinges on the resolution of a periapical lesion, as it indicates the eradication of infection and the resulting healing of any inflammatory changes in the surrounding bone.[2] Non-surgical root canal treatment (NSRCT) is a predictable procedure with a couple of studies indicating that successful outcomes were documented in 80-94% of cases.[3, 4] The high success rate of NSRCT has been attributed to chemo-mechanical removal of bacteria and infected tissue from within the root canals and prevention of reinfection with fluid tight seal. On the other hand, failed root canal treatments are often due to microorganisms that were not fully removed during the procedure.[5] Therefore, it appears to be of utmost importance to address the underlying cause as thoroughly as possible. However, mechanical instrumentation of the canal creates an amorphous, irregular mineralized collagen matrix layer called the smear layer.[6, 7] The creation of a smear layer during root canal therapy could pose a significant challenge to eliminating bacteria from the canal walls and within dentinal tubules.

The smear layer is primarily made of inorganic dentine but also consists of bacteria, organic residues, necrotic materials, and odontoblastic processes.[8] The thickness of the smear layer varies from 0.5 to 2 um, and it can create an obstacle in the tubules known as smear plugs by penetrating the dentin tubules up to a depth of 40um.[9] The complexity of this challenge is further compounded by anatomical factors, including ramifications, accessory canals, isthmuses, and fins, which hinder effective mechanical cleaning.[10] Therefore, root canal irrigation is necessary to address the residual bacterial biofilm from the inaccessible, un-instrumented surfaces.

Sodium hypochlorite (NaOCl) is an effective endodontic irrigant that can eliminate bacteria and biofilm as well as tissue.[11-13] Although NaOCl is useful for removing organic matter, it is inadequate in getting rid of the inorganic component and the accumulated hard tissue debris that resulted from the preparation process.[14, 15]

Ethylenediamine tetra-acetic acid (EDTA) is a calcium chelator that is commonly used and highly effective at removing the smear layer.[9, 16] Nygaard-Ostby introduced chelators to endodontics for the first time in 1957, suggesting the use of a 15% EDTA solution with a pH of 7.3.[17, 18] Future investigators evaluated the use of EDTA as an endodontic irrigant. Yamada et al. demonstrated that the combined application of 10 ml of 17% EDTA, followed by 10 ml of NaOCl effectively removes superficial debris and the smear layer.[14] Calt and Serper demonstrated that application of EDTA for 1 minute is effective in removing the smear layer.[19] Nevertheless, it is important to note that to prevent dentin erosion, the application of EDTA solution should not exceed 1 minute. [13] Additionally, Crumpton and Goodell revealed that utilizing only 1 mL of EDTA is equally as effective as using 10 mL of EDTA.[20]

The necessity of removing the smear layer is currently a subject of ongoing debate and controversy. Nonetheless, numerous in vitro studies have consistently demonstrated the advantages associated with the removal of the smear layer. According to multiple authors, removing the smear layer promotes heightened cleanliness and bolsters the adhesion between sealers and dentin tubules, resulting in reduced vulnerability to apical leakage. Smear layer may hinder the adaption of filling materials to the dentinal walls and decreases the capacity of irrigants and antimicrobial agents to penetrate the dentinal tubules.[8, 15, 21] Furthermore, the presence of the smear layer may serve as a barrier and a source of nutrients for residual bacteria following endodontic treatment.[22] This can facilitate the proliferation of bacteria and reinfection of the supposedly "cleaned" root canal, ultimately resulting in treatment failure.[22] According to Clark-Holke et al.'s research, bacteria leakage occurred after obturation when the smear layer was present, whereas removing the smear layer prevented any bacterial leakage through the apical foramen.[23] Additionally, Sharavan et al. demonstrated that removing the smear layer was the sole factor that resulted in significant improvement in apical seal.[24] Conversely, proponents of retaining the smear layer argue that it may provide a protective barrier against bacterial penetrating into the dentinal tubules and the use of chelating agent can cause harm by eroding the dentin and altering the microstructure of both the organic and inorganic components of dentin.[25-27]

Despite opposing views regarding the value of using canal irrigants to remove the smear layer, to this date, there has been no randomized clinical trial investigating the efficacy of irrigation protocol prior to obturation in permanent teeth of initial nonsurgical endodontic therapy. Multiple in vitro studies have shown that removing the smear layer would improve access of the irrigants into the dentinal tubules and reduce bacterial load.[6, 28, 29] However, there is a lack of in vivo trials directly discerning outcomes of smear layer removal. As a result, there is a need for well-designed randomized controlled clinical trial assessing the effect of smear layer removal on endodontic outcomes.

The primary purpose of this double-blind randomized controlled clinical trial was to evaluate the impact of smear layer removal on the healing status of endodontically treated teeth. Secondarily, the study analyzed the association between pre-endodontic treatment clinical variables and 12-month healing status regardless of smear layer treatment.

CHAPTER 2: Materials and methods

The methods and materials utilized in this study are detailed in Felming et al (2020). A brief summary is provided below.

Study subjects were recruited from the Endodontics Department at the Naval Postgraduate Dental School (NPDS), a military-centric dental treatment center that serves active duty military, their dependents, retired military, foreign military members and other categories of eligible beneficiaries. Inclusion criteria included 18 years or older, American Society of Anesthesiology classification I or II, an initial one-appointment non-surgical root canal therapy, and available to return for a 1-year follow-up examination. Exclusion criteria included a history of periodontal disease, previously initiated or treated root canal therapy, active antibiotic use, the presence of an acute apical abscess, allergies to any medication or dental material used in the study, and pregnant status.

Subjects were randomly assigned to one of two treatment groups (17% EDTA or 0.9% Saline). Orthograde and angled pre-operative periapical radiographs were exposed. Medical conditions, clinical symptoms, diagnostic and treatment data (see **Table A1:** Subject Characteristics Documented Pre-Treatment and at Follow-up) were collected using standardized data collection forms.

Regardless of treatment group, the following standardized treatment protocol was utilized. Subjects were anesthetized and the tooth to be treated was isolated with rubber dam and Oraseal® caulking adhesive (Ultradent Products, South Jordan, UT). Straight-line access was established using #2 round or #557 carbide burs (Henry Schein, Melville, NY) and EndoZ burs (Dentsply Sirona, Tulsa, OK). Coronal flaring was created using #2, #3, and #4 Gates Glidden drills (SybronEndo Corporation, Orange, CA). Canal working lengths were established using a Root ZX® (J Morita, Irvine, CA) and confirmed radiographically. A glide path was created using 0.02 taper #10, #15, #20 FlexoFile® (Dentsply Sirona, Tulsa, OK) stainless steel files to working length. The canals were cleaned and shaped with 0.04 Vortex Blue™ (Dentsply Sirona, Tulsa, OK) rotary files using a crown down technique to at least a master apical file size #35 with .04 taper. Recapitulation was performed with 0.02 taper #10 Flex-O-Files to working length and irrigated with 8.25% NaOCl delivered from a 30-gauge side vented irrigation tip between all file sizes for a total intraoperative irrigation volume not exceeding 2 ml. Canals were dried with sterile paper points (Henry Schein, Melville, NY).

Study providers were given blinded final irrigation solutions, containing 17% EDTA or 0.9% saline and delivered 1 ml of the irrigant 1 mm short of working length over 1 minute per canal. Post-irrigation identical treatment for all subjects resumed.

A final rinse of 3 ml of 8.25% NaOCl per canal was performed and the canals were dried with sterile paper points (Henry Schein, Melville, NY). A System B® (Kerr Corporation, Brea, CA) plugger that bound within the canal 5-7 mm short of working length was selected. Working length was confirmed using a 0.04 taper master gutta percha cone (Diadent, Burnaby, BC, Canada). Roth 801 sealer (Roth International LTD, Chicago, IL) was delivered into the canal and the walls coated. The master cone was seated to working length and the canal was obturated with gutta percha using a continuous wave technique. The canal was backfilled using a thermoplasticized backfill technique. Alcohol-soaked cotton pellets were used to clean the chamber prior to temporizing the access with a sterile cotton pellet and Fuji Triage® (GC America Inc., Alsip, IL) or Cavit™ Temporary Filling Material (3M ESPE Dental, St Paul, MN). A post-operative radiograph was exposed using an XCP® (Dentsply Rinn, York, PA) device with Blu-Mousse® (Parkell Inc., Edgewood, NY) bite registration material in order to reproduce the vertical and horizontal angles of the original radiograph at the one-year follow-up appointment. Subjects were instructed to return to their referring dentist for the permanent restoration.

A follow-up examination was conducted no sooner than 12 months. Providers reviewed health histories and recorded clinical data including results from diagnostic testing on standardized follow-up data collection forms. A follow-up periapical radiograph was taken using the positioning device created during the treatment appointment.

All radiographs were assessed using a modified periapical index (PAI) scoring technique, described by Ørstavik[30]. PAI scoring was conducted by three calibrated, board-certified endodontists. Coronal restorations of the immediate post-operative radiograph and the 1-year follow-up radiograph were masked to eliminate reviewer bias. Radiographs were coded, randomized, individually projected onto a screen in a dark room, and scored by board-certified endodontists. In instances of disagreement, a forced consensus was completed.

Outcomes assessment. Data from the treatment and follow-up exam were utilized to determine the endodontic outcome. Subjects that were classified as “Healed” were defined as asymptomatic with a PAI score of 1 or 2, at the time of follow-up, while “non-healed” subjects were defined as either symptomatic with a PAI score of 3, 4, or 5. A power analysis accounting for an 80% healed at 12 months indicated an initial sample size of 440 subjects (220 per study wing) was required to demonstrate statistical differences in clinical outcomes. However, an interim analysis, conducted after enrolling 362 subjects, indicated that additional recruitment would not alter study results and the study was closed for future enrollment. Chi-square and Fisher's exact tests ($\alpha < 0.05$) were used to perform all statistical comparisons of patient, treatment, and clinical characteristics by healed status at follow up. R v4.0.2 software was used for statistical analysis.

The Institutional Review Board (IRB) at the Walter Reed National Military Medical Center (WRNMMC), Bethesda, Maryland, approved this study for human subject research.

CHAPTER 3: Results

A total of 362 subjects were enrolled in the study with 81.2% (N = 294) completing a 12-month follow-up appointment. Data from 44 subjects were excluded due to various reasons such as extraction of endodontically treatment tooth or protocol deviation, leaving a total of 250 subjects for data analysis.

The proportion of teeth considered healed by 12 months was 68% (N = 82) for cases treated with 0.9% saline irrigation and 66% (N = 85) for cases treated with EDTA irrigation (**Figure 1**). The overall percent healed was 67% (N = 167), and there was no significant difference in healed status between the teeth treated with saline or EDTA (p=0.86).

Irrespective of irrigant (EDTA or saline) status, the following variables were significantly associated with our results: pulpal status, presence of pre-operative radiolucency, presence of pre-operative sinus tract, and subject age. (**Table 1**) Teeth with pulpal necrosis had a significantly lower percent healed of 57% (N = 66) compared to teeth with vital pulps at 75% (N = 101) (p=0.01). Teeth with a pre-operative radiolucency had a significantly lower percent healed of 55% (N = 69) compared to teeth without pre-operative radiolucency at 78% (N = 98) (p<0.001). Additionally, teeth without a pre-operative sinus tract had a higher percent healed of 68% (N = 162) compared to teeth with a pre-operative sinus tract at 39% (N = 5) (p<0.04).

CHAPTER 4: Discussion

This study was the first double-blinded prospective randomized clinical trial assessing the impact of smear layer removal using EDTA on healing status post endodontic treatment. Results indicated that removal of the smear layer was not associated with an increased probability of healing post-NSRCT. Success, defined as healing, was similar between intervention groups with 66% and 68% of NSRCT with and without EDTA determined to be successful, respectively.

One of the limitations of our study that contributed to the results was the utilization of a relatively short and a single follow-up starting at 12 months post treatment. Orstavik reported that 90% of teeth that will heal, will show signs of healing at the 12 month mark.[31] However, multiple studies have shown that certain cases can take up to four years or longer to demonstrate complete healing. [31, 32] Additionally, our study used strict criteria to assess success, categorizing as either "healed" or non-healed" only. "Healing" lesions were all considered "non-healed" which would result in a reduced overall percent healed compared to other published studies that used non-strict criteria.[3] Similarly, Orstavik et al revealed that only 51% of patients who underwent initial endodontic therapy and had a preoperative PAI score of 4 or 5 for their periapical lesions showed signs of healing after a year. Upon incorporation of the "healing" category, the success rate of the procedure was elevated to 88%, demonstrating noteworthy similarity with prior investigations that exhibited strict inclusion criteria with a follow up for at least one year.[33] The reported success rates in these earlier studies ranged between 68% and 85%, a range consistent with the outcome observed in the present study.[34]

The evaluation of preoperative lesion size was not performed in the present study. A review article by Ng et al. indicates that larger lesions are linked to decreased success rates.[3] This could be attributed to the fact that larger lesions are often indicative of longer-standing infections that have larger and more diverse microbial population, deeper invasion of dentinal tubules, stronger biofilm, formation of extra-radicular infection, or cystic transformation. [35-38] The distinct analysis of teeth with lesion sizes larger than 5mm and those smaller than 5mm could have influenced the results.

In accordance with the PAI protocol, only one immediate post-operative radiograph and one follow-up radiograph were considered eligible for evaluation. Therefore, the absence of radiographs taken from various angles posed a limitation in terms of diagnostic accuracy, particularly for teeth with multiple roots.[39] To further enhance diagnostic precision, the utilization of CBCT imaging could be beneficial. In support of this, a study by Von Arx et al. reported that nearly one-third of cases had less healing on CBCT imaging compared to periapical radiography at the one-year follow-up.[40] This combination of factors could have affected the results in the present study.

The standardization of specimens for in vivo experiments is a highly challenging and often infeasible task. To address this challenge, it is crucial to closely analyze various factors to assess their statistical impact on endodontic outcomes. In the present study, lower percent healed were associated with the following four factors: increased age, pre-operative apical radiolucency, presence of a sinus tract, and teeth with necrotic pulp. Kojima et al. in their meta-analysis on success of endodontic treatment on vital and necrotic teeth demonstrated pooled success proportions of 82.8% and 78.9%, respectively, with significant statistical difference in outcome.[41] Likewise, Ng et al. in

2008 reported that teeth with necrotic pulps and periapical lesions exhibited significantly lower success rates than those with vital pulps.[42] Moreover, in 2011 Ng et al. conducted a prospective study and they identified that the presence of a sinus tract was identified as a negative prognostic indicator for tooth survival following non-surgical root canal therapy.[3] While no significant intergroup differences were detected across various age cohorts, Ng et al. noted a declining trend in pooled success rates with increasing age.[42]

The impact of comorbidities on successful healing was highlighted in this study, with diabetes and hypertension emerging as key variables influencing healing success. These results are commiserate with a previous study by Saleh and colleagues that reported that diabetic patients had a nearly three-fold greater incidence of periapical lesions than their nondiabetic counterparts.[43]

Although the removal of smear layer has been shown to enhance chemical disinfection in *in vitro* studies, it did not result in improved clinical outcomes in this study. A possible explanation for this finding is supported by Peters et al., who found no significant differences in healing outcomes when small numbers of bacteria were cultured or not cultured during obturation.[44] Additionally, the use of 8.25% sodium hypochlorite in our study may have been effective enough in reducing the bioload to minimal levels, thus diminishing the additional need for smear layer removal.[13, 45] Furthermore, mechanical disinfection techniques, rotary instrumentation to minimum of size 35/04 in all cases, employed in this study may have adequately disrupted the biofilm and removed infected dentin, making smear layer removal unnecessary.[46] Moreover, it has been observed in several articles that it is virtually impossible to touch all canal surfaces with current rotary instruments, suggesting that smear layer formation may not be significant in cases with wide or oval-shaped canal anatomy.[47, 48] Collectively these findings may suggest that the removal of smear layer may not hold significant clinical meaning in certain clinical scenarios. Further research is needed to fully understand the role and significance of smear layer removal in endodontic treatment.

CHAPTER 5: Conclusions

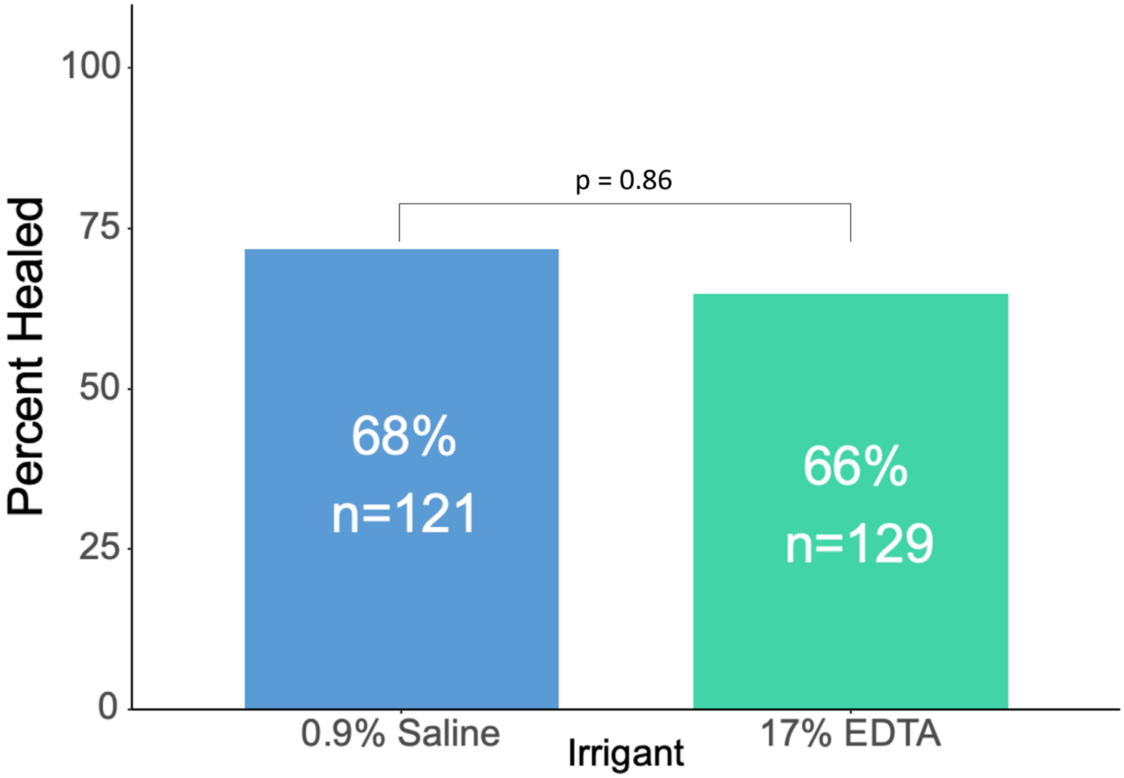
Results from this study indicated that there was no difference in healing outcomes between treatment groups. Healing from nonsurgical endodontic treatment was not dependent on the use of EDTA and the removal of the smear layer. Additionally, increased patient age, presence of pre-operative sinus tract and/or periapical radiolucency, and/or a diagnosis of pulpal necrosis were all associated with lower healing proportions.

Table 1. Pre-treatment Subject Characteristics by Healed Status.

Variables	Healed (N=167)	Non-healed (N=83)	P-value
PATIENT AGE:			
18-35 Years Old	52 (78.8%)	14 (21.2%)	0.036
36-65 Years Old	96 (64.0%)	54 (36.0%)	
>65 Years Old	19 (55.9%)	15 (44.1%)	
SEX:			
Male	123 (68.3%)	57 (31.7%)	0.58
Female	44 (62.9%)	26 (37.1%)	
TOOTH TYPE:			
Single root	76 (71.7%)	30 (28.3%)	0.202
Multiple root	91 (63.2%)	53 (36.8%)	
HYPERTENSION:			
No	133 (70.4%)	56 (29.6%)	0.051
Yes	34 (55.7%)	27 (44.3%)	
DIABETES:			
No	157 (68.6%)	72 (31.4%)	0.088
Yes	10 (47.6%)	11 (52.4%)	
PRE-OP SINUS TRACT:			
No	162 (68.4%)	75 (31.6%)	0.035
Yes	5 (38.5%)	8 (61.5%)	
PRE-OP COLD SENSITIVITY:			
NR	69 (57.0%)	52 (43.0%)	0.006
R/NL	45 (73.8%)	16 (26.2%)	
R/L	53 (77.9%)	15 (22.1%)	
PRE-OP RADIOLUCENCY:			
No	98 (78.4%)	27 (21.6%)	<0.001
Yes	69 (55.2%)	56 (44.8%)	
OVEREXTENSION OF ROOT FILLING:			
No	164 (68.3%)	76 (31.7%)	0.026
Yes	3 (30.0%)	7 (70.0%)	

*Data from the 17% EDTA and 0.9% saline groups were pooled to assess the influence of variables on healing.
*P-values obtained from Chi-square analysis or Fisher's exact tests.

Figure 1. Comparison of the Irrigation Protocols on Percent healed.



Bar graph showing the number of subjects and the percent healed for the two irrigation protocols. The protocol using 0.9% saline did not remove the smear layer, while the protocol using 17% EDTA did remove the smear layer. The percent healed did not statistically differ between the groups ($p = 0.86$).

APPENDIX

Table A1. Subject Characteristics Documented Pre-Treatment and at Follow-up**.**

Sex	Pre-op/Post-op swelling	Presence of pre-op radiolucency
Age	History of ortho treatment	Pre-op pulpal diagnosis
Tooth position	History of external resorption	Pre-op apical diagnosis
Tooth type	History of bleaching	Patency
Pre-op/Post-op diabetes	History of internal resorption	Procedural complications
Pre-op/Post-op hypertension	Pre-op/Post-op caries	Intra-orifice barrier
Pre-op/Post-op smoker	Pre-op/Post-op cold sensitivity	Obturation fill length
Pre-op/Post-op coronary heart disease	Pre-op/Post-op mobility	Post-treatment apical diagnosis
Pre-op/Post-op pain	Pre-op/Post-op bleeding on probing	Post-treatment pulpal diagnosis
Pre-op/Post-op EPT response	Pre-op/Post-op restoration	Time elapsed between initial treatment and permanent restoration
Pre-op/Post-op palpation	Pre-op/Post-op probing depths	Presence of post-op intracanal post
Pre-op/Post-op percussion	Pre-op/Post-op open margin	Follow-up apical diagnosis
Pre-op/Post-op sinus tract	Pre-op/Post-op lamina dura	

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