2023

Impact of portal of exit on the prevalence of apical periodontitis in root canal treated maxillary molars with missed second mesiobuccal canals: A CBCT Study

Jing Ye
Virginia Commonwealth University

Impact of portal of exit on the prevalence of apical periodontitis in root canal treated maxillary molars with missed second mesiobuccal canals: A CBCT Study

A thesis submitted in partial fulfillment of the requirements for the degree of Master of Science in Dentistry at Virginia Commonwealth University.

By

Jing Ye, D.M.D.

B.A., Drexel University, 2014

D.M.D., University of Pennsylvania School of Dental Medicine, 2018

Thesis advisor: Amber Ather, D.D.S., M.S.

Department of Endodontics

Virginia Commonwealth University

Richmond, Virginia

May, 2023

Acknowledgements

First, I would like to thank my thesis committee members Dr. Ather, Dr. Myers, Dr. Carrico, Dr. Andrada, and Dr. Jadhav for their guidance in developing and advancing this thesis project. I am deeply grateful for Dr. Myers, my program director for his mentorship throughout residency and for taking a chance on me from the start.

Secondly, I would like to thank Dr. Tim Finkler and the Commonwealth Endodontics Group for their assistance in this project.

Thirdly, I would like to thank Dr. James DeGracie, Dr. Colton Fischer, and Dr. Joseph Vaughn for their friendship through this chapter of our lives.

Fourthly, I owe everything to my family. My parents - for never-ending love and support toward my dream to become a specialist in endodontics. My sister, brother-in-law, niece, and nephew – for monthly re-fuels of food and heart-warming family time. My husband, Dr. Henry Ma - for being my biggest cheerleader and comedian.

Lastly, this project was supported by the AAE Foundation Resident Research Grant to Jing Ye.

There are no conflicts of interest related to this study.

Table of Contents

List of Tables

List of Figures

Abstract

IMPACT OF PORTAL OF EXIT ON THE PREVALENCE OF APICAL PERIODONTITIS IN ROOT CANAL TREATED MAXILLARY MOLARS WITH MISSED SECOND MESIOBUCCAL CANALS: A CBCT STUDY

By: Jing Ye, D.M.D.

A thesis submitted in partial fulfillment of the requirements for the degree of Master of Science in Dentistry at Virginia Commonwealth University.

Virginia Commonwealth University, 2023

Thesis Advisor: Amber Ather, D.D.S., M.S.

Department of Endodontics

Objective: To evaluate the association of portal of exit (POE) of the second mesiobuccal (MB2) canal with the prevalence of apical periodontitis (AP) in previously treated maxillary molars

Methods: Cone beam computed tomography (CBCT) scans of 106 previously treated maxillary molars seen for either recall or retreatment in the past 3 years were included in the study. Scans were reviewed by one endodontic resident and one board-certified endodontist to determine the POE (separate versus common) of the missed MB2 canal and the presence or absence of a periapical hypo-dense area. Association between AP and portal of exit was assessed using Fisher's exact test. Significance level was set at 0.05

Results: 106 cases with a missed canal were evaluated. Among the 99 cases with apical periodontits, the prevalence of separate POEs was 84% in comparison to 16% for common POE (p-value<0.0001). In teeth with a missed MB2 with separate POE, there was a 94% prevalence of apical periodontitis, in contrast to 89% in teeth with a common POE, with no statistical significance. Teeth with a separate POE were associated with 2.08x the odds of apical periodontitis than those with common canals (95% CI:[0.37-11.65])

Conclusion: A separate portal of exit of MB2 constituted the bulk of cases included in the study. Even though there was a slightly higher prevalence of PARL for separate POEs in comparison to teeth with a common POE, the difference was not statistically significant. Substantial efforts must be directed towards locating and debriding the MB2 canal, irrespective of the portal of exit.

Introduction

The goal of endodontic therapy is to resolve pulpal disease, with or without periradicular involvement, through complete chemomechanical preparation and obturation of the root canal space. Irrespective of the pulp vitality status, the prognosis of root canal treatment depends on the reduction of microbial counts to a level that is physiologically conducive to healing and subsequent prevention of bacterial invasion. Clinical endodontic success can be measured in two ways: 1. Patient based outcomes, which is the resolution of symptoms and the ability to function with the treated tooth. 2. Clinician based outcomes, which is a combination of patient based outcomes and the resolution of signs of disease - such as radiographic evidence of periapical healing. Success rates of endodontic therapy have sustained a high level of predictability, ranging between 82-93%. Over the past several decades, there have been multiple technological and material science-related advancements in the specialty of endodontics (1 , 2, 3). However, the anticipated translation to superior outcomes have not been observed yet, leaving a small proportion of endodontic cases to fail.

Cases which do not respond to endodontic treatment stem from a myriad of reasons: inadequate instrumentation, debridement, or obturation, iatrogenic errors, fractures, and leaking restorations, complex anatomy, and missed canals, to name a few (4, 5). All the above mentioned reasons for post endodontic disease have one thing in common i.e., an opportunity for bacteria to persist or invade the root canal system. This in turn can lead to inflammation of the periapical tissues, also known as apical periodontitis (5, 6). According to a meta-analysis, approximately half of the adult population worldwide have at least one tooth with apical periodontitis. The frequency of apical periodontitis is 3% in non-treated teeth in contrast to 39% in previously treated teeth (7). Post treatment persistent apical periodontitis is often detected by radiographs as a periapical radiolucency in 85% of cases, or in the form of the patient's chief complaint such as pain, present in approximately 50% of the cases (8). Amongst the several causes for post treatment apical periodontitis, a missed canal is presumed to be one of the most common. Interestingly, in a few studies evaluating previously treated teeth, 52-86% of teeth wherein all the canals were located and treated still had signs of apical periodontitis. This demonstrates the multivariate effect that other biological and iatrogenic factors can have on the success of root canal treatment and that locating all canals successfully is only one piece of the puzzle. This, however, does not deny the importance of the undebrided root canal space. Root morphology and anatomical variations still present a technical challenge to clinicians and may result in decreased successful outcomes of root canal treatment. Failure to identify the extra canal, or ability to identify but unable to debride the canal fully, leaves a vulnerable space which can harbor microbes and lead to apical periodontitis (9).

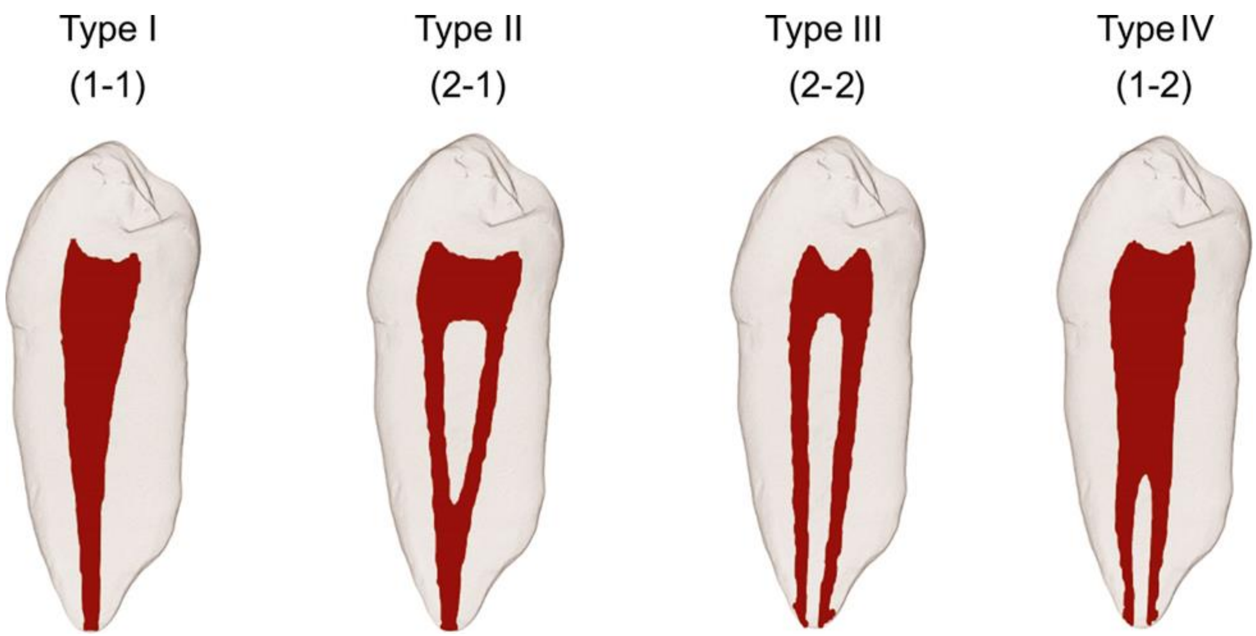
The prevalence of a missed canal in previously endodontically treated teeth ranges between 12-42% (10, 8). The prevalence is lower in incisors and canines (< 1%) and can be as high as 40-59% in maxillary molars (8, 11). The most common cause of endodontic failure for maxillary molars has been reported to be an untreated root canal space (12). Interestingly, the most frequently missed canal in endodontics is located in the most notoriously studied root of our field, the mesiobuccal root of the maxillary molar. Apart from the main mesiobuccal canal, there is often an additional canal located in the palatal portion of the MB root - named the mesiolingual canal, mesiopalatal canal, mesiobuccal 2 canal, or simply, MB2 canal. In 1969, Weine studied the canal configuration of the mesiobuccal root of the maxillary first molar and concluded that the MB2 canal was present in approximately 50% of the cases. The reported prevalence of MB2 canal is 50-90% in maxillary first molars and 30-50% in maxillary second molars (13, 14, 15, 16, 17). With heightened awareness of root canal morphology and improved techniques to detect MB2 canals, along with increased microscope usage in endodontic treatment, the consensus has evolved to assume that the majority of maxillary molars have four canals.

Locating and debriding the MB2 root canal space in initial root canal treatment is critical, but is oftentimes limited both by the experience of the clinician and the accessibility to the complex path of the MB2 canal. In a study conducted by Wolcott et al, the prevalence of the MB2 canal was found to be 6% higher in endodontic retreatments compared to initial root canal treatments (18). On evaluating maxillary molars referred for nonsurgical retreatment, the mesiobuccal root of the maxillary first molar and second molar had a missed canal in 62.8% and 49% of the studied cases, respectively (9). These findings are consistent with a study by Karabucak et al, wherein the MB2 canal was the most frequently missed canal (65%) in maxillary molars (11). When evaluating specifically the mesiobuccal root, the MB2 canal is missed with a significantly higher frequency at 93% when compared to the MB1 canal (10).

The impact of a missed MB2 canal has been found to be significantly related to the development or persistence of apical periodontitis. The virulence of the bacterial reservoir within the missed canal may be dependent on multiple factors. 1) Pre-operative canal status (i.e. vital or necrotic pulp) 2) Quality of chemomechanical debridement and obturation 3) Status of adjacent palatal, distobuccal and main mesiobuccal canals. Despite adequate treatment of surrounding canal spaces, an untreated MB2 space undoubtedly still remains a vulnerable space for microbial invasion or persistence. This persistence may eventually lead to inflammation of the peri-radicular tissues, in which a periapical lesion may form. Studies have demonstrated that a periapical lesion present on a previously treated multi-rooted tooth is usually associated with the root containing an untreated canal (10, 11). In the maxillary first molars, 75% of the missed MB2 cases were associated with a periapical lesion. In the maxillary second molars, 68% of the missed MB2 cases were associated with a periapical lesion. Mesiobuccal roots with a missed MB2 presented with 3.1 higher odds of being associated with periapical pathology than mesiobuccal roots of teeth with all canals identified and filled (9).

Given the high prevalence of apical periodontitis associated with a missed MB2 canal, endodontists have strived to improve the detection and instrumentation of MB2 canals. Better visualization with microscope use, allotment of sufficient clinical time, and implementation of tools for micro-endodontics have significantly increased the detection of MB2 (19). However, detection of the MB2 orifice does not guarantee instrumentation of the entire canal space due to anatomical complexities of the MB2 canal (13). In 39-50% of the cases, the MB root has a Weine class III configuration, wherein the MB2 has its own portal of exit (Figure 1).The presence of a separate exit increases the risk of an untreated canal by 3.03 times (20). Fortunately, approximately 50-60% of the time, the MB root demonstrates a Weine class II configuration, wherein MB1 and MB2 merge into a single portal of exit (13, 17, 20, 21). Based on anecdotal evidence, a missed MB2 canal which joins with MB1 is less likely to affect outcomes as long as MB1 is optimally treated.

Figure 1: Weine classification for root canal configuration (22).



In order to assess the complex morphology of the mesiobuccal root pre-operatively, one of the best clinical tools in endodontics is radiographic imaging. Two dimensional periapical radiographs (PA) have been the main imaging tool for the last several decades. More recently, cone-beam computed tomography (CBCT) has become a critical tool in assessing root morphology and locating missed canals. A limited field of view (FOV) CBCT is recommended by the American Association of Endodontics (AAE) as a supplemental diagnostic tool due to its higher sensitivity in detecting periapical lesions and complex anatomy (23, 24). CBCT has the capability to visualize the canal anatomy in three dimensions - axial, sagittal, and coronal views. As a result, the clinician is able to visualize a missed MB2 canal along with its portal of exit and the location of the recurrent periapical lesion around the apex. Although significantly more MB2 canals have been located when a pre-operative CBCT image was available (25), there has not been an updated CBCT analysis of the entire MB2 canal configuration and its influence on success in root canal treatment.

The aim of this paper is to determine the association of the portal of exit of the MB2 canal in previously treated maxillary molars with apical periodontitis utilizing limited FOV CBCT scans. The null hypothesis is that the missed MB2 canal with a separate POE is not associated with increased prevalence of apical periodontitis when compared to a MB2 canal that merges with the MB1 canal to a common POE.

Methods

This was a retrospective cohort dental chart review study that was approved by the institutional review board (VCU IRB #: HM20024136). Patients with previously treated maxillary molars with a missed second mesiobuccal canal presented to the Graduate Endodontic Practice at Virginia Commonwealth University School of Dentistry (VCU SOD) and a private endodontics practice (Commonwealth Endodontics - CWE) for evaluation for retreatment between July 2020-Feb 2022 (CWE) and January 2021-January 2023 (VCU SOD) were used for this study.

A review of charts was made utilizing a combination of various keywords such as "endodontic failure", "retreatment", "NSRETX", "previously treated", "apical periodontitis" "periapical lesion", "CBCT", "MB2", and "missed canal" were used to locate the patient chart and CBCT file. CBCT image sets were taken for patients who returned for an evaluation for retreatment and/or endodontic microsurgery due to persistent apical periodontitis. Since the CBCT scan was taken prior to conducting the study, the clinical protocol for obtaining a CBCT scan was not altered for the purpose of this study. This yielded a total of 170 charts subject to screening through the inclusion and exclusion criteria listed below.

Inclusion criteria:

- Patients over 18 years old

- Previously treated permanent 1st and 2nd maxillary molars with a missed MB2 canal (defined as an area of low density within mesiolingual portion of the MB root with no evidence of filling material or with filling material exclusively in the cervical third)
- Pre-operative limited field of view cone beam computed tomography scan
- Presence or absence of symptoms of pain, swelling, pain to biting and/or presence of a sinus tract
- Presence or absence of a periapical radiolucency around the MB root
- Obturation quality within 2mm from radiographic apex of the MB root

Exclusion criteria included:

- CBCT scan with artifacts such as scatter and/or beam hardening which rendered the scan not amenable for interpretation
- Prior root resection/apicoectomy surgery
- Evidence of any procedural mishaps such as instrument separations and perforations
- Presence of a post in any canal
- Root resorption
- Root fracture
- Obturation with silver points or carriers (Thermafil and/or Guttacore)
- Lack of well sealed restoration

After selecting the cases that met the inclusion criteria, the corresponding CBCT images were de-identified. A total of 106 cases were included in this study. All CBCT scans were taken with the Carestream 8100 system (Carestream Health; Rochester, HY) at the Graduate

Endodontic Practice at VCU SOD and Morita Veraviewepocs 3D R100 (J Morita; Tokyo, Japan) at Commonwealth Endodontics. All CBCT images were taken using a limited field of view (5 x 5 cm) and a voxel size of 0.075mm. Operating parameters were set at 2-10mA, 60-90 kV, and 12 seconds. Scans were processed on the software provided with the corresponding CBCT unit and viewed in a clinical environment using a Dell Optiplex 990 computer (Dell SA, Geneva, Switzerland), 24 inch monitor (resolution 1920 x 1200 at 60 Hz) provided by the practice location.

Patients' charts were initially reviewed by the primary investigator to gather information. All axial, sagittal, and coronal slices of the scan were screened to confirm that the chart met the inclusion criteria. Each de-identified case had three axial screenshots and two coronal screenshots of the mesiobuccal root. Axial, sagittal and coronal views of the mesiobuccal root were aligned parallel to the long axis of the root (from the apex to the canal orifice) and centered mesially and distally. The first, second, and third axial slices were obtained 1mm, 3mm, and 5mm from the radiographic apex, respectively. If the mesiobuccal root was curved, multiplanar reconstruction was used (26). The first coronal slice was lined up along the long axis of root coronal to curve, and the second coronal slice was lined up with the long axis of the root apical to the curve. A periradicular area of low density was determined when disruption of the lamina dura was detected and the area was at least twice the width of the periodontal ligament space (11).

The screenshots were exported as a .png file, inserted onto a PowerPoint slide (Microsoft; Redmond, WA) and arranged by de-identified case number and the corresponding tooth number. The PowerPoint slides were then evaluated by a final year endodontic resident and a board-certified endodontist. Both evaluators had full access to each software to manipulate the

CBCT scans for viewing when doubts were present. The study was conducted in two phases. The first phase, which was the pilot study utilized for calibration, consisted of 32 CBCT's of previously treated maxillary molars with a missed MB2 canal. The aim of the pilot study was to evaluate the feasibility of the study, clarity of the scans, and assessment procedures to identify if any modifications would be needed in the design of the main study. From the pilot study, the prevalence of separate POE with apical periodontitis was 86% and 14% for common POE with apical periodontitis. The two examiners were calibrated prior to evaluating the patient records that met the inclusion criteria. The de-identified CBCT axial and coronal slices of the mesiobuccal root were presented to the two examiners. Both examiners had ample time to evaluate the provided images of 32 cases carefully and determine whether the missed MB2 had a separate portal of exit, or a common portal of exit with the MB1 canal and whether there was a presence of a periapical radiolucency. Shortly after, the second phase consisted of the examiners evaluating a total of 106 cases with their corresponding CBCT scans. The two evaluators independently arrived at a conclusion for the portal of exit of the missed second mesiobuccal canal and the presence of apical periodontitis, based on the provided CBCT scans.

In addition to imaging, consultation notes were reviewed for presence of signs and symptoms, time since initial treatment, and the qualification of the original provider. Presence of persistent signs and symptoms, such as percussion sensitivity, palpation sensitivity, presence of a sinus tract, or biting pain were gathered from the dental chart. Information regarding the age of the root canal treatment and the qualification of the original provider was based on the dental history. The information was collected on a Microsoft Excel spreadsheet and organized by the deidentified chart number.

Associations between apical periodontitis (as defined by presence of periapical radiolucency) and various case characteristics (portal of exit, gender, tooth type, presence of symptoms) were assessed using Fisher's exact test. The association between portal of exit and various case characteristics (gender, tooth type, and presence of symptoms) were also assessed using Fisher's exact test. The association between patient age and apical periodontitis was assessed using t-test. SAS EG v.8.2 (SAS Institute, Cary, NC) was used for all analyses. Significance level was set at 0.05.

Results

Data from 106 previously treated maxillary molars was included in the analysis. The majority of cases were female patients (68%), first molars (88%), and presented with signs and symptoms (77%) (Table 1). The average patient age was 50.8 years old (standard deviation = 16.6). Additionally, 99 of the included cases had evidence of apical periodontitis with a prevalence of 93%. A separate portal of exit (POE) was demonstrated in 83% of the cases and a common POE in the remaining 17% of cases.

Table 1: Characteristics of cases included

	n	%
Gender		
Female	72	68%
Male	34	32%
Molar		
First	93	88%
Second	13	12%
Signs and Symptoms		
No	24	23%
Yes	82	77%

PARL		
Yes	99	93%
No	7	7%
Portal of Exit		
Separate	88	83%
Common	18	17%

Figure 2: Distribution of portal of exit for cases with and without evidence of apical periodontitis

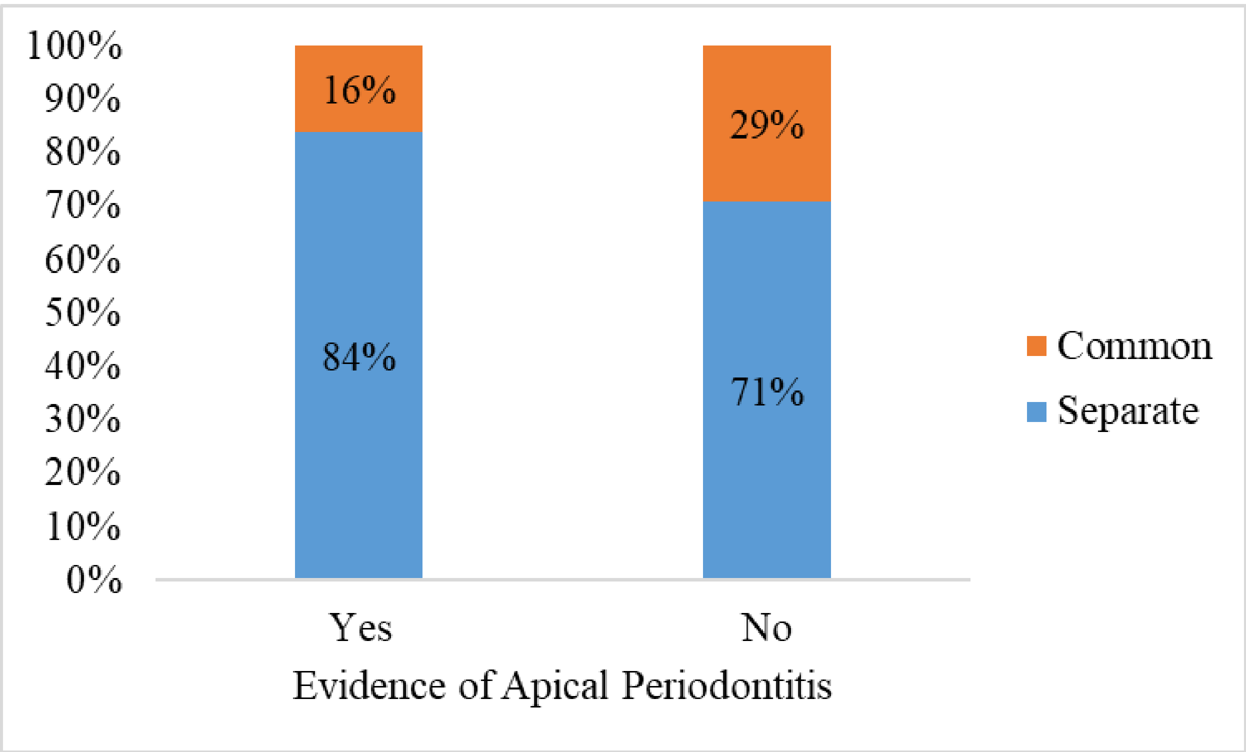
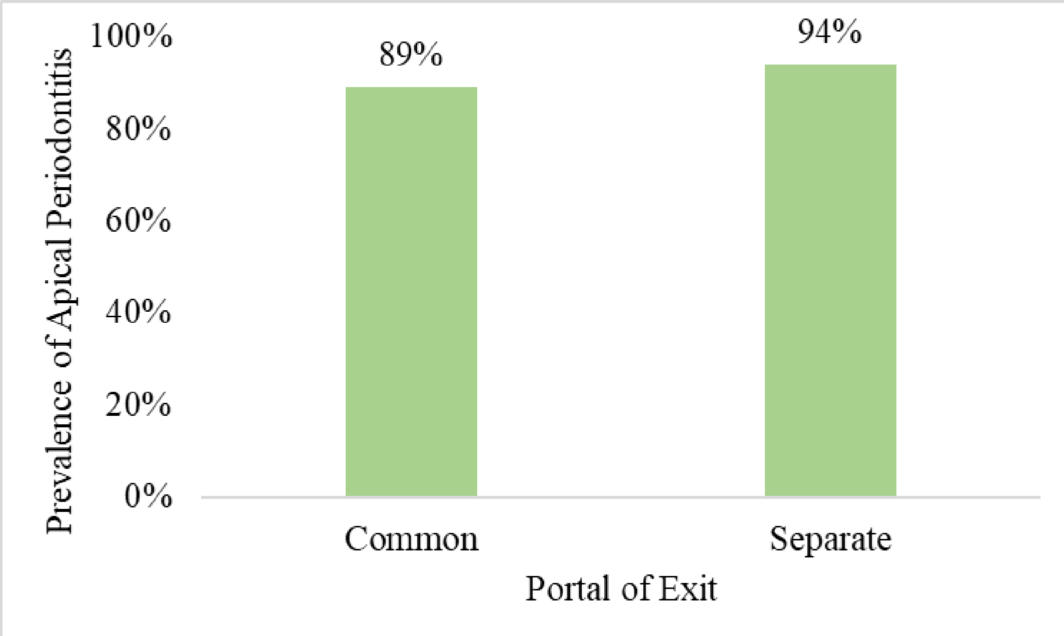


Figure 3: Relationship between apical periodontitis and portal of exit



The average age for patients with apical periodontitis was 50.9 years (SD=16.2) compared to 48.6 years (SD=23.1) for those without evidence of apical periodontitis (p-value=0.7166). There was a marginally significant association between patient gender and apical periodontitis (p-value=0.0938). All 34 cases with male patients had evidence of apical periodontitis and only 90% of the 72 female patients had AP. For cases with apical periodontitis, the prevalence of a separate POE was 84% of cases compared to 16% for a common POE (Figure 2). The prevalence of a separate POE was significantly higher than a common POE for cases with apical periodontitis (p-value<0.0001). When MB2 had a separate POE, there was a 94% prevalence of apical periodontitis. When MB2 had a common POE with MB1, there was an 89% prevalence of apical periodontitis (Figure 3). Teeth with separate POE were associated with 2.08 times the odds of apical periodontitis when compared to teeth with common canals (OR: 2.08; 95% CI:[0.37-11.65]). Although there was a slightly higher prevalence of apical periodontitis for separate POEs, the difference was not statistically significant (p-value=0.3392).

The only variable significantly associated with apical periodontitis was the presence of signs and symptoms. Amongst the 82 patients reporting signs and symptoms, 98% had evidence of apical periodontitis, in contrast to 79% of the 24 asymptomatic patients (p-value=0.0063).

Table 2: Relationship between apical periodontitis and characteristics of cases

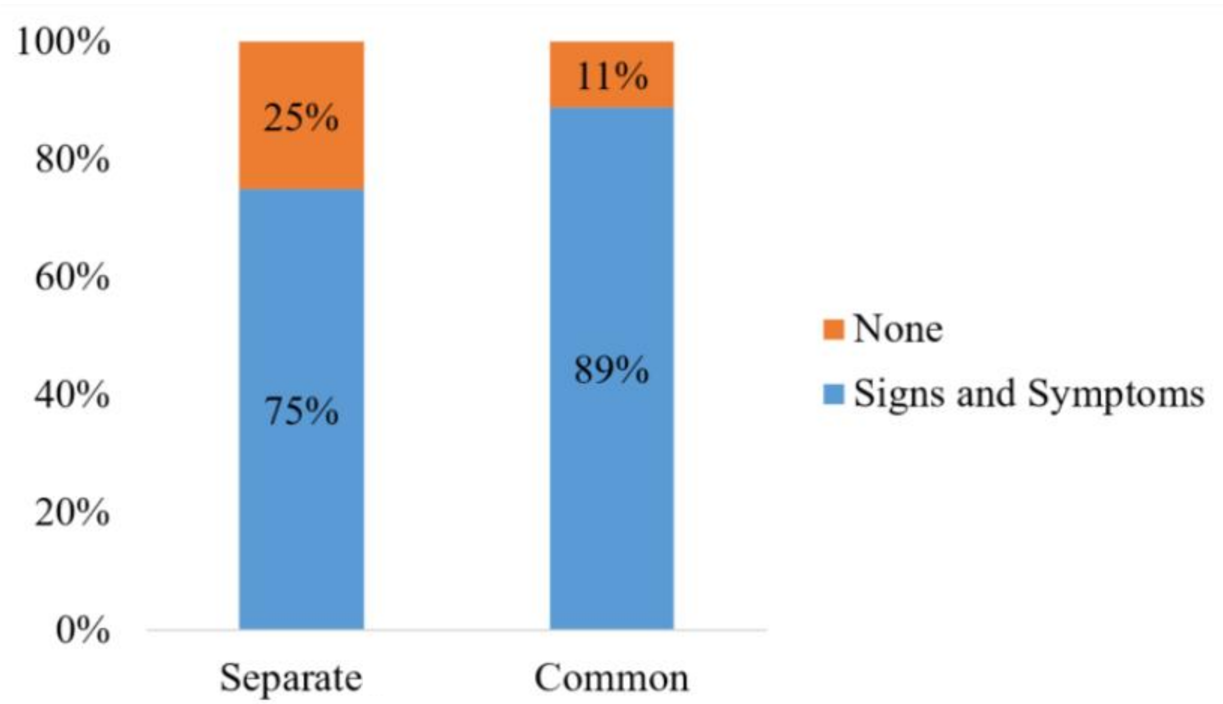
	Apical Periodontitis Yes	No	P-value
Portal of Exit			0.3392
Common	16, 89%	2, 11%	
Separate	83, 94%	5, 6%	
Gender			0.0938
Female	65, 90%	7, 10%	
Male	34, 100%	0, 0%	
Molar			>0.999
First	87, 94%	6, 6%	
Second	12, 92%	1, 8%	
Signs and Symptoms			0.0063
Yes	80, 98%	2, 2%	
No	19, 79%	5, 21%	

Table 3: Relationship between portal of exit and characteristics of cases

	Portal of Exit		
	Separate	Common	P-value
Apical Periodontitis			0.3392
Yes	83, 84%	16, 16%	
No	5, 71%	2, 29%	
Gender			0.1687
Female	57, 79%	15, 21%	
Male	31, 91%	3, 9%	
Molar			0.1187
First	75, 81%	18, 19%	
Second	13, 100%	0, 0%	
Signs and Symptoms			0.3525
Yes	66, 80%	16, 20%	
No	22, 92%	2, 8%	

A separate POE was slightly more prevalent among males (91% vs. 79%, p=0.1687) and in second molars (100% vs. 81%, p = 0.1187), though neither reached statistical significance. Apical periodontitis and the presence of signs and symptoms also did not demonstrate an association with the POE (Table 3). Teeth with signs and symptoms had 0.375 times the odds of having a separate POE than teeth without signs/symptoms (95% CI: 0.08-1.76) (Figure 4).

Figure 4: Association of POE and signs and symptoms



Discussion

An untreated and missed MB2 canal is one of the main reasons previously treated maxillary molars require retreatment. At the outset, the untreated space may be inconsequential to the immediate prognosis of the treated maxillary molar as the majority of the diseased pulpal tissue has been removed. However, the missed canal, along with the dentinal tubules within the root, serve as an extensive network for communication between pathogens from the remaining pulpal tissue and the host. With time, the remnants of pulpal tissue within the untreated space may lead to the development of post-treatment apical periodontitis. This present study aimed to evaluate specifically the association of the portal of exit of the missed MB2 on apical periodontitis in previously treated maxillary molars within the Greater Richmond, Virginia area. A separate POE was demonstrated in 83% of the cases which presented for retreatment. In addition, the prevalence of a separate POE was significantly higher than a common POE for cases with apical periodontitis. We failed to reject our null hypothesis that a MB2 canal with a separate POE is not associated with increased prevalence of apical periodontitis when compared a MB2 canal that merges with the MB1 canal to a common POE.

Many studies have evaluated the incidence of missed canals in previously treated maxillary molars, along with the prevalence of MB2 in various populations and geographic regions (Table 4). Karabucak et al reported on the prevalence of apical periodontitis with an untreated canal in previously treated upper and lower premolars and molars. Of the 1137 previously treated teeth, there were 148 maxillary molars with a missed canal. The study found that in all previously treated upper and lower premolars and molars, the presence of a missed canal was 4.38 times more likely to be associated with a lesion. Costa et al also observed the association between apical periodontitis and missed canals in all teeth. Of the 2294 previously treated teeth, there were 160 maxillary molars with a missed canal (10). Their conclusion was that in all previously treated teeth, the presence of a missed canal was 6.25 times more likely to be associated with apical periodontitis. Most recently, Baruwa et al studied the influence of missed canals and the prevalence of post treatment apical periodontitis. Of the 2305 previously treated teeth observed, there were 199 maxillary molars with a missed canal. Their conclusion was similar to that of Karabucak, in which all teeth with a missed canal were 4.4 times more likely to be associated with a lesion. However, for the first time, a conclusion was made specifically for a missed MB2: 75% of missed MB2 canals had apical periodontitis. While the impact of a missed MB2 and the development of apical periodontitis has been confirmed in these past studies, the focus was not specifically on the missed MB2, or its POE. In addition, the reasons for obtaining the scan, the presence of signs and/or symptoms, and the assessment of the apical extent of fill of previous endodontic treatment, were not reported. Interestingly, even without a missed MB2, 49% of previously treated maxillary molars still presented with apical periodontitis (9). This reflects that root canal treatment success is multifactorial. The weight of impact of a missed MB2 must be isolated from other prognostic factors such as extent of root filling and presence of a permanent restoration. Therefore, definitive inclusion and exclusion criteria were utilized in this present study to isolate a missed canal and its POE as a contributing factor for failure.

Table 4: Comparison of past literature

		Karabucak et al. JOE 2016	Costa et al. IEJ 2018	Baruwa et al. JOE 2020
Clinics		1 Grad Endo	1 Oral Radiology clinic	8 dental clinics
Total # CBCT scans		655	807	1160
Time frame		31 months	4 months	12 months
Voxel size		75	75	75
Total # endo treated teeth		1137 (upper/lower PM and M)	2294	2305
Total # max molars		363		385
	1st Molars	265		230
	2nd Molars	98		155
Teeth with missed canal		262	281	12% (overall)
	Maxillary molars	**148**	**160**	**199**
	Max 1st molar with missed canals	117	114	137
	Max 1st molar with missed MB2	65% (both 1st and 2nd)	106 (93%)	125 (91%)
Odds: AP for teeth with untreated canal		4.38x	6.25x	4.4x
% AP with missed canal		82.8% (of PM and M)		82.6% (of all teeth) 75% (of MB2 missed)
% AP with no missed MB2				49%

Strict inclusion and exclusion criteria were applied to the samples in order to explore the singular impact of the missed MB2 POE on the development or maintenance of apical periodontitis. The apical extent of fill on MB1 canal was critical in qualifying the teeth for the study. This criteria was applied in accordance with previous studies demonstrating obturation length as one of the main predictors for successful endodontic outcome. A root canal filling that is 0-2 mm from the radiographic apex has been considered to be the optimal obturation length. This was substantiated by a recent global cross-sectional study by Meirinhos and Martins et al, which showed that molars with short root fillings (>2mm short of the radiographic apex) were more commonly associated with periapical lesions (27). Therefore, a root canal obturation that terminated within 2mm from the radiographic apex was set as the parameter of sufficient root canal extent of fill for this study. If there was any evidence of overextension or overfill, the samples were excluded. There was no differentiation made between sealer and gutta-percha as the radio-opacity was not discernable on the CBCT scan. A total of 30 scans were disqualified from the study due to concerns with obturation length, with all of them being excluded due to "short fills".

For the 93% of cases with apical periodontitis, 84% had a separate POE and 16% had a common POE, which was statistically significant (p-value <0.0001). However, the overall prevalence of a separate POE included in this study was 83% compared to 17% for a common POE. When MB2 had a separate POE, there was a 94% association with apical periodontitis. When MB2 had a common POE, there was an 88% association with apical periodontitis. Therefore, the prevalence of apical periodontitis associated with a separate POE was higher, but this was not statistically significant (p-value = 0.3392). This is in agreement with Carrion's study - wherein the individual showed that the configuration of the missed MB2 did not have an impact on the development of apical periodontitis (20). In addition, the present study found that when MB2 had a separate POE, the mesiobuccal root was 2.08 times more likely to develop apical periodontitis than when MB2 with a common POE. This adds to the findings from Carrion's study, in which 1000 previously treated maxillary molars were evaluated, and their results showed that the presence of a separate exit for MB2 increases the risk of an untreated canal by 3.03 times (20). Regardless of the portal of exit of MB2, maximum efforts should be made to treat MB2 in its entirety as the missed canal space leaves opportunity for bacteria to thrive.

The presence of apical periodontitis was defined by an area of periapical radiolucency in this current study. It should be noted that the American Association of Endodontists use the term "apical periodontitis" as a periapical diagnosis and further subdivide it into "symptomatic" and "asymptomatic". In the majority of the previous studies, the prevalence of apical periodontitis associated with a missed canal was calculated purely on radiographic appearance of an apical lesion, without factoring in the importance of signs and symptoms. This might potentially lead to omission of cases which may not present with a radiographically visible lesion, but remain symptomatic and would otherwise still be diagnosed as "symptomatic apical periodontitis". This may lead to underreporting of apical periodontitis. In this study, out of the 106 cases referred for retreatment, 82 cases presented with signs and symptoms (77%). Historically, Block et al in 1976 reported that there is no correlation between signs and symptoms and the periapical histology in non-root canal treated teeth (28). However, in a study conducted by Weissman et al (29), there was a significant association between non-pulpal symptoms (such as chewing sensitivity and swelling) and apical periodontitis. Similarly in this study, the presence of signs and symptoms was the only statistically significant variable with relation to apical periodontitis (p-value =

0.0063). For those reporting signs and symptoms (n=82), 98% had apical periodontitis compared to 79% of the 24 patients who did not report signs and symptoms (Table 5).

Table 5: Correlation of signs and symptoms and apical periodontitis

Apical Periodontitis		
Signs and Symptoms	Yes	No
Yes	80 (98%)	2 (2%)
No	19 (79%)	5 (21%)

With regards to the relationship between signs and symptoms and the POE, 75% of the cases with a separate POE had signs and symptoms compared to 89% of those with a common POE. Teeth with a separate POE were less likely to present with signs and symptoms than teeth with a common POE (0.375 times the odds - 95% CI: 0.08-1.76) (Table 6).

Table 6: Association of portal of exit and signs and symptoms

	Separate	Common
Signs and Symptoms	66, 75%	16, 89%
None	22, 25%	2, 11%

Although the sample size in this study is selective toward symptomatic patients, some points may be implied from this observation in which teeth with a common POE were associated with a higher chance of presenting with signs and symptoms (Table 6). The communication of contaminated pulp tissue along with toxins can diffuse through the dentinal tubules and stimulate inflammation. This may cause biting and percussion sensitivity to develop earlier than the time it takes for apical periodontitis to be visible radiographically. When MB2 has a separate POE, the path of least resistance is not hindered by the obturation of the MB canal. The development of apical periodontitis due to the missed MB2 has a direct route through its own POE. This is a proposed theory as to why teeth with a common POE had a higher association with signs and symptoms compared to that of teeth with a separate POE.

There was a marginally significant association between patient gender and apical periodontitis. The majority of patients returning for retreatment were female (n=72, 68%) and 90% of them presented with apical periodontitis. Of the 34 male patients, 100% presented with apical periodontitis (p-value=0.0938). In relation to the POE of MB2, 91% of male patients presented with a separate POE while 79% of the female patients presented with a separate POE. This finding may also be attributed to previous findings that MB2 canals were 1.75 times more common in males than females (30).

There were 7 cases which did not present with apical periodontitis despite having an untreated MB2 space (7%). Of these 7 cases, 2 cases (28%) presented with signs and symptoms and retreatment was still recommended for the resolution of symptoms. However, 5 cases (4.7%) were completely asymptomatic and would otherwise be classified as a successful outcome of the initial root canal treatment. Studies which have reported on teeth without apical periodontitis despite having an untreated root canal range from 2%-37% (9, 10, 11, 20). This may be attributed to the differences in the study design, geographic region, sample size, amongst many others.

There are often communicating channels present between two canals in the form of a fin or an isthmus. Approximately 75% of the time, the presence of isthmuses has been reported connecting the MB1 canal and MB2 canal at all levels of the MB root (31, 32). Isthmus communication could be an accelerating factor for failure if bacteria is present in the MB2 canal space regardless of the POE (6). This confluence between MB1 and MB2 may explain why there was not a statistically significant difference in the association of apical periodontitis with POE. In terms of clinical implications, this supports the decision to retreat the missed MB2 instead of surgery as residual tissue in the untreated space favors bacterial growth.

There were several limitations to this present study. The first being the sample size, as we included 106 previously treated maxillary molars with a missed MB2. This is a smaller sample size than previous CBCT studies evaluating missed canals in root canal treated teeth. However, prior studies included more than just maxillary molars in their CBCT analysis (9, 10, 11). When narrowed down to only previously treated maxillary molars, the sample size relative to the time frame and number of centers involved with data collection is more comparable to previous studies (Table 4).

Although the AAE recommends a limited FOV CBCT scan prior to retreatments, from the initial 170 CBCT scans yielded, 9 scans were disqualified due to the presence of heavy scatter and beam hardening. Additionally, CBCT imaging may not be a true representation of disease as the lesion detected at the time of the scan may have been an apical scar, or in the healing process. While CBCT is more sensitive than periapical radiographs for detecting apical periodontitis (33), there is caution of over-diagnosis when the area of low density is less than 1mm (34). According to Kruse et al (35), 1 in 5 cases detected as mild apical periodontitis on a CBCT scan presented with healthy periradicular tissues when examined histopathologically.

Therefore, CBCT appears to have lower accuracy in root-filled teeth. In ideal settings, removing the obturation material prior to obtaining a scan can yield more accurate findings (36).

The inclusion of signs and symptoms garnered from past clinical charts also had inherent limitations. Only 55 of the 106 cases reported an estimated time frame of when the initial root canal treatment was completed, and the time frame ranged from 1 year to 50 years, with an average of approximately 9 years. 42 of the 55 cases which had information regarding the initial treatment reported on the qualification of the initial provider, with the majority being done by a general dentist. The limitation of this data's significance lies in the fact that the information is based on the patient's recollection, which is approximate, and the questions the provider asked at the consultation visit (37). Information could not be gathered regarding the protocol of disinfection, including the use of rubber dam isolation during the root canal treatment. More importantly, it was not possible to determine the preoperative diagnosis (i.e. vital or necrotic) as that would have provided more input on the bacterial status of the untreated root canal space. Furthermore, the reported signs and symptoms may have been referred pain from high occlusion, inflammation of the distobuccal and/or palatal roots, or a crack that has not yet shown radiographic signs. A follow up of the retreatment procedure to track the resolution of signs and symptoms would have confirmed the signs and symptoms were indeed associated with the missed MB2 canal. Lastly, it should be noted that the current study did not examine cause and effect relationship on the development of apical periodontitis.

Conclusion

The detection of MB2 canals has increased in the past few decades with increased awareness, microscope usage, and micro-endodontic armamentarium. Within the limitations of the study, it can be concluded that the POE of a missed MB2 canal in previously treated maxillary molars have no significant association with the presence of apical periodontitis. However, MB2 with a separate POE were associated with 2.08 times the odds of apical periodontitis than those with a common POE, which is relevant to clinical practice and decision making. This highlights the dire consequences of leaving out even small undebrided spaces and its impact on the development of apical periodontitis. Clinicians should strive to achieve thorough and complete chemomechanical debridement of the most commonly missed canal in endodontics, regardless of its POE.

References

1. Leprince, J. G., & van Nieuwenhuysen, J. -P. (2020). The missed root canal story: aren't we missing the point? *International Endodontic Journal*, *53*(8), 1162–1166.

2. Ng, Y.-L., Mann, V., Rahbaran, S., Lewsey, J., & Gulabivala, K. (2007). Outcome of primary root canal treatment: systematic review of the literature – Part 1. Effects of study characteristics on probability of success. *International Endodontic Journal*, *40*(12), 921–939.

3. Burns, L. E., Kim, J., Wu, Y., Alzwaideh, R., McGowan, R., & Sigurdsson, A. (2022). Outcomes of primary root canal therapy: An updated systematic review of longitudinal clinical studies published between 2003 and 2020. *International Endodontic Journal*, *55*(7), 714–731.

4. Crump, M. C. (1979). Differential diagnosis in endodontic failure. *Dental Clinics of North America*, *23*(4), 617–635.

5. Nair, P. N. R. (2006). On the causes of persistent apical periodontitis: a review. *International Endodontic Journal*, *39*(4), 249–281.

6. Ricucci, D., & Siqueira, J. F. (2010). Biofilms and Apical Periodontitis: Study of Prevalence and Association with Clinical and Histopathologic Findings. *Journal of Endodontics*, *36*(8), 1277–1288.

7. Tibúrcio-Machado, C. S., Michelon, C., Zanatta, F. B., Gomes, M. S., Marin, J. A., & Bier, C. A. (2021). The global prevalence of apical periodontitis: a systematic review and meta-analysis. *International Endodontic Journal*, *54*(5), 712–735.

8. Hoen. M., & Pink, F. (2002). Contemporary Endodontic Retreatments: An Analysis based on Clinical Treatment Findings. *Journal of Endodontics*, *28*(12), 834–836.

9. Baruwa, A. O., Martins, J. N. R., Meirinhos, J., Pereira, B., Gouveia, J., Quaresma, S. A., Monroe, A., & Ginjeira, A. (2020). The Influence of Missed Canals on the Prevalence of

Periapical Lesions in Endodontically Treated Teeth: A Cross-sectional Study. *Journal of Endodontics*, *46*(1), 34-39.e1.

10. Costa, F. F. N. P., Pacheco-Yanes, J., Siqueira, J. F., Oliveira, A. C. S., Gazzaneo, I., Amorim, C. A., Santos, P. H. B., & Alves, F. R. F. (2019). Association between missed canals and apical periodontitis. *International Endodontic Journal, 52*(4), 400–406.

11. Karabucak, B., Bunes, A., Chehoud, C., Kohli, M. R., & Setzer, F. (2016). Prevalence of Apical Periodontitis in Endodontically Treated Premolars and Molars with Untreated Canal: A Cone-beam Computed Tomography Study. *Journal of Endodontics*, *42*(4), 538–541.

12. Song, M., Kim, H.-C., Lee, W., & Kim, E. (2011). Analysis of the Cause of Failure in Nonsurgical Endodontic Treatment by Microscopic Inspection during Endodontic Microsurgery. *Journal of Endodontics*, *37*(11), 1516–1519.

13. Kulid, J. C., & Peters, D. D. (1990). Incidence and configuration of canal systems in the mesiobuccal root of Maxillary first and second molars. *Journal of Endodontics*, *16*(7), 311–317.

14. Baldassari-Cruz, L. A., Lilly, J. P., & Rivera, E. M. (2002). The influence of dental operating microscope in locating the mesiolingual canal orifice. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology*, *93*(2), 190–194.

15. Khalighinejad, N., Aminoshariae, A., Kulild, J. C., Williams, K. A., Wang, J., & Mickel, A. (2017). The Effect of the Dental Operating Microscope on the Outcome of Nonsurgical Root Canal Treatment: A Retrospective Case-control Study. *Journal of Endodontics*, *43*(5), 728–732.

16. Vertucci, F. J. (1984). Root canal anatomy of the human permanent teeth. *Oral Surgery, Oral Medicine, Oral Pathology*, *58*(5), 589–599.

17. Weine, F. S., Healey, H. J., Gerstein, H., & Evanson, L. (1969). Canal configuration in the mesiobuccal root of the maxillary first molar and its endodontic significance. *Oral Surgery, Oral Medicine, Oral Pathology*, *28*(3), 419–425.

18. Wolcott, J., Ishley, D., KENNEDY, W., JOHNSON, S., MINNICH, S., & MEYERS, J. (2005). A 5 Yr Clinical Investigation of Second Mesiobuccal Canals in Endodontically Treated and Retreated Maxillary Molars. *Journal of Endodontics*, *31*(4), 262–264.

19. Stropko, J. J. (1999). Canal morphology of maxillary molars: Clinical observations of canal configurations. *Journal of Endodontics*, *25*(6), 446–450.

20. Carrion, S. J., Coelho, M. S., Soares, A. de J., & Frozoni, M. (2022). Apical periodontitis in mesiobuccal roots of maxillary molars: influence of anatomy and quality of root canal treatment, a CBCT study. *Restorative Dentistry & Endodontics*, *47*(4).

21. Khademi, A., Zamani, Naser, A., Bahreinian, Z., Mehdizadeh, M., Najarian, M., & Khazaei, S. (2017). Root Morphology and Canal Configuration of First and Second Maxillary Molars in a Selected Iranian Population: A Cone-Beam Computed Tomography Evaluation. *Iranian Endodontic Journal*, *12*(3), 288–292.

22. Ahmed, H. M. A., Versiani, M. A., De-Deus, G., & Dummer, P. M. H. (2017). A new system for classifying root and root canal morphology. *International Endodontic Journal*, *50*(8), 761–770.

23. Fayad, M. I., Nair, M., Levin, M. D., Benavides, E., Rubinstein, R. A., Barghan, S., Hirschberg, C. S., & Ruprecht, A. (2015). AAE and AAOMR Joint Position Statement. *Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology*, *120*(4), 508–512.

24. Estrela, C., Bueno, M. R., Azevedo, B. C., Azevedo, J. R., & Pécora, J. D. (2008). A New Periapical Index Based on Cone Beam Computed Tomography. *Journal of Endodontics*, *34*(11), 1325–1331.

25. Studebaker, B., Hollender, L., Mancl, L., Johnson, J. D., & Paranjpe, A. (2018). The Incidence of Second Mesiobuccal Canals Located in Maxillary Molars with the Aid of Cone-beam Computed Tomography. *Journal of Endodontics*, *44*(4), 565–570.

26. Peña-Bengoa, F., Cáceres, C., Niklander, S., & Meléndez, P. (2023). Association between second mesiobuccal missed canals and apical periodontitis in maxillary molars of a Chilean subpopulation. *Journal of Clinical and Experimental Dentistry,* e173–e176.

27. Meirinhos, J., Martins, J. N. R., Pereira, B., Baruwa, A., Gouveia, J., Quaresma, S. A., Monroe, A., & Ginjeira, A. (2020). Prevalence of apical periodontitis and its association with previous root canal treatment, root canal filling length and type of coronal restoration – a cross-sectional study. *International Endodontic Journal*, *53*(4), 573–584.

28. Block, R. M., Bushell, A., Rodrigues, H., & Langeland, K. (1976). A histopathologic, histobacteriologic, and radiographic study of periapical endodontic surgical specimens. *Oral Surgery, Oral Medicine, Oral Pathology*, *42*(5), 656–678.

29. Weissman, J., Johnson, J. D., Anderson, M., Hollender, L., Huson, T., Paranjpe, A., Patel, S., & Cohenca, N. (2015). Association between the presence of apical periodontitis and clinical

symptoms in endodontic patients using cone-beam computed tomography and periapical radiographs. *Journal of Endodontics*, *41*(11), 1824–1829.

30. Colakoglu, G., Kaya Buyukbayram, I., Elcin, M. A., Garip Berker, Y., & Ercalik Yalcinkaya, S. (2022). Association between second mesiobuccal canal and apical periodontitis in retrospective cone-beam computed tomographic images. *Australian Endodontic Journal*.

31. von Arx, T. (2005). Frequency and type of canal isthmuses in first molars detected by endoscopic inspection during periradicular surgery. *International Endodontic Journal*, *38*(3), 160–168.

32. Weller, R. N., Niemczyk, S. P., & Kim, S. (1995). Incidence and position of the canal isthmus. Part 1. Mesiobuccal root of the maxillary first molar. *Journal of Endodontics*, *21*(7), 380–383.

33. Patel, S., Dawood, A., Mannocci, F., Wilson, R., & Pitt Ford, T. (2009). Detection of periapical bone defects in human jaws using cone beam computed tomography and intraoral radiography. *International Endodontic Journal*, *42*(6), 507–515.

34. Torabinejad, M., Rice, D. D., Maktabi, O., Oyoyo, U., & Abramovitch, K. (2018). Prevalence and Size of Periapical Radiolucencies Using Cone-beam Computed Tomography in Teeth without Apparent Intraoral Radiographic Lesions: A New Periapical Index with a Clinical Recommendation. *Journal of Endodontics*, *44*(3), 389–394.

35. Kruse, C., Spin-Neto, R., Evar Kraft, D. C., Vaeth, M., & Kirkevang, L.-L. (2019). Diagnostic accuracy of cone beam computed tomography used for assessment of apical periodontitis: an *ex vivo* histopathological study on human cadavers. *International Endodontic Journal*, *52*(4), 439–450.

36. Vizzotto, M. B., Silveira, P. F., Arús, N. A., Montagner, F., Gomes, B. P. F. A., & Silveira, H. E. D. da. (2013). CBCT for the assessment of second mesiobuccal (MB2) canals in maxillary molar teeth: effect of voxel size and presence of root filling. *International Endodontic Journal*, *46*(9), 870–876.

37. Connolly, D. M., & Silverstein, D. I. (2015). Dermatology consultations in a tertiary care hospital: A retrospective study of 243 cases. *Dermatology Online Journal*, *21*(8).