Interobserver and Intraobserver Reliability and the Accuracy of Periapical Radiographs as a Diagnostic Test in the Identification of Furcation Involvement in Mandibular Molars

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DEDICATION

I dedicate this Thesis to my idols, my mom and dad. You have continuously supported me and pushed me to work hard and be the best that I can be. Without you, I would not have been able to achieve any of my academic goals. Love you both.

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INTRODUCTION

The basis of endodontic treatment involves the prevention and treatment of apical periodontitis which requires complete cleaning, shaping and obturation of the root canal space (1,2). However, in order to come to a decision on the necessity of endodontic treatment a diagnosis must first be established. The diagnosis of endodontic disease involves a combination of subjective findings, dental history, objective clinical findings and testing as well as radiographic findings.

Endodontic diagnosis, specifically in terms of radiographs, has advanced significantly in recent times. In 1899, radiology was first introduced into endodontics when Dr. Edmund Kells inserted a lead wire into a maxillary incisor to determine its length. Since then, the use of radiology in endodontics has continued to evolve. The change from film to digital radiography has made the process of accessing and interpreting radiographs simpler and faster as well as allowing for easier image storage, manipulation and retrieval. Nowadays, the advent of 3-D imaging modalities, particularly cone beam computed tomography (CBCT) imaging, have allowed for radiographic imaging to assume more advanced roles in endodontics. Limited field of view (LFOV) CBCT is utilized in many applications including, but not limited to, diagnostic evaluation of canal morphology, surgical treatment planning, assessment of perforations and resorptions and the detection of periapical pathosis. As the advent of LFOV CBCT continues to change the landscape of radiology in endodontics, it remains that digital periapical radiographs are still the most accessible and widely used radiographic diagnostic tool utilized for the detection of periapical pathosis (3). Furthermore, while numerous studies have evaluated the accuracy of CBCT compared to 2-D periapical imaging in terms of ability to correctly diagnose apical periodontitis as well as evaluating the role that anatomical structures like cortical bone play in the ability to diagnose such lesions, no study to date has focused on a particular anatomic area of the tooth, the furcation area and the ability of these radiographic tests to assess this area.

The furcation area of multi-rooted teeth is clinically relevant due to the presence of accessory canals also known as furcation canals in this specific area. Moreover, studies have shown that periapical pathosis when expanding spread first in a vertical direction toward the furcation and possibly involving the furcation depending on its size (4,5). Furcation canals are especially present in mandibular molars and upon infection may lead to the presence of pathosis in the area of the furcation.

The mandibular first molar is the most frequently endodontically-treated tooth owing in part to the series of anatomical challenges it poses. With a variation in the number of roots, once accessed, within each root can be found a wide variation in canal morphology. These variations include isthmuses, apical ramifications and accessory canals including lateral and furcation canals. Furthermore, the buccal bone is thickest in the mandibular molar area possibly making it more difficult to interpret pathosis in this area (6,7). However, mandibular molars pose certain advantages in terms of evaluating the furcation area, namely the separation of roots in a mesial and distal direction, with minimal anatomic structures overlapping the area of the furcation. For this reason, the furcation of mandibular molars may be more systematic to evaluate compared to other multi-rooted teeth.

Numerous studies have evaluated the ability of our traditional imaging techniques to identify pathosis in the periapical area (PA) of teeth as well as the reliability of these techniques however, no study to date has evaluated the role of our common endodontic imaging modalities in evaluating furcation involvement of endodontic origin. Thus, the aim of this study will be to assess the interobserver and intraobserver reliability of periapical radiograph interpretation in the identification of furcation involvement in mandibular molars as well as to determine the accuracy of periapical radiographs as a diagnostic test in the detection of furcation involvement in mandibular molars.

REVIEW OF THE LITERTURE

2-D vs 3-D imaging modalities in Endodontics

Radiographic imaging plays a significant role in most aspects of endodontic practice. They are important for diagnosis, treatment planning, monitoring details during treatment, observing details at the conclusion of treatment, and for follow-up of treatment outcome. Although now considered essential, the use of radiographs was not available to the dental profession until early in the last century. Fourteen days after Professor Roentgen's discovery announcement about the properties of cathode rays, Dr. Otto Walkoff was already taking the first dental radiograph in his own mouth. Three years later in 1899 and Dr. Kells introduced radiology into endodontics (8). Since that time to the use of radiographs in the present day, numerous discoveries and advancements have continuously changed and shaped the landscape of radiology in endodontics.

Periapical (PA) radiographs are the technique of choice for assessment, diagnosis and management of endodontic disease (3,9). However, clinicians must understand that they are two-dimensional reflections of a three-dimensional reality. As clinical and radiographic signs of endodontic disease often are small and undefined, clinicians are required to analyze unspecific variations in radiographic appearance of tooth and supporting structures. According to Goldman, "we do not read radiographs; we interpret them" (10). This study reported a relatively low interobserver and intraobserver reliability when interpreting conventional radiographs which was also confirmed by studies evaluating digital radiographs (10,11). Although radiographic interpretation has been shown to be subjective, it is still an essential component in the diagnosis of endodontic disease.

Most endodontic studies evaluating the diagnostic ability of radiographs focus on the presence or absence of a periapical rarefying osteitis since identification of apical periodontitis critically dictates the health and treatment of a tooth. Classically, Bender & Seltzer in the 1960s created artificial bone lesions in mandibles of human cadavers and found that in order to detect radiolucency on a film PA radiograph, the bone cortex must be affected, and lesions confined to only cancellous bone are not visible. If lesions erode the junction area of cortical/cancellous or perforate cortical bone, then they can be distinguished with PA radiographs (12). This finding was further confirmed with studies using digital radiography (13). Future studies began to challenge this idea postulating that lesion detection had more to do with factors like lesion location and thickness of the cortical bone rather than whether it erodes any amount of cortical bone. A recent in vivo study by Chang further challenged this, concluding that lesions confined to cancellous bone can be detected on PA radiography at a rate of 91.6%. and that lesion size is what is correlated with correct identification of a PA lesion, rather than involvement of junctional and cortical bone which had no significant effect (14).

Furthermore, numerous techniques and adjuncts have aimed to improve on the accuracy of PA imaging methods for detection of apical periodontitis. Increasing the number of radiographs exposed with angled radiographs as well as the utilizing digital radiography over film significantly improved detection of apical periodontitis (15,16). However, arguably no advancement in dental radiology is as studied in our current literature as 3-D imaging with cone-beam computed tomography (CBCT).

CBCT scanning for maxillofacial imaging was introduced in 1998 (17). Limited field of view (LFOV) options allow small volume scans with minimal distortion at high resolutions and lower radiation doses, increasing the ability to use CBCT imaging in endodontics. Various studies documented the greater accuracy and specificity of CBCT imaging to detect endodontic radiographic findings compared with conventional periapical radiographs. Clinical studies demonstrate that periapical radiolucency was detected in 20% of cases using PA radiographs, compared to 48% using CBCT (18). Furthermore, CBCT had significantly higher diagnostic accuracy in detecting apical periodontitis compared to PA radiographs, using human histopathological findings as a reference standard (19,20). Finally, in a systematic review and meta- analysis, periapical radiographs (digital and conventional) reported good diagnostic accuracy on the discrimination of artificial apical periodontitis from no lesions, whereas CBCT imaging showed excellent accuracy values (20). Besides diagnosis of endodontic diseases and identifying the extent of apical periodontitis, endodontic applications of CBCT also include the identification of root and root canal anatomy; internal, external, cervical, and apical resorptions; localization and detection of missed canals, separated instruments, and other foreign body materials before retreatment; identification and extent of apical periodontitis trauma, including root and alveolar fractures; and surgical treatment planning (21).

Although CBCT presents certain advantages over PA imaging, it also presents disadvantages. These include artifacts (beam hardening, metal artifact, noise artifact) the significantly higher cost of CBCT to the practitioner and the patient, accessibility and availability of CBCT and especially the radiation dose to the patient. According to a CBCT review study, the approximate ionizing radiation dosages for LFOV CBCTs ranged from 4.7-38.3μSv depending on the location of the of the scan and CBCT manufacturer. The dosage for one digital periapical radiograph was approximately 6μSv, as shown in Table 1 (22). Thus, the benefit to the patient must outweigh any potential risks of the additional radiation exposure, which should be kept as low as reasonably achievable (ALARA) and decision to utilize of CBCT should be determined on an individual basis (23).

Table 1: Approximate Ionization Radiation Dosages[22]

Activity	Effective Dose in μSv	Dose as Days of Equivalent Background Radiation
1 digital PA radiograph	6	1
Kodak© CBCT focused field, anterior	4.7	0.71
Kodak© CBCT focused field, maxillary posterior	9.8	1.4
Kodak© CBCT focused field, mandibular posterior	38.3	5.47
3D Accuitomo, J. Morita	20	3

Despite advances in radiographic imaging technology with 3-D imaging, the periapical radiograph and intraoral imaging in general, has successfully maintained its presence and remains indispensable in endodontic practice. Thus, the continued evaluation into the diagnostic ability of these radiographs is important and beneficial to our understanding and treatment approach especially in multi-rooted teeth like mandibular molars.

Radiographic Attenuation and Supporting Structures

The radiographic interpretation of odontogenic disease requires a sound knowledge of the radiographic appearance of normal structures. For structures surrounding and supporting the teeth this includes the alveolar crest, the periodontal ligament (PDL) space, lamina dura, cancellous bone and adjacent cortical plates. When evaluating the periapical condition of teeth with necrotic pulps, lamina dura continuity and shape as well as PDL width and shape were the most consistent features for diagnosis and by looking at them separately detection is more sensitive (24).

Depending on the tooth being evaluated, certain anatomical structures may also influence the interpretation of disease such as the intermaxillary suture or nasal spine for anterior maxillary teeth as well as the floor of the maxillary sinus or zygomatic process of the maxilla for posterior teeth. When focusing specifically on the furcal area of the tooth the roots of the teeth themselves may also prevent the complete visualization of the area on 2-D radiographs. The mandibular molar often only has 2 roots separated mesio-distally not superimposed, allowing for better visualization of the furcation region. However, difficulty in interpretation in this area is often attributed to the overall thickness of bone and specifically cortical bone. In the mandible, at the level of the root apex, buccal bone thickness averaged 2.19 mm over the root of the 2nd premolar, 2.30 mm over the mesial root of the 1st molar, 3.00 mm over the distal root of the 1st molar, 5.16 mm over the mesial root of the 2nd molar and 6.35 mm over the distal root of the 2nd molar. Furthermore lingual bone thickness progressively increased from the distal root of second molar (2.42mm) to the 2nd premolar (4.50mm) (6). Although usually located closer to the apex of teeth rather than the furcation region, the external oblique ridge forms a substantial bony buttress merging with the buccal cortical plate, and on the lingual surface, the internal oblique and mylohyoid ridges are bony structures that may attenuate the x-ray beam. Lastly, thick anterior border of the overlying masseter muscle may add additional attenuation to the incident beam.

Mandibular Molars

Molar teeth frequently require endodontic treatment with mandibular 1st molars being the tooth most frequently treated (25). A more recent study at the University of Pennsylvania found that in general, out of all teeth, mandibular molars most commonly receive initial root canal treatment (26). Besides being the most treated tooth, mandibular molars also pose various anatomical complexities and canal irregularities contributing to the challenge of treating mandibular molars. These include the multi-canal nature of mandibular molars as well as canal irregularities including isthmuses and accessory canals.

Mandibular first molars and second molars both present with multiple canals. According to different morphological studies, mandibular first molars present with 2 roots 98% of the time and within these 2 roots, 3 canals about 64% and 4 canals about 29-35% (27,28). In mandibular second molars, the reported incidence of three canals was about 81% and 5-10% had four canals (29). An added significance of the presence of multiple canals in mandibular molars is that any time there is a presence of multiple canals there may be the presence of isthmuses. The isthmus has been defined by Weller as “a narrow, ribbon-shaped, communication between two root canals that contains pulp or pulpally derived tissue” (30). In a CBCT study by Estrela, the highest isthmus frequency was found in the group of mandibular first molars (87.8 %). Mandibular second molars had the second highest frequency of root canal isthmuses at 66.3% (31). The increased incidence of isthmuses present in mandibular molars is of importance considering they contain necrotic debris and tissue remnants and can harbor bacteria allowing them to grow and multiply, ultimately causing failure of the nonsurgical and surgical endodontic procedures (9,32).

Another morphological variation present in mandibular molars are accessory canals. As defined by the AAE glossary of terms an accessory canal is any branch of the main pulp canal or chamber that communicates with the external surface of the root. Depending on their location along the length of the tooth, these include lateral canals, apical ramifications and furcation canals which will be discussed more in depth in a later subsection. Lateral canals are accessory canals located in the coronal or middle third of the root, usually extending horizontally from the main canal space. In mandibular first molars, Vertucci's dye study found a 45% incidence of lateral canals in the mesial root and a 30% incidence of lateral canals in the distal root. Regarding the second mandibular molar, an incidence of 49% in the mesial root and 34% in the distal root (33). DeDeus separately evaluated the body of the root and the apical portion and found lateral canals in the main body of the root in 10.4% and secondary canals in the apical region in 19.4% of mandibular first molars. In mandibular second molars, lateral canals were found in the main body of the root in 5.0% of teeth and secondary canals in the apical region in 17.5% (34). Furthermore, apical ramifications in mandibular first molars were evaluated in a study by Harris and defined as portals of exit distinct from the main canal(s) occurring in the apical 0.5 mm of the tooth. Among the mesial roots, there was an average of 3.73 portals of exit in the apical 0.5 mm compared with an average of 3.36 in distal roots (35). The presence of lateral canals and apical ramifications, because separate from the main canal(s) and hard to reach, are unlikely to be mechanically debrided with endodontic instruments and, therefore, are often only chemically debrided, if cleaned at all.

<u>Furcation</u>

The furcation of a tooth is where the roots of multirooted teeth divide and separate from one another. Mandibular molars generally have two roots thus a furcation is called a bifurcation while maxillary molars have three roots and are called a trifurcation. Furcation involvement is defined as an area of bone loss at this branching point of a tooth root. Its etiology includes anatomic factors like furcation canals, root fractures, trauma from occlusion, extension of periodontal disease and periapical pathosis extending cervically to involve the furcation. Of particular importance exclusively to endodontics are the presence of furcation canals, the extension of periapical pathosis and the presence of fractures since these situations either require endodontic treatment for resolution or, in the case of fractures, present with endodontic treatment as a common etiology.

According to Seltzer, necrotic pulps produce periodontal lesions by passage of toxic products through canals whether main or lateral canal (36). Grossman stated that “pulp disease, if untreated, usually results in the destruction of the attachment apparatus wherever main foramina or large accessory foramina exit into the periodontal ligament” (37). As discussed previously, accessory canals have different names depending on their location within the tooth. One of the final anatomical complexities to discuss related to mandibular molars are furcation canals which the AAE defines as an accessory canal located in the furcation (38). Numerous articles have established the interrelationship of pulpal and periodontal tissues through furcation canals. Gutmann’s dye study found accessory canals in furcation region of molars 28% of the time which includes 4mm root apical to the pulpal floor (39). Vertucci’s SEM study determined that accessory foramina on both the pulp chamber floor and the furcation surface were found in 32% of mandibular first molars, and 24% of mandibular second molars. Furthermore, mandibular teeth had a higher incidence (56%) of foramina involving both the pulp chamber floor and furcation surface than did the maxillary teeth (48%) (40). In a more recent study from Dammaschke, 79% of molar teeth had accessory furcation foramina that varied from 10 µm to 200µm in diameter and alveolar bone loss in the furcation regions of molars can be induced by pulp inflammation and necrotic or caries-involved pulps through these canals (41).

In addition to or in combination with furcation canals, endodontic pathosis may involve the furcation through the extension of periapical pathosis in a cervical direction. Histologic studies have differed as to the initial direction of spread of inflammation. A histologic study from Walton has shown that inflammation tends to follow the path of least resistance. With marrow spaces being susceptible and the periodontal ligament being resistant to the spread of inflammation, inflammation spreads primarily towards the furcation (5). Whereas a study from Yamasaki demonstrated that apical lesions extended first in a mesiodistal direction followed by a vertical expansion (42). Regardless, of the initial direction of lesion expansion, further significance lies in that lesions extending to involve the furcation are often lesions of increased size. There is a consensus among endodontic outcome studies as to the presence of apical periodontitis decreasing the success rate of non-surgical root canal treatment (NSRCT) both initial treatment and retreatment (43–46). Furthermore, with regard to the size of the lesion, the results are still inconclusive as to whether larger lesion size affects success in primary and secondary endodontic treatment (43,44,46,47). For surgical endodontic treatment lesion size and type both affect the outcome of bone healing. Barone found that when the crypt diameter was >10 mm it resulted in a decrease in healing from 80% to 53% (48). Kim's study evaluating lesion type affecting success of surgical endodontic treatment, found the successful outcome for isolated endodontic lesions was 95.2% whereas it was 77.5% in endodontic-periodontal combined lesions (49). Thus, being able to detect the extent of the lesion and whether furcation is involved, may be a factor in prognosis or outcome of treatment.

Lastly, of possible endodontic origin involving the furcation, are cracks and vertical root fractures (VRFs). Cracks are defined as a thin surface disruption of enamel and dentin and possibly cemcntum of unknown depth or extension and these include VRFs (38). VRFs specifically differ from cracks in that they usually occur in a buccal-lingual direction and progress apically to coronally whereas cracks occur in a mesio-distal direction and progress coronally to apically. Endodontic treatment is suggested to be a major etiologic factor for VRFs likely related to strains and forces during the obturation phase of treatment however, excessive reduction of dentin will predispose a tooth to fracture as well (50,51). The etiology of cracks has been related to several factors including trauma, excessive parafunctional forces or interferences, but also to restorative materials and procedures because of thermal expansion and contraction coefficients (52). In a histologic study, Walton showed that the fracture spaces contained a combination of irritants: bacteria, necrotic debris, sealer, and degraded inflammatory cells. Root surfaces consistently demonstrated an inflammatory lesion adjacent to the fracture (51). Similarly, Ricucci and Siqueira found that cracks are always colonized with bacterial biofilms (53). Diagnosis of VRF is, at times, difficult due to lack of specific signs, symptoms and/or of typical radiographic features. However, when visible radiographically, the 'halo' appearance also known as the 'J-shaped' lesion, which is a combination of periapical and lateral radiolucency, was associated with a high probability of VRF as was an angular resorption of the crestal bone along the root (54). VRFs extending to the furcation are important to diagnose as they are often a devastating event as treatment involves either extraction of a single-rooted tooth, or at least root amputation or hemi-section of a molar. Cracks that involve the furcation are most commonly from two sources: a crack running mesio-distally through he pulpal floor or a crack that has extended apically and progressed to a split tooth which appears as a large periapical radiolucency that is contiguous with the furcation (55). According to a recent systematic review from Olivieri, in both these situations when the extension of the cracks results in complete root involvement or extends across the pulpal floor, extraction will be the most viable treatment option (52).

With the presence of all these anatomic complexities in mandibular molars it becomes very important to obtain a complete diagnostic picture when evaluating mandibular molars for treatment. Therefore, the radiographic exam and the value of assessing furcation involvement is of particular importance in these teeth.

SPECIFIC AIMS

1. To assess the interobserver and intraobserver reliability of periapical radiograph interpretation in the identification of furcation involvement in mandibular molars

2. To determine the accuracy of periapical radiographs as a diagnostic test in the detection of furcation involvement in mandibular molars.

MATERIALS AND METHODS

The IRB at the University of Minnesota has determined that this study meets the criteria for exemption from IRB review: Exemption (HRP-312). No patient identifiable data was collected for any CBCT or PA radiograph.

Image Selection

A minimum of 43 mandibular CBCT scans demonstrating furcation involvement has been calculated as the minimum sample size required for ROC analysis with multiple observers. In this study we assigned a desired half width of 0.15 with a confidence interval of 95%, an estimated AUC of 0.7 and a desired ratio of about 3:1 for presence of furcation involvement to absence of furcation involvement. The sample size determination for ROC was calculated according to the equation outlined by Zhou 2011 (Appendix) (56).

As per the policy at the Graduate Endodontics department at the University of Minnesota, the decision to utilize LFOV CBCT imaging is made on a case-by-case basis according to the recommendations outlined by the AAE and AAOMR Joint Position Statement: Use of Cone Beam Computed Tomography in Endodontics—2015/2016 Update (57). CBCT scans and associated PA radiographs were collected from two sources: 1) The records of all patients having received non-surgical root canal treatment of either the first or second mandibular molar at the University of Minnesota Graduate Endodontics clinic between August 2017 and December 2021 were reviewed retrospectively for pre-operative CBCT scans, 2) CBCT scans of mandibular molars were collected retrospectively from an existing database at a private endodontic practice in Minnesota, Metropolitan Endodontics LLC, from the period of November to December 2021.

Images of first or second mandibular molars of patients in which LFOV CBCT scans taken with the following characteristics were excluded:

1. Patients below the age of 18 years

2. CBCT scans that do not have 2 corresponding PA radiographs exposed at different horizontal angulations

3. CBCTs of mandibular molars with vital pulp diagnosis (pulp diagnosis of previously treated or previously initiated treatment were included in the study)

4. CBCTs with no clear visualization of the furcation region of the mandibular molar such as mandibular molars with fused roots

5. Images of poor quality because of radiographic artifacts or other obstructions making them non-diagnostic

If the CBCT scans did not fall under any exclusion categories, they were included in the study with their associated PA radiographs of the mandibular first molar (1 straight on image and 1 horizontally angled image). All scans from the University of Minnesota Endodontics department were taken with a CS 8100 3D unit (Carestream Health, Inc, Rochester, NY) (figure 1) with a voxel size of 76 µm, 5mA, 90kVP and all periapical radiographs were taken with RVG 6200 (Carestream Health, Inc, Rochester, NY) (figure 3) at 7mA and 70kVp with a pixel dimension of 19µm and measured resolution of 24 line pairs/mm. The CBCT and periapical radiographs were stored on the Carestream Imaging software. All CBCT scans from Metropolitan Endodontics were taken with Veraviewepocs 3D F40 (J Morita MFG Corp, Kyoto Japan) (figure 2) with a voxel size of 125µm, 5mA and 90kVp and stored on the i-Dixel Software (J Morita MFG Corp, Kyoto Japan). All periapical radiographs were taken with Schick 33 Intraoral sensor (Dentsply Sirona Inc, York, PA) (figure 4) at 7mA and 70kVp with a pixel size of 15µm and a measured resolution of 28 line pairs/mm and stored on the Schick CDR DICOM 5 Digital X-Ray Software (Dentsply Sirona Inc, York, PA).

Figure 1- Carestream 8100 CBCT

Figure 2- Veraviewepocs 3D F40 CBCT

Figure 3- Carestream RVG 6200 Sensor **Figure 4- Schick 33 Intraoral Sensor**

All CBCTs were reviewed by the two authors individually (AA and LK) who classified the scans of mandibular molars into one of two categories: presence of furcation involvement visualized on CBCT image or furcation involvement absent on CBCT image. Scans were classified as displaying mandibular first or second molars with furcation involvement if a clear radiolucency was present involving the furcation region of mandibular first or second molars. This includes periapical lesions extending coronally to include the furcation area of mandibular molars (figure 5) or appearance of “halo lesions” or “J-shaped lesions” (54) involving the furcation commonly observed in cases of vertical root fracture (VRF) (figure 6) as well as well-defined furcal radiolucency of endodontic origin confined only to the furcation area (figure 7). CBCT scans of mandibular first and second molars demonstrating any evidence of generalized horizontal bone loss characteristic of periodontitis causing furcation involvement of periodontal origin (i.e horizontal, crestal bone loss exposing a furcation area) were excluded from the study at this point. This was done to ensure that only furcation involvement of endodontic origin was included. If there was any disagreement between the authors in terms of the presence or absence of identifiable furcation involvement, the scans were reviewed by the

Oral and Maxillofacial Radiologist at the University of Minnesota (LG) for final determination.

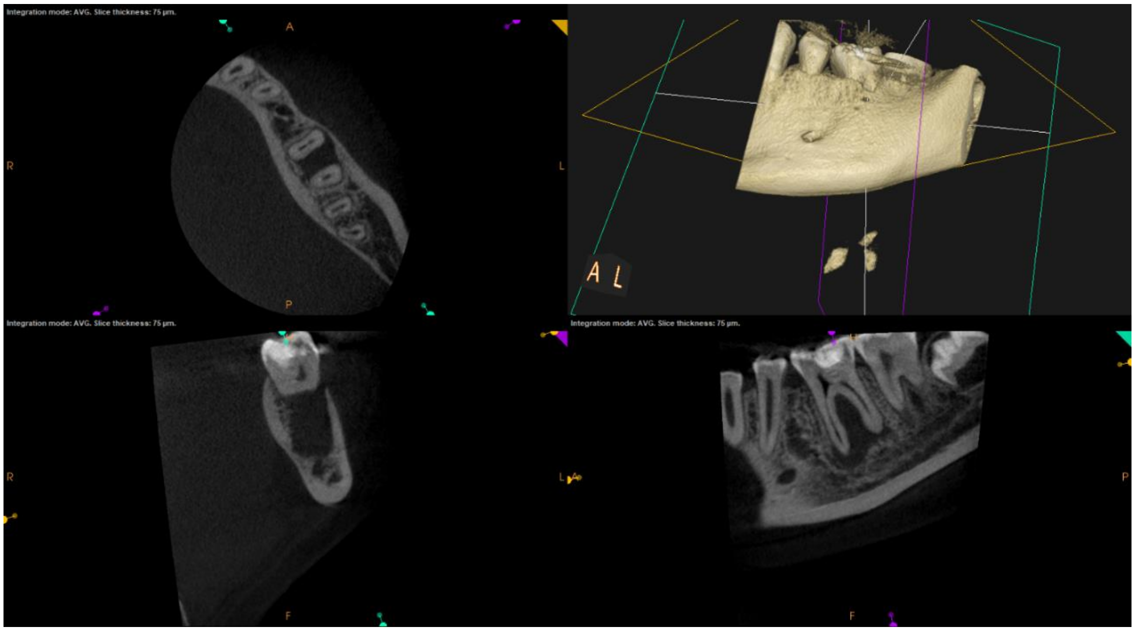

Figure 5- Example of a CBCT image slice of mandibular first molar furcation involvement in which periapical radiolucency extends coronally to include furcation area.

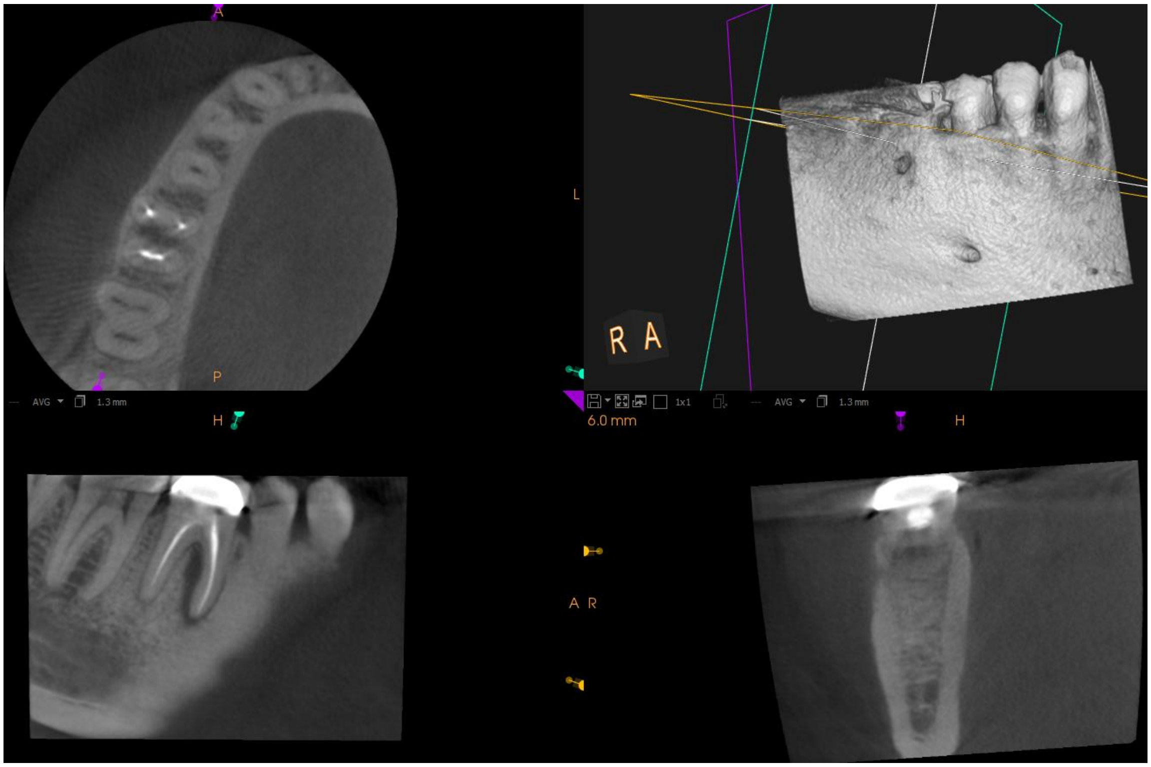

Figure 6: Example of a CBCT image slice of mandibular first molar furcation involvement with 'J shaped' radiolucency in which pathosis is caused by vertical root fracture.

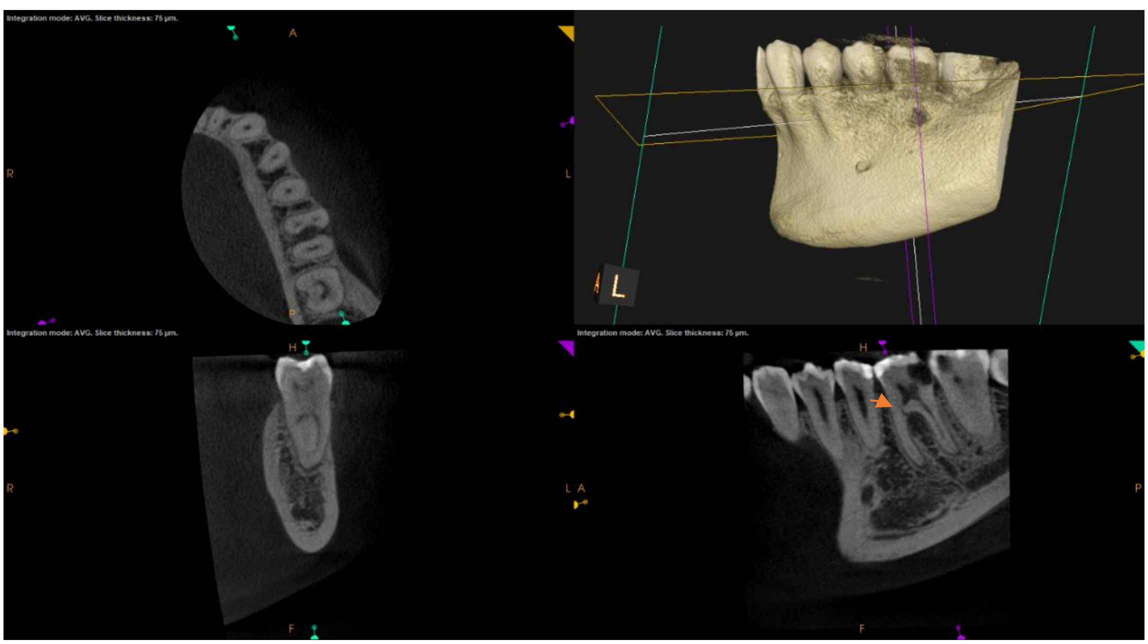

Figure 7- Example of a CBCT image slice of mandibular first molar furcation involvement due to furcal pathosis confined only to furcation area. Furcation canal visible on sagittal slice (orange arrow).

From the numerous CBCT scans that were collected of mandibular first and second molars that did not demonstrate the presence of furcation involvement, 20 CBCT scans were randomly included, with the associated 2 PA radiographs each, to serve as negative controls.

Lesion Identification

A total of 84 cases were thus included for observation (64 presence of furcation involvement on CBCT and 20 absence of furcation involvement on CBCT, the control group) for a total of 168 periapical images. The observers, a board-certified endodontist (observer 1), a board-certified periodontist (observer 2), a board-certified oral and maxillofacial radiologist (observer 3) and 2 second-year endodontic residents (observers 4 and 5) separately viewed the corresponding 84 cases (168 PA radiographs total). The periapical radiographs that were collected from the University of Minnesota Carestream software and Metropolitan Endodontics Schick CDR software were saved as DICOMs, rendered anonymous using the DICOMAnonymize tool, assigned a random case number (www.randomizer.org) and exported to RadiANT DICOM Viewer (Medixant, Posnow, Poland) to consolidate the PA images. RadiANT DICOM Viewer was chosen due to its simple and intuitive interface to facilitate viewing for the observers. Each of the 84 cases were saved as a separate folder with the 2 corresponding periapical images on the RadiANT software. Each case was viewed using a Dell P1913Sf LCD Monitor (Dell, Round Rock, TX) with a resolution of 1280 x 1024 at 60Hz in a dark, radiograph interpretation room in the radiology department at the University of Minnesota (figure 9). The AAPM TG-18 QC test pattern was performed as a check of monitor calibration prior to analysis. The only information provided to the observers regarding the case was the tooth number to interpret.

Evaluation

One week prior to interpretation, observers were calibrated as to what constituted presence (Y), maybe (M) or absence (N) of furcation involvement on PA radiographs. All observers were also calibrated on how to operate the viewing software and were permitted to use all functions that they believed would aid in image interpretation including magnification, brightness/contrast and measurement tools. No time restrictions were placed on the observers. Individually, the observers were asked to evaluate and rate the PA radiographs for furcation involvement to create dual 3-point and 4-point data sets. They first indicated the presence of furcation on a 3-point scale: No, Maybe or Yes. If the observers indicated maybe, they were then asked to indicate whether they were more inclined to observe furcation involvement or not (Yes or No) to be able to further generate a 2-point (No, Yes) and 4 point scale (No, Maybe No, Maybe Yes and Yes).

<u>3-point scale definition (for all cases):</u>

No : Furcal destruction of bone almost definitively not present

Maybe: Unsure

Yes: Furcal destruction of bone almost definitely present

<u>4- point scale definition (for cases initially rated as unsure):</u>

No: Furcal destruction of bone almost definitively not present

Maye No: Furcal destruction of bone probably not present

Maybe Yes: Furcal destruction of bone probably present

Yes: Furcal destruction of bone almost definitely present

The cases were then reordered using random number set generator (www.randomizer.org) and evaluation of the images was conducted by the same observers for a second time, 2 weeks after the first evaluation, to ensure observers would not recall previous findings.

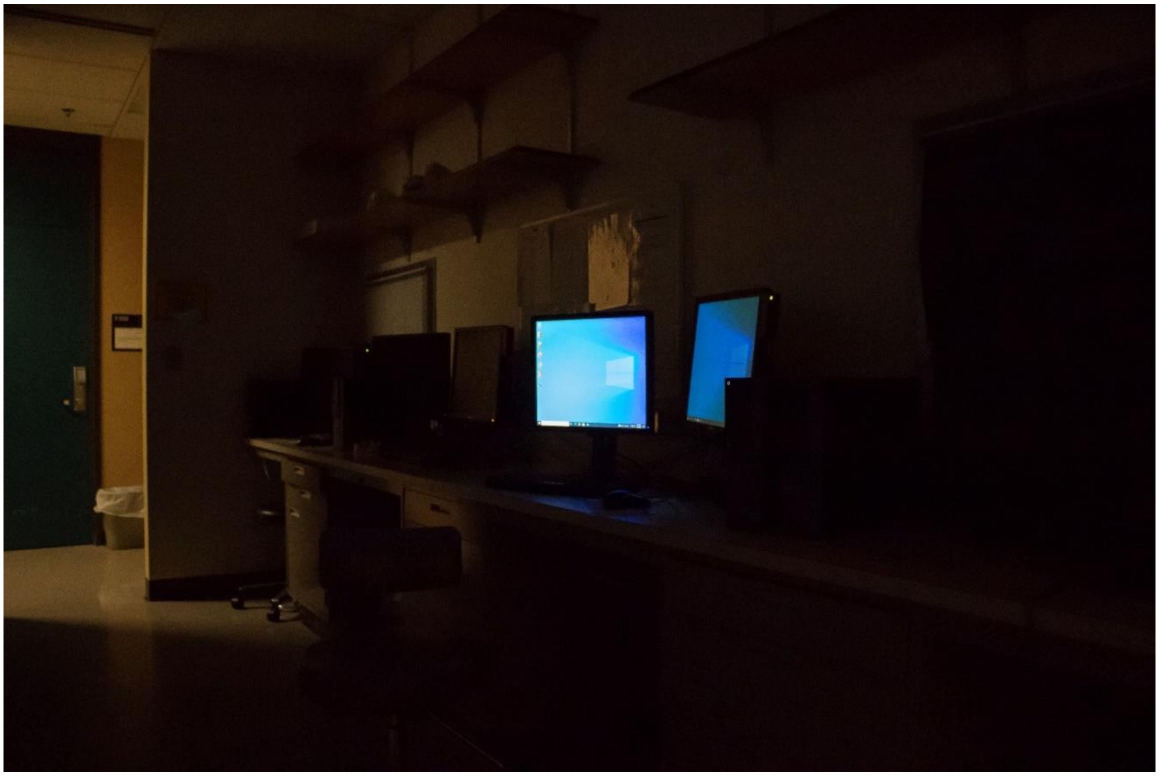

Figure 8- Dark, radiograph interpretation room

Statistical Analysis

The evaluations of the 5 observers as to the presence or absence of furcation involvement per the periapical radiographs were subjected to statistical analysis. Intra- and inter-observer agreement for binary (No/Yes) ratings was assessed using the Fleiss kappa statistic. Rater agreement for 3-level (No/Maybe/Yes) and 4-level (No/Maybe No/Maybe Yes/Yes) ratings was assessed using the weighted Fleiss kappa statistic with linear weights and interpreted according to Landis and Koch 1977 table for interpreting kappa values (Table 2) (58). Binary ratings were compared to the CBCT reference standard and summarized using overall accuracy (proportion of correct ratings), sensitivity, specificity, and positive and negative predictive values. Receiver operating characteristic curve (ROC) were plotted and the area under the ROC curve (AUC) was calculated for each observer and each session to evaluate the diagnostic accuracy of PA radiographs in the detection of FI across all diagnostic test thresholds of the 4 point confidence scale. The average AUC was calculated using the method from described by

Gallas (59), as implemented in the R package iMRMC version 1.2.3 (https://CRAN.R-project.org/package=iMRMC). AUC values were interpreted according to Swets' commonly used AUC value range for interpretation of accuracy (Table 3) (60).

Table 2- Fleiss Kappa Statistical Analysis Ranges

Kappa Value (κ)	**Degree of Agreement**
< 0.00	Poor
0.00 – 0.20	Slight
0.21 – 0.40	Fair
0.41 – 0.60	Moderate
0.61 – 0.80	Substantial
0.81 – 1.00	Near perfect

Table 3- Accuracy Classification by AUC for a Diagnostic Test

AUC Value	**Diagnostic Accuracy of Test**
<0.50	Due to Chance Result
0.50 – 0.70	Low Accuracy
0.70 – 0.90	Moderate Accuracy
>0.9	High Accuracy

RESULTS

Reliability Results

The Fleiss kappa (κ) for the 5 observers during the first round of interpretation was 0.53, 0.40, 0.38 (for each point scale 2-point, 3-point, 4-point) and 0.51, 0.38, 0.41 for the second round of interpretation. The mean Fleiss kappa coefficient for interobserver reliability for each point scale was 0.52, 0.39, 0.40 with 95% Confidence Intervals (CI) (Table 4). This indicates a moderate level of agreement among the observers when evaluated using a 2-point scale and a fair level of agreement when evaluated with either the 3- or 4- point scale

Table 4- Inter-observer Agreement, Fleiss' (Weighted) Kappa Statistic with 95% Confidence Interval (CI)

	Session 1 (CI)	**Session 2 (CI)**	**Mean**
2-point scale	0.53 (0.42,0.65)	0.51 (0.39, 0.63)	0.52
3-point scale	0.40 (0.28,0.48)	0.38 (0.31,0.52)	0.39
4-point scale	0.38 (0.28,0.47)	0.41 (0.30,0.51)	0.40

*Weighted Fleiss kappa statistics for 3- and 4- point scale

The Fleiss kappa coefficients for intra-observer reliability was 0.62, 0.53, 0.50 for observer 1, 0.63, 0.63, 0.63 for observer 2, 0.73, 0.56, 0.57 for observer 3, 0.62, 0.61, 0.61 for observer 4 and 0.48, 0.49, 0.49 for observer 5 evaluated using the 2-point scale, 3-point scale and 4-point scale respectively. These results indicate that when evaluated with the 2-point confidence scale, substantial levels of agreement for all observers was achieved except observer 5, with a moderate level of agreement. When evaluated with the 3- point scale or 4-point scale, a moderate level of agreement was observed for all observers except observer 4 with a substantial level of agreement (Table 5). Observer 2 was excluded from analysis for the 3-and 4-point scale because they evaluated all cases using only a binary scale.

Table 5- Intra-rater Agreement, Fleiss' (Weighted) Kappa Statistic with 95% CI:

	Observer 1 (CI)	**Observer 2 (CI)**	**Observer 3 (CI)**	**Observer 4 (CI)**	**Observer 5 (CI)**
2- Point Scale	0.62 (0.44, 0.79)	0.63 (0.45, 0.80)	0.73 (0.56, 0.90)	0.62 (0.45, 0.79)	0.48 (0.29, 0.71)
3- Point Scale	0.53 (0.38, 0.68)	0.63 (0.45, 0.80)	0.56 (0.40, 0.71)	0.61 (0.46, 0.75)	0.49 (0.30, 0.68)
4-Point Scale	0.50 (0.36, 0.65)	0.63 (0.45, 0.80)	0.50 (0.40, 0.65)	0.61 (0.47, 0.75)	0.49 (0.30, 0.68)

*Weighted Fleiss kappa statistics for 3- and 4-point scale

Binary Results

Binary ratings were then compared to the CBCT reference standard in the detection of furcation involvement. The mean sensitivity of the periapical radiographs in detection of furcation involvement was 0.78 indicating that the presence of furcation involvement in mandibular molars was correctly identified in 78% of cases. The mean specificity was 0.85 indicating that the absence of furcation involvement was correctly identified by PA radiographs in 85% of cases. The mean negative predictive value was 0.57 indicating a low probability that a negative diagnosis of furcation involvement with PA images is indeed absent with CBCT as a reference standard, but the mean positive predictive value was 0.95 indicating a high probability of positive diagnosis with PA radiographs, actually presenting with furcation involvement. The mean accuracy of PA radiographs in detecting furcation involvement was 0.79 thus, when evaluated on a 2-point binary scale on average, 79% of the time the PA evaluation for furcation involvement is making the correct diagnosis. The accuracy, sensitivity, specificity, and positive and negative predictive values for each observer and each session is presented in table 6 as well as the average. Table 7 presents a 2x2 table of the binary results of the diagnostic testing with PA radiographs for the presence of furcation involvement compared to the CBCT reference standard for each observer and each session.

Table 6- Sensitivity, Specificity, PPV, NPV, and Diagnostic Accuracy (true positives + true negatives) for Periapical Images Considering all Observers.

	Accuracy	Sensitivity	Specificity	PPV	NPV
Observer 1 Session 1 (S1)	0.80	0.75	0.95	0.98	0.54
Observer 1 Session 2 (S2)	0.70	0.64	0.90	0.95	0.44
Observer 2 (S1)	0.82	0.78	0.95	0.98	0.58
Observer 2(S2)	0.74	0.72	0.80	0.92	0.47
Observer 3 (S1)	0.86	0.89	0.75	0.92	0.68
Observer 3 (S2)	0.82	0.86	0.70	0.90	0.61
Observer 4 (S1)	0.71	0.64	0.95	0.98	0.45
Observer 4(S2)	0.76	0.72	0.90	0.96	0.50
Observer 5 (S1)	0.89	0.94	0.75	0.92	0.79
Observer 5 (S2)	0.83	0.83	0.85	0.95	0.61
Average	**0.79**	**0.78**	**0.85**	**0.95**	**0.57**

Table 7- Binary results of Diagnostic Testing with PA radiographs for the Presence of Furcation Involvement Diagnosed by CBCT as Standard Reference for each Observer and each Session

PA Furcation Involvement		CBCT Furcation Involvement: Yes	CBCT Furcation Involvement: No
Observer 1 (S1)	Yes	48	1
	No	16	19
Observer 1 (S2)	Yes	41	2
	No	23	18
Observer 2 (S1)	Yes	50	1
	No	14	19
Observer 2 (S2)	Yes	46	4
	No	18	16
Observer 3 (S1)	Yes	57	5
	No	7	15
Observer 3 (S2)	Yes	55	6
	No	9	14
Observer 4 (S1)	Yes	41	1
	No	23	19
Observer 4 (S2)	Yes	46	2
	No	18	16
Observer 5 (S1)	Yes	60	5
	No	4	15
Observer 5 (S2)	Yes	53	3
	No	11	17

ROC Curves and AUC

A single ROC curve per observer was plotted on a graph for session 1 with the respective AUC values (figure 9). Figure 10 is a separate graph for session 2, plotting a single ROC curve per observer with their respective AUC values.

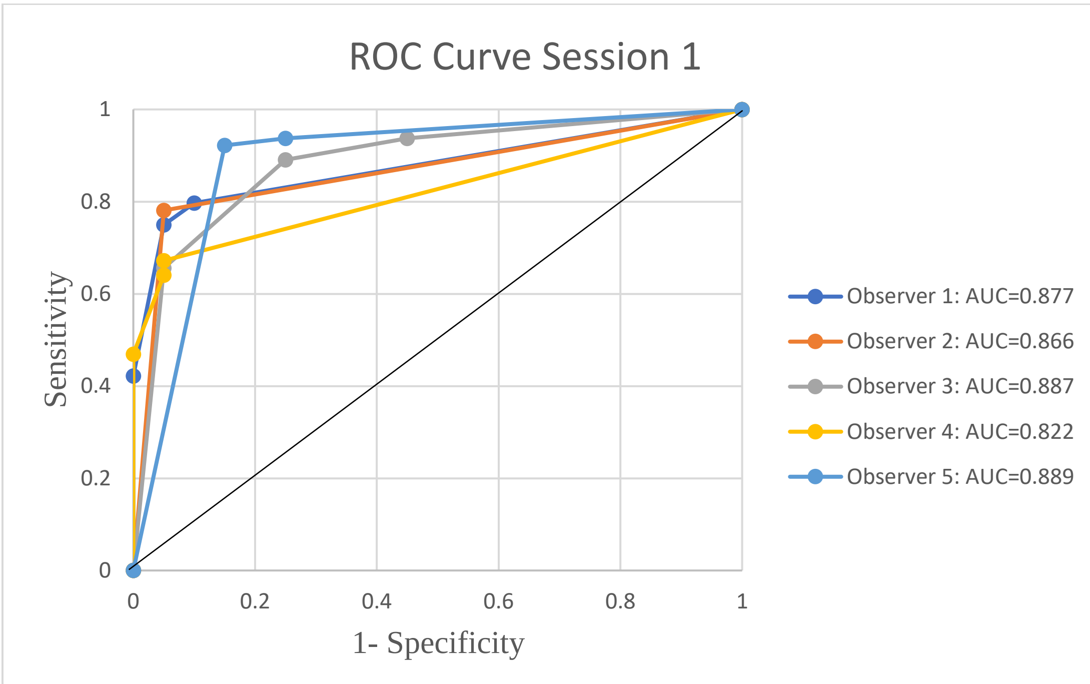

Figure 9- ROC Curves for each Observer in Session 1 and Associated AUC

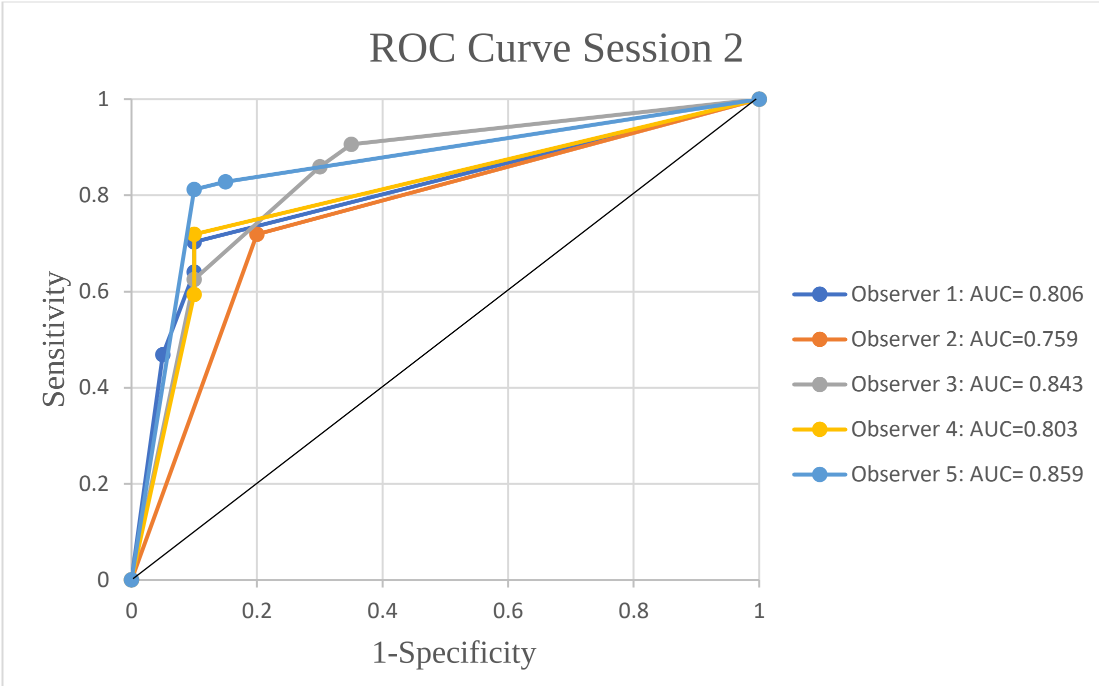

Figure 10- ROC Curves for each Observer in Session 2 and Associated AUC

The average AUC for all observers across both sessions was 0.841 with a 95% CI of (0.792, 0.890). The null hypothesis H0: AUC = 0.5 was rejected with $p<0.001$. AUC multiple comparison, via Bonferroni test was used to statistically evaluate the difference between the observers with NSD ($p>0.05$).

DISCUSSION

Literature is yet limited regarding 2-D radiographic-based assessment of furcation involvement of endodontic origin in patients, let alone CBCT based assessment. Therefore, the main goal of the present study was to evaluate the ability of PA images to investigate the existence of furcation involvement in mandibular molars. Since periapical radiographs are still the most frequently employed and accessible radiographic imaging modality in detection of lesions of endodontic origin, data on their accuracy is of pivotal relevance and proper assessment of furcation involvement is also important for adequate treatment management of endodontic patients.

The gold standard method to identify furcation involvement would be by surgically exposing the furcation area as well as histopathologic analysis. For practical and more importantly ethical reasons, this is not possible when there is no clear indication for surgical exposure. Histopathologic studies have previously been used as a gold standard in the evaluation of diagnostic accuracy of CBCT vs. periapical imaging in the diagnosis of apical periodontitis (19,61). CBCT was used as gold standard in the present study because of their accessibility and availability to the graduate endodontics department at the University of Minnesota given the increased utilization of CBCT in endodontics for various purposes previously outlined. Moreover, CBCT has been shown to be an adequate gold standard in studies describing high levels of agreement between CBCT and histopathological studies for the detection of apical periodontitis (19,61). In addition, in periodontic literature, CBCT images in the detection of furcation involvement shows high levels of agreement with intra-surgical findings (62,63).

The usefulness of a diagnostic test is evaluated in terms of its validity or ability to detect subjects with disease as well as its capacity to exclude subjects without disease (64). Reliability is also a key feature of a diagnostic test as results should be repeatable with high interobserver agreement (65).

Interpreting Reliability results

Despite advancements in technology, interpreting radiographs continues to be a subjective exercise. Every attempt was made in the present study to limit the variables that would affect interpretation as each observer viewed the images on the same computer monitor in the same room with the same lighting. With these efforts the mean Fleiss kappa coefficients for the 2-point confidence scale for the presence of furcation involvement was 0.52 indicating a moderate level of agreement between observers. However, when evaluated with the 3-point and 4-point confidence scale the mean weighted Fleiss kappa coefficient was 0.39, 0.40 respectively, indicating a fair level of agreement between observers. In terms of agreement with themselves over time, when evaluated on a binary scale, the mean Fleiss kappa coefficients indicated a substantial level of agreement for all observers with a range of 0.62-0.73 except for observer 5 with a Fleiss kappa coefficient of 0.48 indicating a moderate level of agreement. When evaluated with the 3- point or 4-point scale, a moderate level of agreement was observed for all observers with a range of 0.49-0.56 respectively, except for observer 4 with a substantial level of agreement (κ= 0.61). According to Goldman, we do not read radiographs; we interpret them. In their classic study, interpreting radiographs for endodontic success, observers agreed with each other 47-73% of time and with themselves 75-83% of time (10). More recently, when looking at the presence of apical periodontitis using PA radiographs, kappa values indicated reliability was fair to moderate at best (11,66,67). This study agreed with the results from previous studies, although regarding identifying furcation involvement rather than apical periodontitis. This similarity in results may be explained by the same interferences that would be hindering the reliability of detecting apical periodontitis also hindering the reliability of detecting furcation involvement in mandibular molars such as the dense and thick buccal and lingual cortical plates of the mandible. Moreover, the more numerous subdivisions in the confidence scale resulted in lower levels of reliability and consistency. More classifications render the interpretation more demanding on the observer (24,68) and this may explain why the kappa values were higher for the dichotomized values. This study demonstrates that with the traditional 2-D periapical radiograph imaging technique, the interpretation of furcation involvement in mandibular molars is quite subjective and Goldman's observation of interpreting rather than reading radiographs still holds true.

<u>Interpreting Binary Results</u>

An approach for evaluating the validity of a test is to use paired measures at a specific test threshold, using sensitivity, specificity, positive predictive value, negative predictive value (PPV and NPV) and accuracy as was calculated in this study. With an average sensitivity of 0.78, if a mandibular molar has furcation involvement, there is a 78% chance that the PA will correctly diagnose it as present (true positive rate). Figure 11 demonstrates an example of PA radiographs in which all observers correctly detected furcation involvement. With an average specificity of 0.85, periapical radiography will correctly return a negative result for 85% of teeth without furcation involvement (true negative rate). Figure 12 demonstrates an example of PA radiographs in which all observers correctly detected absence of furcation involvement. The accuracy of PA radiographs in diagnosing furcation involvement on a binary scale was 0.79 thus, the true positive and true negative diagnoses of furcation involvement occurred in 79% of cases. However, these results further indicate that 22% of furcation involvement will be missed using PA radiographs (figures 13 and 14 respectively, show examples of cases where all and some observers recorded false negatives). Moreover, it indicates a false positive rate of 15% and figure 15 shows an example of a case in which 4/5 observers recorded a false positive. Previous studies reporting sensitivity and specificity of PA radiographs in detection of apical periodontitis varied with sensitivity between 0.38-0.77 and specificity 0.99-1 (16,19,20). Our study was somewhat consistent with studies evaluating furcation lesions of periodontal origin using PA radiographs where the sensitivity was 0.56 and 0.79 for the specificity (69).

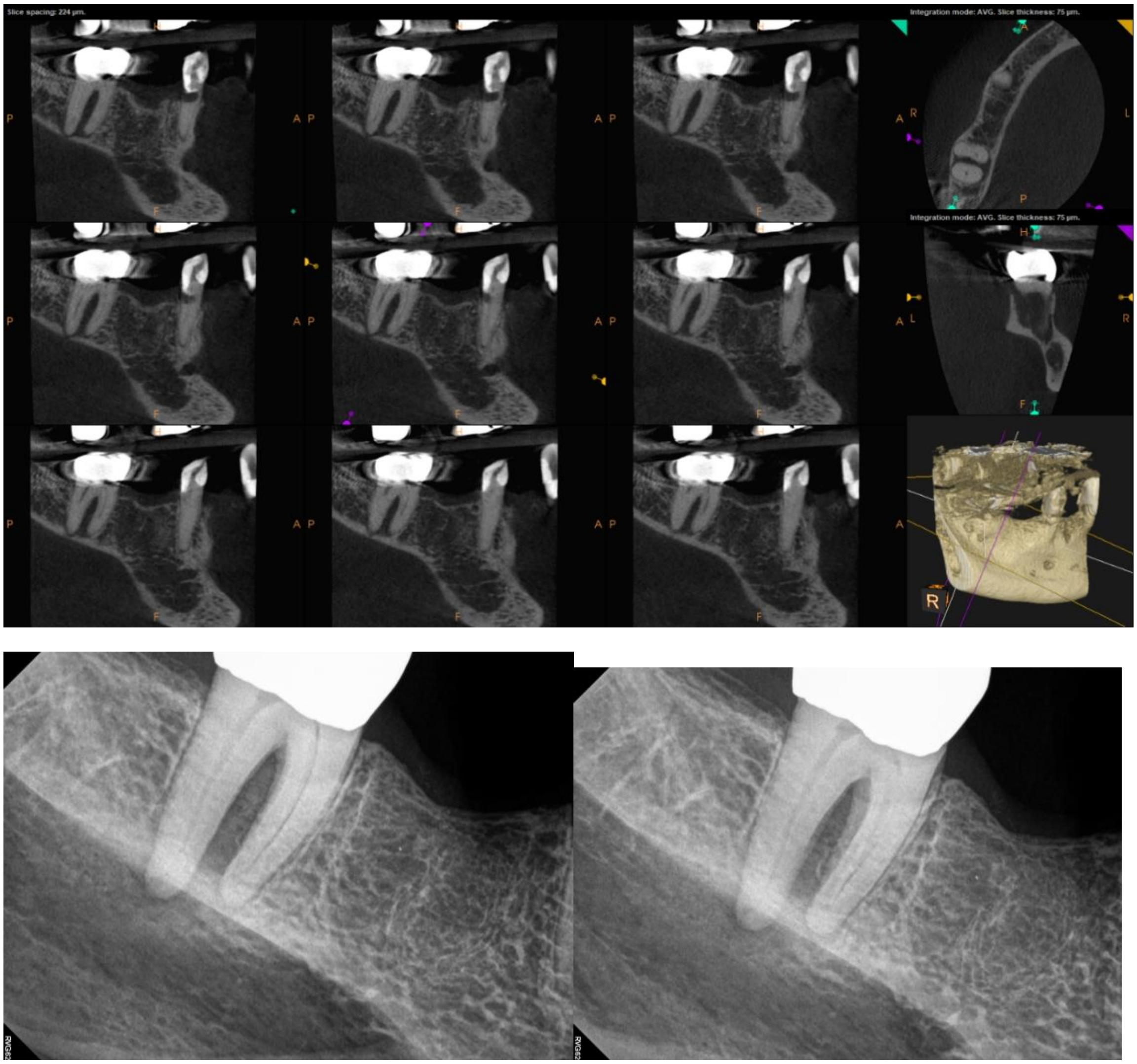

Figure 11- CBCT image slice of tooth #31 demonstrating furcation involvement with associated PAs in which all observers responded "YES" to the prescence of FI. All repsonses resulting in true positive.

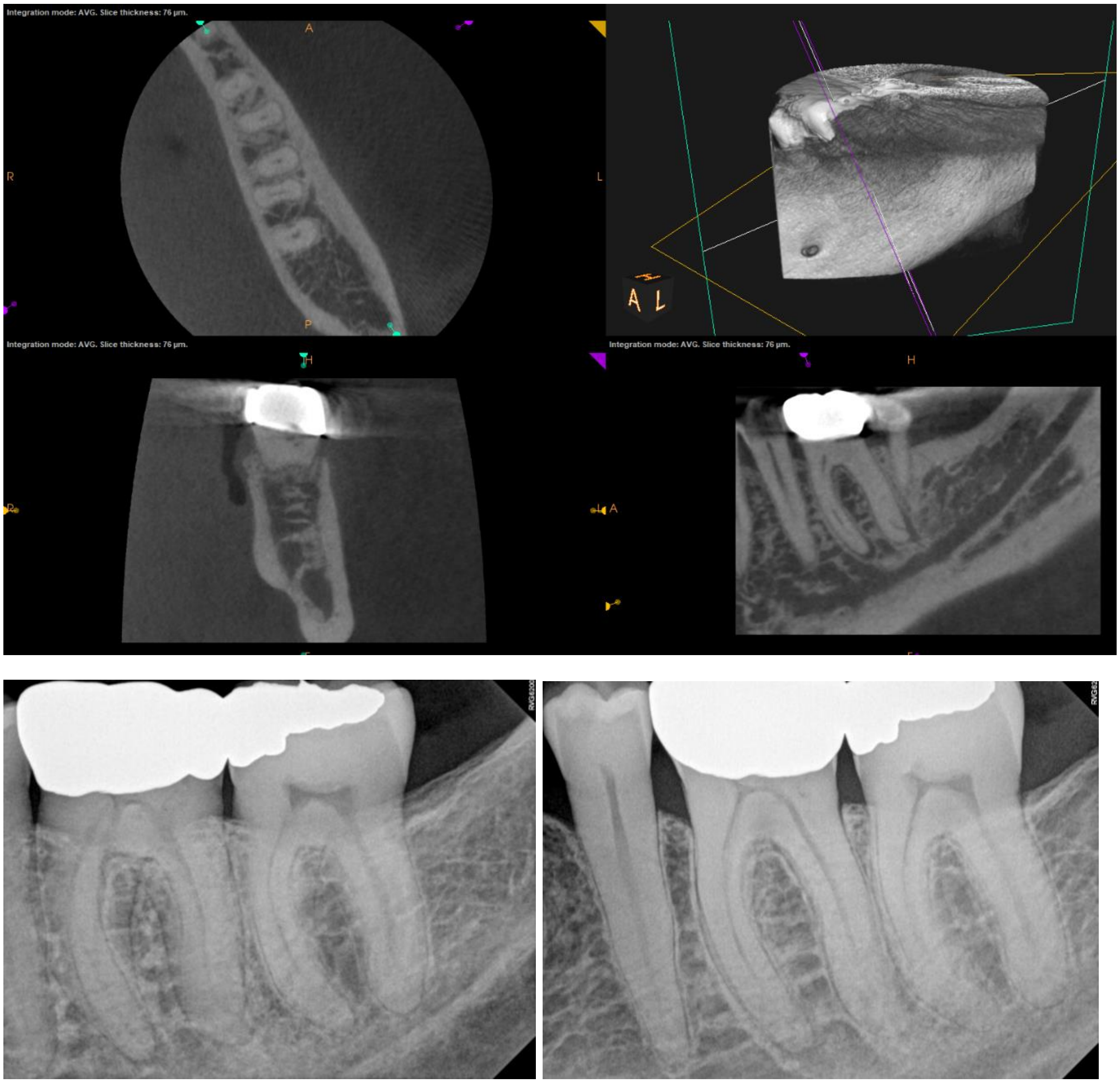

Figure 12- CBCT image slice of tooth #19 with no furcation involvement (control group) in which all observers responded "NO" to the prescence of FI. All responses resulting in true negative.

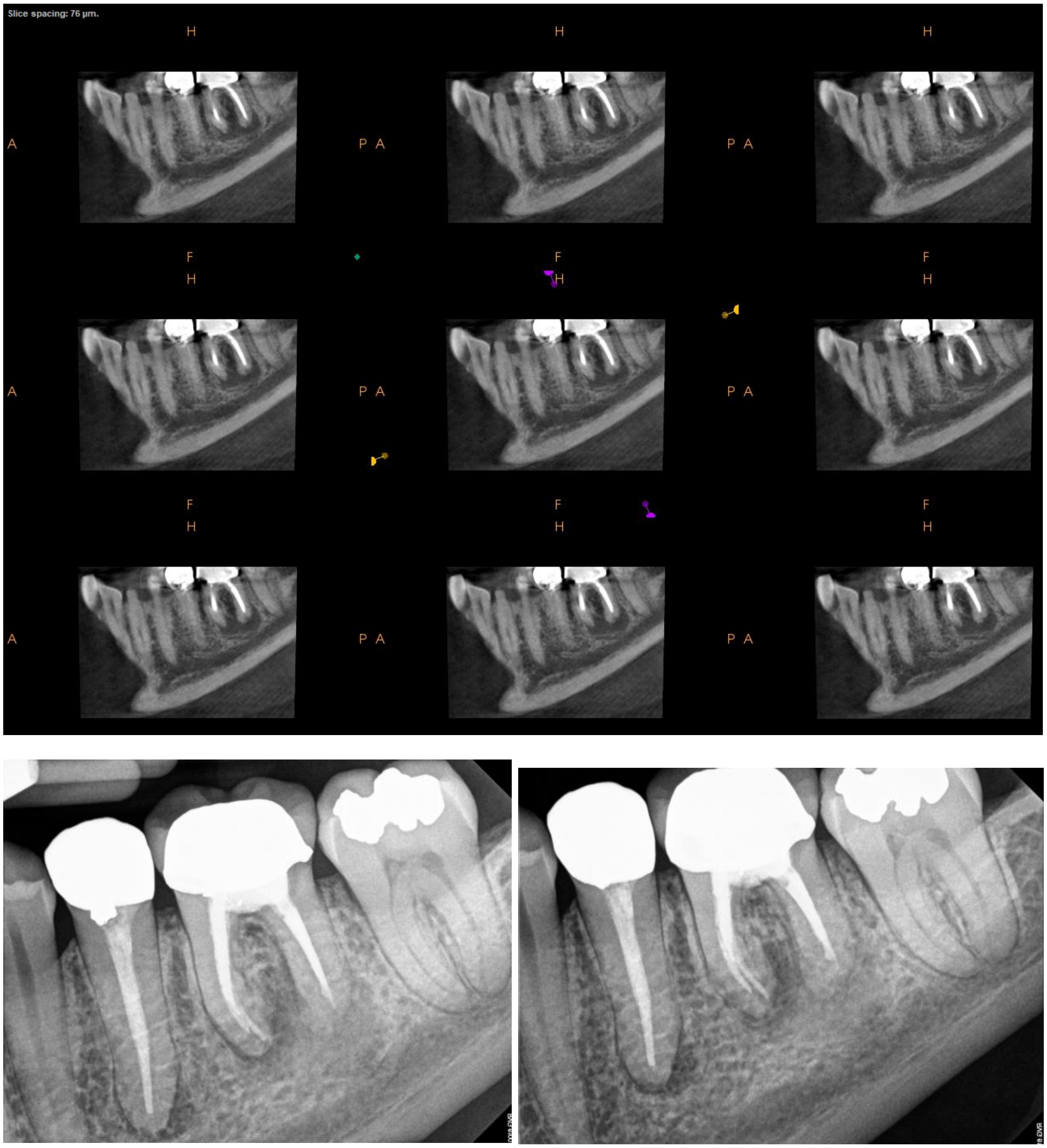

Figure 13- Sagittal slices of CBCT image of tooth #19 demonstrating furcation involvement with associated PAs in which all observers responded “NO” to the prescence of furcation involvement. All responses resulting in false negative.

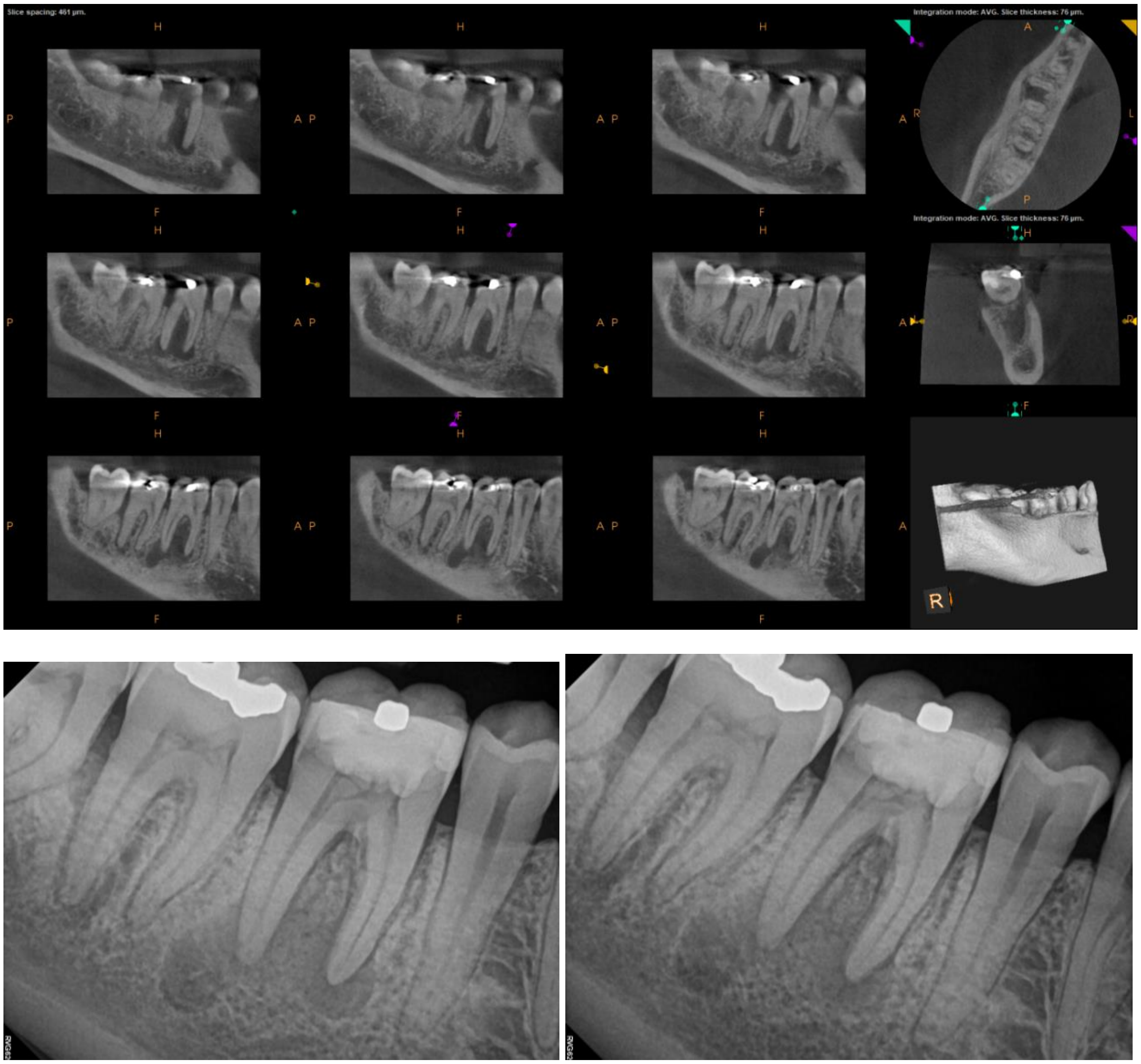

Figure 14- Sagittal slices of CBCT image of tooth #30 demonstrating furcation involvement with associated PAs resulting in disagreement regarding the prescnce of furcation involvement among observers also resulting in false negative.

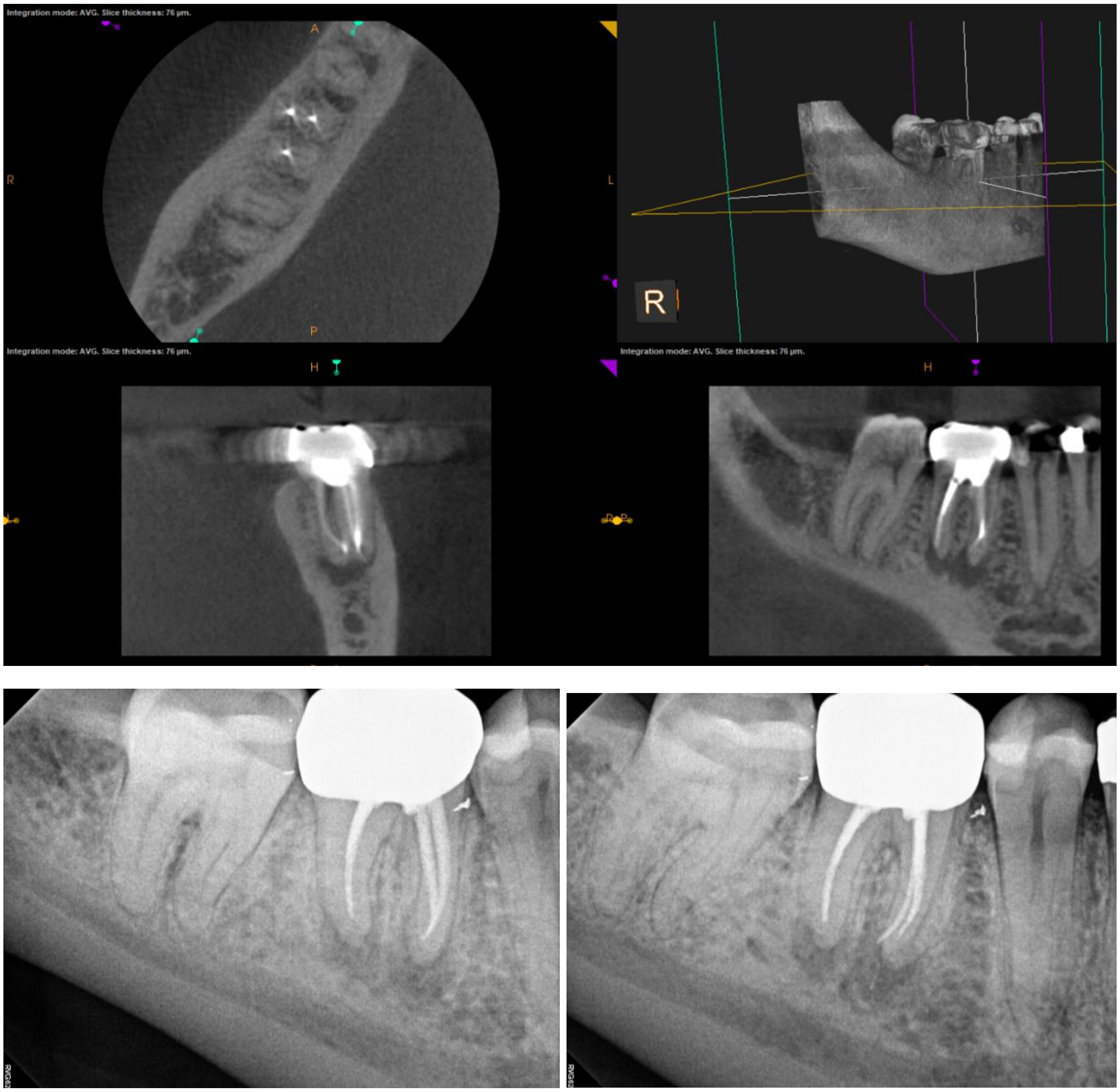

Figure 15- CBCT image slice of tooth #30 with no furcation involvement (control group) in which 4/5 observers responded "YES" to the prescence of furcation involvement resulting in FP in both sessions.

PA radiographs in the detection of furcation involvement displayed low NPV values with an average of 0.57, meaning that that 57% of mandibular molars judged as negative for furcation involvement with PA images, will lack furcation involvement. This is a rather low probability that a negative diagnosis of furcation involvement on PA radiographs, correctly indicates absence of furcation involvement. However, PA radiographs displayed a very high PPV with an average of 0.95 meaning that 95% of teeth in which furcation involvement was observed on PA radiographs, have furcation involvement. The sensitivity and specificity of a screening test are characteristics of the test's performance at a given cut-off point. However, the PPV and NPV of a diagnostic test will be influenced not only by the sensitivity and specificity of the test, but also by the prevalence of the disease in the population. A limitation however, in interpreting these results, is that case-control selection bias may have occurred when selecting cases to be interpreted. Because PPV and NPV depend on the prevalence of disease in population, to achieve accurate results, sample population should have been randomly selected or match the prevalence of the population. Since prevalence of endodontic furcation involvement in endodontically treated teeth or teeth requiring NSRCT in the population is not known from our studies and because pre-test prevalence was not performed, a 3:1 ratio of prevalence of furcation involvement to absence of furcation involvement was arbitrarily selected. Unless the presence of furcation involvement in mandibular molars with pulp necrosis is lower than 75% then the PPV will be overestimated and NPV will be underestimated which may have been the case in this study. With that considered, the results for PPV and NPV of this study agree with previous studies evaluating PA radiographs for the detection of AP with PPV ranging from 0.99-1 and NPV ranging 0.44-0.55 (16,19,31). Overall, these results indicate that PA radiographs would be able to diagnose a certain number of teeth with furcation involvement when it is present but will also miss many cases of furcation involvement. Comparing this to studies evaluating CBCT in the detection of periapical lesions with histopathologic studies as a gold standard; PPV and specificity were 1, sensitivity about 0.89-0.91 and NPV ranges from 0.46-0.81. Although we cannot make direct comparisons, the predictive values and diagnostic accuracy of CBCT for diagnosing apical periodontitis are quite high and significantly higher than PA radiographs for diagnosing apical periodontitis. The question becomes whether these same results translate to furcation involvement in mandibular molars.

Interpreting ROC curves and AUC

A second approach to determine diagnostic accuracy is to examine the test's performance across all diagnostic test thresholds which was another reason why observers were asked to evaluate the presence of furcation involvement in mandibular molars on a 4-point confidence scale. ROC curves characterize a diagnostic test's accuracy, in this case how well PA radiographs discriminate between subjects with furcation involvement versus without furcation involvement. In order to assess accuracy, a reference standard is needed which in this case is LFOV CBCTs. For both sessions 1 and 2 we can appreciate that the empirical ROC curves for each observer never falls on the chance diagonal (AUC=0.5) indicating that the diagnosis of furcation involvement by PA radiographs does have discriminatory value and the correct diagnosis is not by chance.

The AUC which summarizes the diagnostic accuracy of the test determines the probability that the diagnostic test assigned a higher score to the subject with the condition than to the subject without the condition. The greater the area under the ROC curve, the higher the accuracy to discriminate the presence of the condition from control data and the more useful the radiographic method will be. Based on our results, for furcation involvement in mandibular molars, PA imaging provided a moderate ability to discriminate and diagnose patients with and without the condition accurately with an average AUC of 0.841. AUC values for all observers and sessions was also above 80% except for observer 2 session 2 with an AUC=0.759 with no significant difference between observers ($p>0.05$). PA radiographs have reasonable discriminatory ability as a diagnostic test for furcation involvement considering the average AUC value of 0.841 is greater that AUC=0.5 which is the null hypothesis that the results are due to chance alone with a 95% CI of (0.7921, 0.8900) and $p< 0.001$. However, considering the AUC values for each observer, it indicates no better than a moderately accurate test for furcation involvement in mandibular molars. These results are very similar to the systematic review and meta-analysis from Leonardi Dutra, evaluating the diagnostic accuracy of digital periapical imaging in the detection of apical periodontitis where it also demonstrated moderate diagnostic accuracy, with an AUC value of 0.73(20). ROC analysis suggests that furcation involvement is somewhat accurately identified with conventional methods like PA radiographs. However, an important factor from previous studies, that was not analyzed in this study, was the stage of the lesion or source of furcation involvement. Lesions progressing from AP to involve the furcation, which were a large proportion of our cases, are usually larger than those confined to the furcation. Thus, this may have increased the AUC results and influenced the ability of PA to correctly identify furcation as our recent studies confirm that lesion size, not the degree of cortical involvement, significantly affected the ability to accurately detect lesions with 2-D imaging (14). Further sub analysis differentiating by lesion source and size may be useful for future studies to obtain more accurate results. An interesting observation from the results of this study was that diagnostic parameters of PA radiography were not affected by the experience of the clinician. We predicted that the oberservers' level of experience or dental specialty may have an impact but, it did not appear to be the case with $p>0.05$. For reference, from previous studies, CBCT provided the highest diagnostic accuracy with an AUC of 0.97 (20) indicating a near perfect ability to distinguish a normal from an abnormal patient based on the image ratings.

The ability to accurately and reliably detect furcation involvement using periapical radiographs is clinically significant in terms of proper diagnosis, adequate treatment and improved healing of endo-perio lesions. The isolated periodontal lesion in the furcation area of a posterior tooth, without bone loss elsewhere in the mouth is most likely to be of pulpal origin alone. This pathosis in the furcation region, without concurrent destruction in the periapical bone, should resolve completely after non-surgical root canal treatment (NSRCT) without periodontal intervention, considering that bone in the furcation region is thin and inflammation usually begins in the coronal portion of the pulp and progresses apically. Thus, inflammatory products may cause damage in this region long before they reach the periapical tissues (70). This again is significant because if we are able to detect the presence of furcation involvement in these situations, we are detecting inflammatory changes to the pulp in its early stages. This can arrest the progression of inflammation before it reaches the critical zone. Baumgartner cultured the apical 5mm of the canal in teeth with periapical lesions and found 50 strains of bacteria (71). Simon describes the apical 3mm of the canal system the critical zone because it is the space that may harbor the most viable bacteria, their byproducts and endotoxins (72). And although we lack outcome studies on the success of NSRCT and re-treatment when furcation involvement is present and confined to the furcation of multi-rooted teeth, we have an array of studies that demonstrated that the presence of apical periodontitis significantly reduces the success rate of primary and secondary NSRCT (43–46) as well as surgical outcomes in endo-perio lesions (67). Thus, the earlier furcation is diagnosed the greater the chance for healing and success.

Clinical management of cases exhibiting signs of pulp-induced periodontal lesions in the furcation region of molars requires endodontic treatment to eliminate the causative factors. These accessory canals or accessory foramina might be contaminated and filled with necrotic tissue and plaque, which may tend to perpetuate furcation lesions, making successful treatment difficult (73). Hence, a thorough evaluation of the status of the furcation region is crucial and with the results of this study we have determined that PA radiographs of mandibular molars may not be a reliable and valid means of evaluating furcation involvement. This is significant, especially when trying to decide whether PA radiographs are sufficient as the only radiographic means of detecting furcation involvement. In a survey of endodontist members of the AAE, 80.30% of the participants had access to a CBCT scan, of which 50.69% (n = 443) were on-site and 19.30% of all respondents denied having access to CBCT imaging (21). The accessibility of CBCT in general practice dentistry is even lower than this. Furthermore, financially, PA radiographs are a significantly more cost-effective means of diagnosis for both the patient and practitioner compared to LFOV CBCT. Lastly when evaluating safety, 2 PA radiographs produce approximately 1/3rd the ionizing radiation dose to the patient as a LFOV CBT of the posterior mandible. Thus, one must consider these accessibility, feasibility and safety factors as well, when interpreting the results of this study for the detection of furcation involvement with PA radiographs in mandibular molars.

This study demonstrated that conventional PA radiography certainly has its limitations and thus, further imaging may be of value. LFOV Cone-beam computed tomographic (CBCT) imaging is increasingly being used for diagnosis and treatment planning in endodontics. In studies that compare the abilities of periapical radiography and CBCT imaging in the detection of periapical lesions, it was found that CBCT imaging could identify more periapical lesions than PA radiographs in vitro and in vivo (18). Other studies report that in all reliability and diagnostic accuracy parameters, CBCT had significantly higher sensitivity, specificity, PPV, NPV and AUC values. How this translates to furcation involvement however, is still to be determined. Also, although this study is an observational study regarding the detection of furcation involvement and future research is needed to directly compare the two imaging modalities in detecting furcation involvement, it is worth taking into consideration when deciding whether the benefits outweigh the risks for CBCT imaging.

A limitation of this study is that the most reliable method of evaluating an imaging technique is to compare its ability to detect pathologic changes with the true state of the object (74), it is accepted that histopathological diagnosis is the reference standard for detection of apical periodontitis (75,76). CBCT is not the gold standard for detection of furcation involvement but in our study is used as the reference standard for the ethical and practical reasons described earlier in the discussion section. A variable that a study from Kruse found that does affect the diagnostic accuracy of CBCT is the treatment status of the tooth (77). For non-endodontically treated teeth, the diagnostic accuracy of CBCT is high and all diagnostic accuracy parameters were lower for endodontically treated teeth. This may be due to artifacts present on CBCT which do not affect PA radiographs thus, a future study would be not only to compare the diagnostic accuracy of PA vs CBCT in the detection of furcation involvement, but also to see if there is any difference in untreated vs root filled teeth. Similarly, Strong asserted that the radiographic appearances of the coronal and intraradicular areas influence the interpretation of periapical areas (78). In our study the coronal area was not hidden because in doing so would mask part of the furcation thus, another possible limitation in the validity of the results. A further limitation of this study is the inherent study design issues when assessing diagnostic tests that require subjective interpretation by human observers. First, observers will inevitably assign confidence scores differently. For example, in our study observer 2 did not use answers MY and MN in the 4-point confidence scale while observers 1 and 3 spread their confidence most evenly across the given range. Thus, their AUCs may be similar, but the observers' scores for individual responses will not agree. Although a calibration was performed prior to analyses, still we were not able to achieve the utilization of the full confidence scale among observers. For this reason, following the recommendation of Obuchowski (79), the confidence scores from multiple readers were not pooled together. Rather, an ROC curve was constructed for each reader separately for each session; then, a summary measure of accuracy, such as the AUC, was calculated for each reader and averaged across readers. Moreover, for this same reason, instead of only a single AUC to describe the diagnostic test's accuracy, the accuracy was also represented by a distribution of AUCs for better representation (74). Lastly, PA radiographs differed between the University of Minnesota Graduate Endodontics Clinic and Metropolitan Endodontics. Although mA and kVp values were the same, different intraoral sensors and image storing software were utilized. Although both the RVG 6200 and the Schick 33 are high quality imaging sensors with high resolution there is a slight difference in pixel size and line pairs that may affect the detection of furcation involvement depending on which sensor was used. Again, this should not affect the results of the inter- and intra- observer reliability but may influence the results for accuracy of the PA radiograph as a diagnostic test.

Because PA images were only compared to a reference standard, the results of this study are observational rather than conclusive. Other future areas of research are warranted for direct comparison of conventional radiographic techniques like PA radiographs to LFOV CBCTs rather than using LFOV CBCTs as reference standard. There is also potential with this same study design to be employed for further sub-analysis on extent of furcation involvement (size) and type of furcation involvement. Furthermore, this study may serve as a building block to encourage future studies which evaluate the effects of furcation involvement on the outcome of primary and secondary NSRCT. Lastly, different tooth types or anatomical variations could be a future research direction using this study design. An evaluation of teeth with more anatomical distractors in the furcation area such as maxillary premolars or molars which have three furcation entry points, may offer more insight into the value of CBCT in the detection of furcation involvement.

CONCLUSION

Under the tested conditions and within the limitations of this investigation, it can be concluded that:

1) PA radiographs in the detection of furcation involvement in mandibular molars are moderately reliable at best when evaluating interobserver reliability but, moderately to substantially reliable when evaluating intraobserver reliability depending on the confidence scale.

2) Furcation involvement in mandibular molars can be correctly identified with conventional methods but relying exclusively on PA radiographs to detect furcation will result in a certain amount of undiagnosed furcation involvement in mandibular molars.

3) Similarly, PA radiographs also had a moderate diagnostic accuracy in its ability to distinguish between mandibular molars with furcation involvement and without furcation involvement when evaluated across all potential diagnostic thresholds rather than at a specific threshold.

Overall intraoral PA radiography, is an accurate diagnostic method but has its limitations in both reliability and validity in the detection of furcation involvement in mandibular molars and these must be considered when interpreting these radiographs for the presence of furcation involvement.

REFERENCES

1. Schilder H. Filling Root Canals in Three Dimensions. Dent Clin North Am. 1967 Nov;11:723–44.

2. Schilder H. Cleaning and Shaping the Root Canal System. 1974 Apr;18(2):269–96.

3. European Society of Endodontology. Quality guidelines for endodontic treatment: consensus report of the European Society of Endodontology. Int Endod J. 2006 Dec;39(12):921–30.

4. Vertucci FJ. Root canal morphology and its relationship to endodontic procedures. Endod Top. 2005 Mar;10(1):3–29.

5. Walton, Richard E G Jerry J. The Histology of Periapical Inflammatory Leisons in Permanent Molars in Monkeys. J Endod. 1986 Feb;12(2):49–53.

6. Chiona D, Koivisto T, Milroy LL, Roach SH, McClanahan SB, Ahmad M, et al. CBCT Analysis of Mandibular Posterior Teeth: Impact on Endodontic Microsurgery. Northwest Dent J. 2017;96(4):35+.

7. Porto OCL, Silva BS de F, Silva JA, Eestrela CR de A, de Alencar AHG, Bueno M dos R, et al. CBCT assessment of bone thickness in maxillary and mandibular teeth: an anatomic study. J Appl Oral Sci. 28:e20190148.

8. Ingle JI, Bakland LK, Baumgartner JC. Ingle's endodontics 6. 2008.

9. Nair PNR, Henry S, Cano V, Vera J. Microbial status of apical root canal system of human mandibular first molars with primary apical periodontitis after "one-visit" endodontic treatment. Oral Surg Oral Med Oral Pathol Oral Radiol Endodontology. 2005 Feb 1;99(2):231–52.

10. Goldman M, Pearson AH, Darzenta N. Reliability of radiographic interpretations. Oral Surg Oral Med Oral Pathol. 1974 Aug;38(2):287–93.

11. Tewary S, Luzzo J, Hartwell G. Endodontic radiography: who is reading the digital radiograph? J Endod. 2011 Jul;37(7):919–21.

12. Bender IB, Seltzer S. Roentgenographic and direct observation of experimental lesions in bone: I. J Am Dent Assoc. 1961 Feb 1;62(2):152–60.

13. Folk RB, Thorpe JR, McClanahan SB, Johnson JD, Strother JM. Comparison of two different direct digital radiography systems for the ability to detect artificially prepared periapical lesions. J Endod. 2005 Apr;31(4):304–6.

14. Chang L, Umorin M, Augsburger RA, Glickman GN, Jalali P. Periradicular Lesions in Cancellous Bone Can Be Detected Radiographically. J Endod. 2020 Apr;46(4):496–501.

15. Brynolf I. Roentgenologic periapical diagnosis. II. One, two or more roentgenograms? Sven Tandlakare Tidskr Swed Dent J. 1970 May;63(5):345–50.

16. Kanagasingam S, Hussaini HM, Soo I, Baharin S, Ashar A, Patel S. Accuracy of single and parallax film and digital periapical radiographs in diagnosing apical periodontitis - a cadaver study. Int Endod J. 2017 May;50(5):427–36.

17. Mozzo P, Procacci C, Tacconi A, Tinazzi Martini P, Bergamo Andreis IA. A new volumetric CT machine for dental imaging based on the cone-beam technique: preliminary results. Eur Radiol. 1998 Nov 1;8(9):1558–64.

18. Patel S, Wilson R, Dawood A, Mannocci F. The detection of periapical pathosis using periapical radiography and cone beam computed tomography - part 1: pre-operative status. Int Endod J. 2012 Aug;45(8):702–10.

19. de Paula-Silva FWG, Wu M-K, Leonardo MR, da Silva LAB, Wesselink PR. Accuracy of periapical radiography and cone-beam computed tomography scans in diagnosing apical periodontitis using histopathological findings as a gold standard. J Endod. 2009 Jul;35(7):1009–12.

20. Leonardi Dutra K, Haas L, Porporatti AL, Flores-Mir C, Nascimento Santos J, Mezzomo LA, et al. Diagnostic Accuracy of Cone-beam Computed Tomography and Conventional Radiography on Apical Periodontitis: A Systematic Review and Meta-analysis. J Endod. 2016 Mar;42(3):356–64.

21. Setzer FC, Hinckley N, Kohli MR, Karabucak B. A Survey of Cone-beam Computed Tomographic Use among Endodontic Practitioners in the United States. J Endod. 2017 May 1;43(5):699–704.

22. Ludlow JB, Timothy R, Walker C, Hunter R, Benavides E, Samuelson DB, et al. Effective dose of dental CBCT—a meta analysis of published data and additional data for nine CBCT units. Dentomaxillofacial Radiol. 2015 Jan;44(1):20140197.

23. Fayad MI. Colleagues for Excellence: The Impact of Cone Beam Computed Tomography in Endodontics: A New Era in Diagnosis and Treatment Planning [Internet]. American Association of Endodontics; [cited 2021 Jul 13]. Available from: https://f3f142zs0k2w1kg84k5p9i1o-wpengine.netdna-ssl.com/specialty/wp-content/uploads/sites/2/2018/05/COL042Spring2018CBCTinDiagnosis.pdf

24. Kaffe I, Gratt BM. Variations in the radiographic interpretation of the periapical dental region. J Endod. 1988 Jul;14(7):330–5.

25. Wayman BE, Patten JA, Dazey SE. Relative frequency of teeth needing endodontic treatment in 3350 consecutive endodontic patients. J Endod. 1994 Aug;20(8):399–401.

26. Iqbal M, Chan S, Ku J. Relative frequency of teeth needing conventional and surgical endodontic treatment in patients treated at a graduate endodontic clinic—a Penn Endo database study. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2008 Jul 1;106(1):e62–7.

27. Hartwell G, Bellizzi R. Clinical investigation of in vivo endodontically treated mandibular and maxillary molars. J Endod. 1982 Dec 1;8(12):555–7.

28. Skidmore AE, Bjorndal AM. Root Canal Morphology of the Mandibular First Molar. OOOOE. 1971 Nov;32:778–84.

29. Weine FS, Pasiewicz RA, Rice T. Canal Configuration of the Mandibular Second Molar Using a Clinically Oriented In Vitro Method. J Endod. 1988 May;14(5):207–13.

30. Norman Weller R, Niemczyk SP, Kim S. Incidence and position of the canal isthmus. Part 1. Mesiobuccal root of the maxillary first molar. J Endod. 1995 Jul 1;21(7):380–3.

31. Estrela C, Rabelo LEG, Souza JB de, Alencar AHG, Estrela CRA, Neto MDS, et al. Frequency of Root Canal Isthmi in Human Permanent Teeth Determined by Cone-beam Computed Tomography. J Endod. 2015 Sep 1;41(9):1535–9.

32. Kim S, Jung H, Kim S, Shin S-J, Kim E. The Influence of an Isthmus on the Outcomes of Surgically Treated Molars: A Retrospective Study. J Endod. 2016 Jul 1;42(7):1029–34.

33. Vertucci FJ. Root canal anatomy of the human permanent teeth. Oral Surg Oral Med Oral Pathol. 1984 Nov;58(5):589–99.

34. De Deus QD. Frequency, location, and direction of the lateral, secondary, and accessory canals. J Endod. 1975 Nov;1(11):361–6.

35. Harris SP, Bowles WR, Fok A, McClanahan SB. An Anatomic Investigation of the Mandibular First Molar Using Micro–Computed Tomography. J Endod. 2013 Nov 1;39(11):1374–8.

36. Seltzer S. Endodontology : Biologic Considerations in Endodontic Procedures. McGraw-Hill Education; 1971.

37. Grossman L. Endodontic Practice [Internet]. 7th Edition. Philadelphia: Lea &Febiger; [cited 2021 Jul 18]. 448 p. Available from: https://www.thriftbooks.com/w/endodontic-practice_louis-irwin-grossman/1710875/

38. American Academy of Endodontists. Glossary of Endodontic Terms. 2020;10th Edition:48.

39. Gutmann JL. Prevalence, location, and patency of accessory canals in the furcation region of permanent molars. J Periodontol. 1978 Jan;49(1):21–6.

40. Vertucci FJ, Anthony RL. A scanning electron microscopic investigation of accessory foramina in the furcation and pulp chamber floor of molar teeth. Oral Surg Oral Med Oral Pathol. 1986 Sep;62(3):319–26.

41. Dammaschke T, Witt M, Ott K, Schäfer E. Scanning electron microscopic investigation of incidence, location, and size of accessory foramina in primary and permanent molars. Quintessence Int Berl Ger 1985. 2004 Oct;35(9):699–705.

42. Yamasaki M, Kumazawa M, Kohsaka T, Nakamura H, Kameyama Y. Pulpal and periapical tissue reactions after experimental pulpal exposure in rats. J Endod. 1994 Jan;20(1):13–7.

43. Sjögren U, Hägglund B, Sundqvist G, Wing K. Factors affecting the long-term results of endodontic treatment. J Endod. 1990 Oct;16(10):498–504.

44. Chevigny C de, Dao TT, Basrani BR, Marquis V, Farzaneh M, Abitbol S, et al. Treatment Outcome in Endodontics: The Toronto Study—Phases 3 and 4: Orthograde Retreatment. J Endod. 2008 Feb 1;34(2):131–7.

45. de Chevigny C, Dao TT, Basrani BR, Marquis V, Farzaneh M, Abitbol S, et al. Treatment Outcome in Endodontics: The Toronto Study—Phase 4: Initial Treatment. J Endod. 2008 Mar;34(3):258–63.

46. Ng Y-L, Mann V, Gulabivala K. A prospective study of the factors affecting outcomes of nonsurgical root canal treatment: part 1: periapical health. Int Endod J. 2011 Jul;44(7):583–609.

47. Chugal NM, Clive JM, Spångberg LS. A prognostic model for assessment of the outcome of endodontic treatment: Effect of biologic and diagnostic variables. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2001 Mar 1;91(3):342–52.

48. Barone C, Dao TT, Basrani BB, Wang N, Friedman S. Treatment outcome in endodontics: the Toronto study--phases 3, 4, and 5: apical surgery. J Endod. 2010 Jan;36(1):28–35.

49. Kim E, Song J-S, Jung I-Y, Lee S-J, Kim S. Prospective Clinical Study Evaluating Endodontic Microsurgery Outcomes for Cases with Lesions of Endodontic Origin Compared with Cases with Lesions of Combined Periodontal–Endodontic Origin. J Endod. 2008 May;34(5):546–51.

50. Tamse A. Vertical root fractures in endodontically treated teeth: diagnostic signs and clinical management. Endod Top. 2006;13(1):84–94.

51. Walton RE, Michelich RJ, Smith GN. The histopathogenesis of vertical root fractures. J Endod. 1984 Feb;10(2):48–56.

52. Olivieri JG, Elmsmari F, Miró Q, Ruiz X-F, Krell KV, García-Font M, et al. Outcome and Survival of Endodontically Treated Cracked Posterior Permanent Teeth: A Systematic Review and Meta-analysis. J Endod. 2020 Apr;46(4):455–63.

53. Ricucci D, Siqueira JF, Loghin S, Berman LH. The cracked tooth: histopathologic and histobacteriologic aspects. J Endod. 2015 Mar;41(3):343–52.

54. Tamse A, Kaffe I, Lustig J, Ganor Y, Fuss Z. Radiographic features of vertically fractured endodontically treated mesial roots of mandibular molars. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2006 Jun;101(6):797–802.

55. Mamoun JS, Napoletano D. Cracked tooth diagnosis and treatment: An alternative paradigm. Eur J Dent. 2015;9(2):293–303.

56. Zhou X-H, McClish DK, Obuchowski NA. Statistical Methods in Diagnostic Medicine. 2nd edition. Hoboken, N.J: Wiley; 2011. 592 p.

57. AAE/AAOMR. AAE/AAOMR Joint Position Statement: Use of Cone Beam Computed Tomography in Endodontics. 2015 Update. 2015.

58. Landis JR, Koch GG. The Measurement of Observer Agreement for Categorical Data. Biometrics. 1977;33(1):159–74.

59. Gallas BD. One-shot estimate of MRMC variance: AUC. Acad Radiol. 2006 Mar;13(3):353–62.

60. Swets JA. Measuring the accuracy of diagnostic systems. Science. 1988 Jun 3;240(4857):1285–93.

61. Kanagasingam S, Lim CX, Yong CP, Mannocci F, Patel S. Diagnostic accuracy of periapical radiography and cone beam computed tomography in detecting apical periodontitis using histopathological findings as a reference standard. Int Endod J. 2017 May;50(5):417–26.

62. Walter C, Weiger R, Zitzmann NU. Accuracy of three-dimensional imaging in assessing maxillary molar furcation involvement. J Clin Periodontol. 2010 May;37(5):436–41.

63. Qiao J, Wang S, Duan J, Zhang Y, Qiu Y, Sun C, et al. The accuracy of cone-beam computed tomography in assessing maxillary molar furcation involvement. J Clin Periodontol. 2014 Mar;41(3):269–74.

64. Akobeng AK. Understanding diagnostic tests 3: receiver operating characteristic curves. Acta Paediatr. 2007;96(5):644–7.

65. Zakariasen KL, Scott DA, Jensen JR. Endodontic recall radiographs: how reliable is our interpretation of endodontic success or failure and what factors affect our reliability? Oral Surg Oral Med Oral Pathol. 1984 Mar;57(3):343–7.

66. Molven O, Halse A, Fristad I. Long-term reliability and observer comparisons in the radiographic diagnosis of periapical disease. Int Endod J. 2002 Feb;35(2):142–7.

67. Lam EWN, Law AS, Nguyen RHN, Basile S, Austah O, Gilbert GH, et al. Inter-examiner Agreement in the Radiologic Identification of Apical Periodontitis/Rarefying Osteitis in the National Dental PBRN PREDICT Endodontic Study. J Endod [Internet]. 2021 Jul 16 [cited 2021 Jul 19];0(0). Available from: https://www.jendodon.com/article/S0099-2399(21)00485-4/abstract

68. Plascencia H, Díaz M, Ordinola-Zapata R, Vázquez-Sánchez ME, Juárez-Broon N, Ruíz-Gutiérrez A, et al. Intra- and Interobserver Agreement during the Assessment of the Different Stages of Root Development Using 4 Radiographic Classifications. J Endod. 2021 Jun 1;47(6):906–13.

69. Berghuis G, Cosyn J, De Bruyn H, Hommez G, Dierens M, Christiaens V. A controlled study on the diagnostic accuracy of panoramic and peri-apical radiography for detecting furcation involvement. BMC Oral Health. 2021 Mar 12;21:115.

70. Vertucci FJ, Williams RG. Furcation canals in the human mandibular first molar. Oral Surg Oral Med Oral Pathol. 1974 Aug 1;38(2):308–14.

71. Baumgartner JC, Falkler WA. Bacteria in the apical 5 mm of infected root canals. J Endod. 1991 Aug;17(8):380–3.

72. Simon JH. The apex: how critical is it? Gen Dent. 1994 Aug;42(4):330–4.

73. Seltzer S, Bender IB, Nazimov H, Sinai I. Pulpitis-induced interradicular periodontal changes in experimental animals. J Periodontol. 1967 Apr;38(2):124–9.

74. Kullendorff B, Nilsson M. Diagnostic accuracy of direct digital dental radiography for the detection of periapical bone lesions. II. Effects on diagnostic accuracy after application of image processing. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 1996 Nov;82(5):585–9.

75. Green TL, Walton RE, Taylor JK, Merrell P. Radiographic and histologic periapical findings of root canal treated teeth in cadaver. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 1997 Jun;83(6):707–11.

76. Brynolf I. A histological and roentgenological study of the periapical region of human upper incisors. [Uppsala]: Almqvist & Wiksell; 1967.

77. Kruse C, Spin-Neto R, Wenzel A, Væth M, Kirkevang L-L. Impact of cone beam computed tomography on periapical assessment and treatment planning five to eleven years after surgical endodontic retreatment. Int Endod J. 2018;51(7):729–37.

78. Strong JW, Woodmansey KF, Khademi JA, Hatton JF. Coronal and Intraradicular Appearances Affect Radiographic Perception of the Periapical Region. J Endod. 2017 May;43(5):723–7.

79. Obuchowski NA, Bullen JA. Receiver operating characteristic (ROC) curves: review of methods with applications in diagnostic medicine. Phys Med Biol. 2018 Mar;63(7):07TR01.

APPENDIX

Sample size calculation (53)

Confidence Level	Alpha	Alpha/2	z alpha/2
90%	10%	5.0%	1.645
95%	5%	2.5%	1.96
98%	2%	1.0%	2.326
99%	1%	0.5%	2.576

$$n_1 = \frac{\left[(z_{\alpha/2})\sqrt{V}\ \right]^2}{L^2}$$

$\eta_{1=}$ number of diseased cases required.

$$V = (0.0099 \times e{-}(a^2/2)) \times ([5a^2 + 8]+[a^2 + 8]/K)$$

$$V = \left(0.009 \text{ x } e^{-\frac{0.742^2}{2}}\right) \times \left((5(0.742)^2 + 8) + \frac{(0.742^2 + 8)}{1/3}\right)$$

$$V = 0.249$$

For the purposes of our study, we assumed an AUC of 0.70 with a 95% CI with a width of 0.30 (i.e. L=0.15). Considering we have decided an approximate 3:1 ratio of diseased to non-diseased for our sample size (i.e. K = 1/3). Under these conditions, a = 0.742, $z_{\alpha/2}$ = 1.960 and according to above calculations V = 0.249.

$$n_1 = \frac{\left[(z_{\alpha/2})\sqrt{V}\ \right]^2}{L^2}$$

$$n_1 = \frac{\left((1.960)\sqrt{0.2}49\right)^2}{0.15\text{^}2}$$

$$n_1 = 43$$

Minimum number of disease cases (furcation involvement) required is 43.